ABDOMINOPELVIC DISEASES AND EMERGENCIES

Editor
Munire BABAYIGIT, MD, Assoc. Prof.

LIVRE DE LYON
2023

Health Sciences

Abdominopelvic Diseases and Emergencies

Editor
Munire BABAYIGIT, MD, Assoc. Prof.

LIVRE DE LYON
Lyon 2023

Abdominopelvic Diseases and Emergencies

Editor
Munire BABAYIGIT, MD, Assoc. Prof.

LIVRE DE LYON
Lyon 2023

Abdominopelvic Diseases and Emergencies

Editor •. Munire BABAYIGIT, MD, Assoc. Prof. • Orcid: 0000-0002-5090-3262
Cover Design • Motion Graphics
Book Layout • Motion Graphics
First Published • February 2023, Lyon

ISBN: 978-2-38236-521-2

Publisher • Livre de Lyon
Address • 37 rue marietton, 69009, Lyon France
website • http://www.livredelyon.com
e-mail • livredelyon@gmail.com

PREFACE

"Entrust me to Turkish physicians" Mustafa Kemal ATATÜRK

Turkish physicians work devotedly under very different conditions in different geographical regions of Turkey. In addition, they are gaining prestige in the medical community by leading scientific developments in every branch of medicine. As in this book we have prepared, they create scientific resources for their colleagues and give permanent works.

Turkish physicians, who made their mark in history with the services they provided at the front and behind the front during the First World War, rushed to provide health services to people in many disasters such as floods, fires and earthquakes. While I was writing these lines, Turkey was struggling with an unprecedented disaster. As a result of 2 consecutive earthquakes in 10 different cities of our country, we lost thousands of our citizens, thousands of our citizens were injured, and rescue efforts are still continuing. Thereupon, hundreds of my colleagues and hundreds of health workers rushed to help the region. All my colleagues organize the treatment of our injured citizens by establishing a nationwide communication network. I believe that in this difficult process, self-sacrificing Turkish physicians will have their names written in history again with their extraordinary efforts.

We know that the power we need is in the noble blood in our veins.

Münire BABAYİĞİT, M.D.
08 FEB 2023

SCIENCE BOARD

CONTENTS

CHAPTER I

ABDOMINOPELVIC EMERGENCIES

Hasan Okmen[1] & Sundus Zeynep Kucuksumer Ertek[2]

[1](MD), Department of General Surgery, Health Sciences University, Turkish Ministry of Health Istanbul Research and Training Hospital, Istanbul, Turkey
hasanokmen@hotmail.com
ORCID: 000-0002-2297-3386

[2](MD), Department of General Surgery, Health Sciences University, Turkish Ministry of Health Istanbul Research and Training Hospital, Istanbul, Turkey
hasanokmen@hotmail.com, zkucuks13@gmail.com
ORCID: 0000-0002-0150-3959

In 1920, Sir Zachary Cope wrote in his book Early Diagnosis of the Acute Abdomen, "Severe abdominal pain that lasts more than six hours is caused by some condition of surgical import' (1). This sentiment, to this day, retains some truth although due to advances in medicine and science, there are more than 20 differential diagnoses of the acute abdomen, both surgical and medical.

Acute abdomen is defined as a sudden onset abdominal pain which requires urgent medical attention (2). Acute abdomen has many reasons surgical and non-surgical. Nonsurgical causes include diabetes, acute intermittent porphyria, Addison's crisis, FMF, sickle cell crisis et cetera. Surgical causes may include GI tract perforations, obstructions, acute appendicitis and so on. A careful physical examination and patient history as well as modern imaging modalities will help the diagnosis.

1. COLORECTAL EMERGENCIES

1.1 COLON PERFORATION

The most common causes of non-iatrogenic colon perforation are diverticulitis, colorectal carcinomas, foreign body ingestion, ischemia, trauma, and inflammation.

1.1.1 Penetrating and Blunt Colorectal Injury

Penetrating colorectal injuries are very common in abdominopelvic traumas and have a high rate of mortality (3,4). Management of a patient with a penetrating colorectal wound depends on various factors. Type of treatment, surgical or otherwise, depends on the overall condition of the patient, degree of intra abdominal contamination, the time delay between the injury and the treatment, and the condition of the colon. The surgeon must decide carefully to choose the best candidates for primary repair vs an ostomy. In a hemodynamically stable, relatively young patient, primary repair may be the best option if the degree of the peritoneal contamination is low. If the patient is in shock, has a high level of intraabdominal contamination, and the surgery has started after more than 6 hours after the injury, then primary repair of the colon is contraindicated (4). The nature of the penetrating trauma should also be taken into consideration. High-energy injuries such as gunshot wounds are often associated with increased levels of organ damage, peritoneal contamination, and hemodynamic instability (Table 1). below, the deciding criteria for ostomy are shown (3).

Table 1. Indications for an Ostomy
High-velocity shotgun wounds
Blast wounds
Crush injury
Condition of the patient
Inflamed and highly infected tissue
Insufficient blood supply
Shock findings
Hemorrhage > 1L
Multiple organ injuries
Thoracoabdominal penetration

Penetrating rectal injuries are even more difficult to manage. This is due rectum's anatomy and physiology: penetrating the rectum tends to result in a higher degree of fecal contamination and its anatomy makes the surgical repairs more challenging. Although the general consensus is not clear, the majority of rectal injuries are best managed with an ostomy to divert the fecal matter (5,6). Anastomotic leaks tend to be more frequent when the injury is more distally located (6).

Blunt injuries to the colon and rectum are less frequent. Rarely blunt trauma to colon or rectum may result in perforation, and the management criteria are similar to primary penetrating traumas. Blunt traumas such as crush injuries may cause small mucosal tears or serosal hematomas. Small mucosal tears can be treated with primary suturing. Serosal hematomas don't always need to be treated however a close inspection of the bowel must be performed to avoid missing a perforated section. Pelvic crush injuries with bone fractures are the one of the most serious types of injury and often need to be managed with a diverting ostomy, debridement of the nonviable tissue, and a rectal washout (3).

1.1.2 Colorectal Carcinomas

Colorectal carcinomas can result in perforation by way of two mechanisms: necrosis and perforation at the primary tumor site or perforation proximal to the obstruction caused by the tumor ("blowout perforation"). The most common location for the second type of perforation is the cecum. Perforation caused by colorectal carcinomas have a high rate or mortality, 12-19% (5). The patient typically presents with symptoms of peritonitis such as guarding, rebound, and tenderness of the abdomen. The diagnosis may be made by performing a detailed physical examination, an X-ray of the abdomen, and a CT scan. In cases of perforation, computed tomography is the most reliable method for diagnosis. Presence of extraluminal air in the abdomen is the main finding in a CT scan. In some cases, free air may be seen under the diaphragm in an abdominal x-ray.

The management of colorectal perforation is surgical. Exploration of the intestines and thoroughly irrigating the abdomen is the first step. If colorectal carcinoma is the cause of the perforation, the resection should be compliant with the oncological surgical principles as long as the patient is stable (6). The decision between an anastomosis or an ostomy is a challenging one for surgeons. Emergency surgery alone is a risk factor for anastomotic leaks (7). Although colostomies seem to be the safer choice, they also have complications such as narrowing of the opening, skin irritation, and parastomal hernias. It has been demonstrated that the majority of the colostomies made in the emergency settings were never reversed therefore the patient's comfort in the future should also be taken into consideration (7).

1.1.3 Perforated Diverticulitis

Perforated diverticulitis is one of most common causes of the acute abdomen. It typically presents with tenderness in the left lower quadrant, fever,

and leukocytosis. Sigmoid colon is the most common location for this pathology however diverticulitis can happen in any segment of the colon.

Primary resection and anastomosis in selected cases is the mode of treatment if surgical treatment is indicated. The stage of the diverticulitis determines the treatment. Hinchey classification is widely used for the staging, demonstrated in Table 2 (8). According to Moore et al. stages I and II may be treated with IV antibiotics and bowel rest (8). Stages III and IV may present with sepsis and septic patients should be resuscitated accordingly before the surgery. Surgery may entail resection and primary anastomosis (a diverting loop ileostomy is recommended) or lavage and drainage in lower risk patients. For stage III and IV patients, primary resection anastomosis still carries a high rate of mortality (10%) (8). During surgery, deciding between a primary resection anastomosis, with or without a diverting loop ileostomy, (PRA) and Hartmann's Procedure (HP) may be difficult. Several RCT studies demonstrated that PRA and HP have similar mortality and morbidity rates (7).

1.1.4 Infectious and Inflammatory Causes

Colon perforation due to infectious and inflammatory causes is rare. IBD or infectious colitis etiologies (CMV, HIV, pseudomembranous colitis) sometimes result in toxic megacolon. Toxic megacolon is a highly mortal complication and is characterized by intense dilation of the colon.

Surgery is indicated when there are symptoms of perforation. Additionally, it has been shown that prophylactic surgery (to prevent perforation) reduced mortality significantly, from 40% to 2 % (4). Segmental resection with an ostomy is the ideal choice.

1.2 VOLVULUS

Volvulus is defined as the twisting of an air-filled colonic segment about its own mesentery (3). Patients present with abdominal distension, tenderness, inability to have bowel movements, and nausea. The most common location is the sigmoid colon, and the second most is the cecum. In the absence of an acute abdomen, the first line of treatment is endoscopic detorsion, in sigmoid volvulus. Raveenthiran et al. stated that endoscopic detorsion should be used as a bridge and a temporary treatment and the main goal of treatment should be to resect the redundant sigmoid colon segment (9). Additionally, Raveenthiran et al. propose that primary resection anastomosis has good outcomes and should

be preferred. Cecal volvulus cannot be endoscopically managed and surgical exploration is indicated (3). Complicated cases of sigmoid or cecal volvulus (resulting in perforation and intraabdominal sepsis) are shown to be highly mortal and need surgical intervention.

1.3 ISCHEMIC COLITIS

Ischemic colitis is the result of interrupted or insufficient blood supply to the colon. This condition mainly affects the elderly and has a female predominance. Patients present with abdominal tenderness, distention, diarrhea, and rectal hemorrhage. Computed tomography is the primary method for screening in suspected patients. Typical CT findings include colonic distention, pneumatosis, and fat stranding (4). The most common location for ischemic colitis is the splenic flexure. Majority of ischemic colitis patients can be treated conservatively with antibiotics and bowel rest (3). Colonoscopy is recommended after the patient completes their recovery in order to rule out strictures and other colon pathologies (3). If symptoms and signs of peritonitis are present, necrosis and perforation may be suspected and surgical exploration is indicated. Resection of the necrotic bowel is necessary and primary anastomosis should not be performed (3).

2. ACUTE APPENDICITIS

Acute appendicitis is the inflammation of the appendix, most commonly due to obstruction of its lumen by fecaliths, foreign bodies such as food, and neoplasms. Patients present with right lower quadrant pain, nausea, leukocytosis, and anorexia. Migratory pain from the umbilicus to the right lower quadrant is typical. McBurney's point is the most tender location; it is found between the anterior superior iliac spine and the umbilicus and is 1/3rd of the distance to the ASIS. A CT scan or an ultrasound imaging can also be utilized for accurate diagnosis. Appendectomy is the mainstay treatment (3).

3. PEPTIC ULCER DISEASE

Peptic ulcers are mucosal defects that reach into the submucosal layers. Peptic ulcers are commonly seen in the stomach or the duodenum and may cause various complications such as hemorrhage, perforation, and obstruction. Ulcers develop due to imbalances of the aggressive and defensive factors in the mucosa. Patients with peptic ulcers have epigastric pain (usually a burning

sensation), nausea, bloating, and dyspeptic complaints. Duodenal ulcer pain gets worse 2-3 hours after meals and can wake the patient up from their sleep. Most patients with hemorrhage, approximately 75%, will stop bleeding with PPI therapy and ceasing oral intake. The rest of the patients will need either endoscopic or surgical treatment modalities. Surgery should be considered after two failed endoscopic treatments. According to Schwartz's Principles of Surgery, in the elderly patients, early elective surgery after a successful endoscopic treatment may be life-saving because these patients may not be able to tolerate periods of intense hemodynamic instability should the re-bleeding occur (3). Perforated PUD is almost always treated surgically. Simple patch closure is the most common method however patch closure and HSV (highly selective vagotomy) or patch closure with V+D (vagotomy and drainage) can be performed in selected patients. Biopsy should be taken in perforated ulcers in order to rule out gastric cancers.

4. SMALL BOWEL OBSTRUCTION

Obstruction of the small bowel presents with abdominal tenderness, colicky pain, nausea, vomiting, and distention. Reasons include adhesions, foreign bodies, tumors, and strictures. Patients may present with an excessive amount of vomiting and dehydration therefore fluid resuscitation is the first step of the treatment regimen. Nasogastric tube should be used in order to alleviate the distention of the stomach. A nonoperative approach for 48 hours with an NG tube and bowel rest is the preferred treatment for nonischemic obstructions (3). If the symptoms of the patient don't improve, surgery is recommended. Surgery depends on the etiology of the obstruction. After treating the obstruction (e.g. removing the tumor or the foreign body or adhesions), the viability of the remaining small bowel should be explored. Any nonviable, necrotic segments should be resected. If uncertain, a second-look operation may be performed within 24-48 hours of the first surgery.

5. ABDOMINAL SOLID ORGAN INJURY

In current medical practice, most of the solid organ injuries are managed nonoperatively if the patient is hemodynamically stable. In a study conducted in Italy by Cipressi et al. 75% of spleen and 95% of liver trauma patients were successfully treated nonoperatively (4).

4.1 Liver

According to the classification of liver injuries by American Association for the Surgery of Trauma Organ Injury Scale, grade 4 and grade 5 liver injury patients who are hemodynamically unstable should be treated surgically (10). The main goal of the surgical treatment is to stop the hemorrhage. Abdominal packing to stop the parenchymal bleeding of the liver and non-anatomical resections and ligations are preferred to reduce the surgery duration and decrease mortality (4). Recently angioembolization has become a viable option in selected cases. Major anatomical liver resection for extensive liver damage is discouraged due to high mortality rates however it can be performed in cases of a major destruction of the liver tissue or a severe bile leak from intrahepatic bile ducts. According to Hommes et al. out of the 125 patients with liver injuries, only 10 of them presented with biliary leaks. Nine of those patients were treated either with ERCP or percutaneous drainage and only 1 of the patients needed surgery (11). It should be kept in mind that anatomical resection of the liver is very complicated and should only be performed by experienced surgeons(4).

4.2 Pancreas

Pancreatic injuries are classified according to the American Association for the Surgery of Trauma Pancreas Organ Injury Scale, shown in Table 4 (12). It is recommended that Grade 3 and 4 injuries should be treated surgically. A CT scan and MRCP are recommended before surgical treatment in order to assess the extent of the damage. MRCP is especially essential for evaluating the pancreatic duct system. ERCP can be utilized as part of the nonoperative management and can be helpful for preventing fistulas and pseudocysts (13). Surgical method depends on the involvement of duodenum, location of the pancreatic duct and tissue injury. For example, if the duct injury is to the left of the SMV, a distal pancreatectomy is suggested (4). Lesions of the pancreatic head are the most challenging and the indication for a pancreaticoduodenectomy is still unclear.

4.3 Spleen

AAST classification for splenic injuries are used to determine the extent of the damage (Table 5) (11). As stated before, 75% of spleen injuries can be managed nonoperatively according to the AAST classification. CT with IV

contrast is the gold standard for evaluating the injury in hemodynamically stable patients (4). Angioembolization is effective in cases of "vascular blushing" in CT scan or a grade 3 injury in hemodynamically stable patients. If observation is the mainstay treatment, the patient needs to be closely monitored. Since delayed splenic ruptures may occur even after 10 days, monitorization must be conducted in a center where the option of surgical treatment is available. In hemodynamically unstable patients or in cases of grade 5 injury, surgery is recommended. Splenectomy is the most common procedure. Partial splenectomy or other salvage procedures depend on the expertise of the surgeon however according to Coccolini et al. partial splenectomy is not recommended. Additionally, laparotomy is the gold standard in penetrating spleen traumas and laparoscopic surgery is not recommended(14).

5. BILIARY PATHOLOGIES

Biliary pathologies are uncommon causes of acute abdomen however these pathologies should be considered in the differential diagnosis of the acute abdomen.

Acute calculous cholecystitis typically present with colicky right upper quadrant pain, nausea, and a positive Murphy's sign. An ultrasound is the gold standard for evaluating the gallbladder. US criteria for acute calculous cholecystitis are: a wall thickness >5 mm, echo of the stone, pericholecystic fluid, and a positive sonographic murphy sign (4). All patients should be started on broad-spectrum antibiotics and IV fluids. Treatment depends on the patient however early cholecystectomy (within 72 hours of the symptoms) is recommended if the patient is fit enough to tolerate the surgery. If a patient is not a good fit for surgery, a cholecystostomy can be utilized to decompress the gallbladder. In 5-10% of the patients, cholecystitis can become complicated; necrosis of the gallbladder or perforation can develop. In these instances, the patient may present with an acute abdomen and surgical treatment may become necessary (15).

REFERENCES

1. Silen W, Cope Z. Cope's Early Diagnosis of the Acute Abdomen. Oxford University Press, USA; 2005.

2. Townsend CM, Beauchamp RD, Evers BM, Mattox KL, Sabiston DC. Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice. St. Louis, MO: Elsevier; 2022.

3. F Charles Brunicardi, Andersen DK, Billiar TR, et al. Schwartz's Principles of Surgery. Mcgraw-Hill; 2019.

4. Baer C, Menon R, Bastawrous S, Bastawrous A. Emergency presentations of colorectal cancer. Surgical Clinics of North America. 2017;97(3):529-545.

5. Chiara O, ed. Trauma Centers and acute care surgery. Updates in Surgery. 2022. doi:10.1007/978-3-030-73155-7

6. Pisano M, Zorcolo L, Merli C, et al. 2017 WSES guidelines on colon and rectal cancer emergencies: obstruction and perforation. World Journal of Emergency Surgery. 2018;13(1).

7. Ginesi M, Steinhagen E. A brave new world: Colorectal anastomosis in trauma, diverticulitis, peritonitis, and colonic obstruction. Seminars in Colon and Rectal Surgery. 2022;33(2):100881.

8. Moore, F.A., Catena, F., Moore, E.E. et al. Position paper: management of perforated sigmoid diverticulitis. World J Emerg Surg 8, 55 (2013). https://doi.org/10.1186/1749-7922-8-55

9. Raveenthiran V, Madiba TE, Atamanalp SS, De U. Volvulus of the sigmoid colon. Colorectal Disease. 2010.

10. Coccolini F, Coimbra R, Ordonez C, et al. Liver trauma: WSES 2020 guidelines. World Journal of Emergency Surgery. 2020;15(1).

11. Hommes M, Kazemier G, Schep NW, Kuipers EJ, Schipper IB. Management of biliary complications following damage control surgery for liver trauma. European Journal of Trauma and Emergency Surgery. 2013;39(5):511-516.

12. Injury Scoring Scale. The American Association for the Surgery of Trauma. Published August 27, 2009. https://www.aast.org/resources-detail/injury-scoring-scale#pancreas

13. Al-Hassani A, Jabbour G, ElLabib M, Kanbar A, El-Menyar A, Al-Thani H. Delayed bile leak in a patient with grade IV Blunt Liver trauma: A case report and review of the literature. International Journal of Surgery Case Reports. 2015;14:156-159.

14. Coccolini F, Montori G, Catena F, et al. Splenic Trauma: WSES classification and guidelines for adult and pediatric patients. World Journal of Emergency Surgery. 2017;12(1).

15. Kim S, Kim JW, Jung PY, et al. Diagnostic and therapeutic role of Endoscopic Retrograde Pancreatography in the management of traumatic pancreatic duct injury patients: Single Center experience for 34 years. International Journal of Surgery. 2017;42:152-157.

CHAPTER II

SYMPTOMS AND PHYSICAL EXAMINATION IN ABDOMINAL DISEASES

Akif Doğantekin

(MD), Private Gaziantep Emek Hospital, Department of Internal Diseases,
E- mail : akifdogantekin@gmail.com
ORCID : 0000-0001-6078-540X

Symptoms are the complaints that the patient describes. Symptoms are subjective, not measurable. For example, stomachache. The doctor cannot understand the nature of the abdominal pain and what it looks like with the examination, he learns subjectively by asking the patient. The simultaneous coexistence of three or more symptoms that are related to each other is expressed as a "symptom cluster" ("symptom group" or "symptom cluster"). The symptoms that make up the symptom group need not have the same etiology (1).

1. Symptoms

• Regurgitation (Water in the mouth) • Rumination • Pyrosis (Burning in the chest) • Globus • Dysphagia • Odynophagia • Dyspepsia • Nausea and Vomiting • Anorexia • Gas and bloating • Constipation • Diarrhea • Malnutrition • Acute abdominal pain (Acute abdomen) • Chronic abdominal pain (Chronic abdomen) • Jaundice • Ascites • Abdominal mass • Gastrointestinal bleeding

1.1. Regurgitation

Regurgitation is a symptom of painful, sour stomach contents coming into the mouth and throat spontaneously, without nausea and vomiting. The symptom of regurgitation is sometimes confused with rumination.

1.2. Rumination

Rumination, on the other hand, is the situation in which food that has been eaten a while ago comes into the mouth and then swallowed again without nausea

or vomiting. Basically, regurgitation in rumination occurs immediately after or during a meal, but is not triggered by nausea or gurgling. Patients often have lived with this symptom for years and may have consulted a physician many times with this complaint. Rumination syndrome is a clinical picture that can be easily confused with treatment-refractory vomiting, gastroparesis, burping, especially gastroesophageal reflux, and therefore can be overlooked. In fact, rumination is a method that mechanically assists the digestion of herbivores and animals with a multi-chambered stomach. However, it should be defined as a disease in humans. While it is more common in children and individuals with mental and developmental delays, it is increasingly defined in healthy adults (2).

1.3. Pyrosis

Pyrosis is a symptom felt in the form of a burning sensation that starts around the xiphoid on the stomach and spreads retrosternally upwards. It can also spread to the throat and back. It usually happens in the postprandial period. Although the symptom of pyrosis is valuable in the diagnosis, the severity of this symptom is not proportional to the presence and severity of esophagitis (3).

1.4. Globus

Globus pharyngeus; It is a clinical symptom that is described as a lump or foreign body sensation in the throat, which is painless, occurs continuously or intermittently, and generally increases during eating. Globus-like symptoms were first described by the Egyptians around 1900 BC. In today's literature, various definitions such as "globus", "globus pharyngeus", "globus hystericus", "pseudodysphagia" and "globus syndrome" are used to describe the symptom (4).

In a recent study conducted with 122 individuals diagnosed with globus, 44% of the patients stated that they experienced problem-related anxiety, while the most common pathological findings in this patient group were 15.6% reflux, 10.6% post-infectious inflammation and 7%, 4 nasal cavity pathologies were detected (5).

1.5. Dysphagia

Terminologically, dysphagia is a Greek term derived from the words dys (difficulty) and phagia (to eat). Dysphagia is a symptom that occurs as a

result of mechanical inhibition of the transfer of ingested food from the mouth to the stomach, decreased strength of the muscles that provide the swallowing movement, or deterioration of coordination. It may occur in the oropharyngeal or esophageal stages of swallowing. Oropharyngeal dysphagia, also called transfer dysphagia, is mostly caused by neurological, myopathic and metabolic causes. Oropharynx, larynx, and upper esophageal sphincter functions. Oesophageal dysphagia is often caused by intrinsic diseases of the esophagus. Dysphagia can also be seen due to medication, caustic substance intake and viral causes. In these cases, dysphagia accompanies odynophagia (6).

1.6. Odynophagia

Odynophagia is defined as painful swallowing. Caustic substance intake, drug-induced esophagitis, radiation damage and infectious esophagitis (candida, herpes viruses and citomegalovirus) are the most important causes of odynophagia. Odynophagia can also be seen in cases where ulcerative esophagitis develops in gastroesophageal reflux (7).

1.7. Dyspepsia

Dyspepsia; indigestion. Dys=Hard, Pepsis=Digest. Dyspepsia is a complex of symptoms rather than a disease. Abdominal pain (epigastric), burning, tightness, early satiety, fullness, bloating and belching are some of this symptom complex. The feeling of discomfort is not relieved by defecation, 25% is due to an organic cause, and 75% does not find a cause. Dyspepsia is therefore examined under two headings: 1. Organic 2. Functional (8).

1.8. Nausea and Vomiting

Although nausea and vomiting can be seen together, they are different conditions. Nausea is an uncomfortable feeling in the back of the throat and stomach and can result in vomiting. Nausea may be accompanied by increased salivation, dizziness, sweating, difficulty in swallowing, pale skin, inability to lift one's head, slow heartbeat, drop in blood pressure, changes in body temperature and palpitations. Vomiting is the expulsion of stomach contents through the esophagus and mouth with a strong reflex. An irresistible feeling of vomiting may develop after nausea. Food poisoning, viral gastroenteritis (infection of the stomach and intestines caused by a virus), and certain medications are the most common causes of sudden nausea and vomiting (9).

1.9. Anorexia Nervosa

Anorexia nervosa is characterized by body image disorder, which is mostly seen in adolescence. Tertiary, psychological reasons, life-threatening reduction of food intake and advanced it is an eating disorder that is highly resistant to treatment, accompanied by weight loss. Individuals with anorexia nervosa often make severe restrictions on the amount of food they eat to prevent weight gain or continue to lose weight. They may vomit after eating or abuse tools such as laxatives, diet pills, diuretics, or enemas to control the calorie intake the body needs. In addition, they may try to lose weight by exercising excessively. For individuals suffering from anorexia nervosa, the amount of weight they lose is not enough and they continue to fear gaining weight. Anorexia is basically not about food. It is an extremely unhealthy and in many cases life-threatening method of dealing with emotional problems. Individuals who suffer from anorexia nervosa often equate weakness with self-worth (10).

1.10. Gas

Gas is also normally present in the gastrointestinal tract (GIS). Changes and disorders related to the formation, distribution, excretion and amount of gas can cause some symptoms. Gas-related symptoms (20-40%) are the main reasons for most of the patients who apply to gastroenterology outpatient clinics. patients gas; excessive belching, visibly in the abdomen or with one or more of the complaints of unseen bloating and excessive flatulence. Its prevalence in the general population is between 16-30%. There are 5 gases (nitrogen, oxygen, carbon dioxide, hydrogen and methane), all of which are odorless, which normally make up about 99% of the gas present in the GIS. The main complaints of gassy patients are: recurrent frequent burping, abdominal bloating, feeling of fullness and discomfort; excessive winding (11).

1.11. Constipation

Constipation in general; It is defined as insufficient defecation characterized by few defecations, difficult stool passage, or both. The normal number of defecations is accepted as 3 times a day to 1 time in 3 days. Constipation is generally not described as a disease, but as a collection of symptoms that vary from person to person. Rome IV criteria also support this subjective description (12).

1.12. Diarrhea

Diarrhea is a symptom that occurs due to infectious or non-infectious causes, which causes stooling more than 3-4 times a day and in quantity more than 200-250 grams (may vary depending on age and nutritional factors), increased fluid and electrolyte loss. Diarrhea is defined as a decrease in stool consistency or an increase in fluidity. Acute diarrhea is usually defined as diarrhea that lasts up to 3 weeks, while chronic diarrhea is any diarrhea that lasts longer than that in stool consistency. Chronic diarrhea, defined as reduction lasting more than four weeks, is a common and challenging clinical Picture (13).

1.13. Malnutrition

Malnutrition; It has been defined as a whole consisting of malnutrition, overnutrition, specific nutrient deficiencies and imbalance due to disproportionate nutrient intake due to insufficient nutrient intake. Malnutrition; It is a medical term formed by the prefix 'mal' meaning abnormal, bad, diseased to the word 'nutrition' which means nutrition. Therefore, malnutrition can be defined as malnutrition. In the past, while malnutrition was mostly used to mean deficient and inadequate nutrition, today concepts such as overnutrition and obesity are also included in the scope of malnutrition. Malnutrition occurs as a result of deficient or excessive consumption of various foods or food groups (14).

1.14. Acute Abdomen

Acute abdomen is abdominal pain in which signs and symptoms shorter than '1 week' are concentrated in the abdomen, except for female patients with known abdominal trauma and approximately 20 weeks of pregnancy. The 2 most common causes are nonspecific abdominal pain (34%) and appendicitis (28%). Abdominal pain can be classified into 3 categories: Visceral pain, somatoparietal pain and referred pain. Visceral pain; pain experienced when stimuli trigger visceral receptors. The pain is usually blunt pain that is not well localized in the midline, epigastrium, periumbilical region, or lower middle abdomen because the abdominal organs send sensory afferents to both sides of the spinal cord. Somatoparietal pain is caused by stimulation of the parietal peritoneum. It is usually more severe than visceral pain and can be more precisely localized. An example of the differences between these 2 types of pain; It is vague periumbilical visceral pain seen in the early phase of acute appendicitis, followed by localized

somatoparietal pain at McBurney's point due to inflammatory involvement of the parietal peritoneum. Referred pain is pain felt in places distant from the diseased organ. This pain occurs when visceral afferent neurons combine with somatic afferent neurons from different anatomical regions on second-order neurons located in the same spinal segment in the spinal cord. Referred pain may be felt in the skin or deeper tissues but is usually well localized (15,16).

1.15. Chronic abdominal pain

Chronic abdominal pain is pain that lasts for 3-6 months and affects the daily activities of patients. Gastrointestinal causes and pathologies should be excluded in the evaluation. The best treatment is to accept the pain and reassure the patient that there is no possibility of a serious underlying disorder.

1.16. Jaundice

Jaundice is the yellowing of the skin and mucous membranes due to the accumulation of bilirubin pigment as a result of the imbalance between the production and clearance of bilirubin pigment. Cholestasis is a term that covers the physiological, morphological and clinical changes that occur as a result of the inability of bile to flow into the intestine. Bilirubin level may be found to be normal in cholestasis. Bilirubin is a tetrapyrrole compound that is formed as a result of the metabolism of the heme ring, which is formed by the degradation of free heme and hemoproteins such as cytochromes, catalase, peroxidase, tryptophan pyrolase, especially hemoglobin, and is yellow in color (17).

1.17. Ascites

When ascites is mentioned, it should be understood that free fluid accumulation in the peritoneal cavity. Abscesses, cystic-localized fluid accumulations are excluded from this definition. The most common cause (80%) is cirrhosis. In men, the peritoneal cavity is closed and normally only very small amounts of intraperitoneal fluid are present. In women, the peritoneal cavity is continuous with the female reproductive organs and up to 20 ml of fluid can accumulate depending on the menstrual phase. Normally, there is less than 100-200 ml of fluid in the peritoneal cavity, pathological fluid accumulation in this space is called ascites (18).

Increased abdominal circumference; It may develop as a result of ascites, gas-induced distention, hepatomegaly, obesity and widespread tumors. Ascites

can be difficult to diagnose by physical examination in obese patients. Dullness in the lateral parts of the abdomen is the most specific physical examination finding. If there is no dullness in the lateral parts of the abdomen, it is probably absent in ascites. If dullness is detected; The patient should be placed in the partial decubitus position and displaced dullness should be sought. Looking at the fluid wave is rarely helpful, as this is usually detected in patients with massive ascites (19).

1.18. Abdominal Mass

An abdominal mass can be defined as a localized swelling or enlargement in one area of the abdomen. Abdominal masses may originate from the abdominal wall, abdominal organs, or retroperitoneal region. However, intra-abdominal masses, especially those in the retroperitoneal region, may not attract attention until they reach large sizes. It is detected incidentally during routine controls or when presenting with another complaint. Sometimes, complaints such as pain, vomiting, constipation that occur due to the mass that takes the patient to the doctor, and sometimes intestinal or urinary obstruction findings. The mass may be due to diffuse enlargement of the intra-abdominal organs, or it may be palpable as a separate tumor. The palpable mass may be due to a simple cause such as fecaloma, or it may be due to anomalies and cysts in the gastrointestinal tract, inflammatory diseases or benign neoplasms. More importantly, abdominal mass is one of the most common findings of malignant diseases (20).

1.19. Gastrointestinal bleeding

It is used for all bleeding in the digestive system starting from the mouth and continuing to the anus.

1.19.1. Hematemesis

Bloody vomit – Coffee-ground-colored (hematinized blood by stomach acid) or bright red, fresh blood. It is seen in hemorrhages above the level of the ligament of Treitz.

1.19.2. Melena

It is tar-like black, slimy and foul-smelling stool containing digested blood. Melena-shaped defecation is usually seen in upper GI bleeding. However, melena

can also be seen in bleeding from the proximal levels of the small intestines and colon. At least 50 ml. blood can cause melena. 1000 ml of bleeding can cause melena for 5 days (21).

1.19.3. Hematochezia

Fresh, bright, red bloody stool from the rectum. It is usually seen in bleedings below the ileo-cecal valve. Hematochezia can be seen in heavy upper GI bleedings (10%).

1.19.4. Occult Bleeding

These are light and insidious bleedings that show signs of occult blood positivity in the stool. In patients; Symptoms of iron deficiency anemia such as pallor, dyspnea, decreased effort capacity and anginal pain are prominent. It is recognized by the presence of iron deficiency anemia and the presence of occult blood in the stool. It can be of either upper or lower gastrointestinal origin. It may be the first sign of gastrointestinal cancers, especially in men over 40 and postmenopausal women (22).

2. Abdominal Examination

The patient is taken to the examination room, information is given about the procedures to be performed, hands are washed for each examination, and consent is obtained for the examination. By preparing a suitable environment, it is ensured that the patient lies on the examination table and the abdomen is completely open. To relax the abdominal muscles, the knees are brought to half flexion. The patient's head should be turned to the left (23).

The examination is to lie in a supine position in a well-lit and comfortable environment, with the arms to either side or over the rib cage, and knees moderately low. The abdominal muscles are relaxed and the patient is made ready for examination. The part of the abdomen from the xiphoid process to the symphysis pubis should be open. In a patient with abdominal pain, the examination is to start from the farthest point from the place of pain and finally to evaluate the area of pain. Although it is more important especially in young children, it is very important for patient cooperation to ensure that the diaphragm part of the stethoscope and our hands are warm enough to not disturb the patient (24).

The first method used to divide the abdomen into topographic regions is to divide it into four quadrants with two horizontal and vertical lines passing through the umbilicus. The main organs in the abdomen are distributed in these quadrants as follows :

Right upper quadrant: 1. Liver 2. Gallbladder and biliary tract 3. Duodenum 4. Ascending colon, right curvature of colon (hepatic flexure) and transverse colonproximal half 5. Pancreas 6. Right kidney and adrenal gland

Left upper quadrant: 1. Stomach 2. Spleen 3. Distal half of the transverse colon, left curvature of the colon (splenic flexure), and descending colon 4. Pancreas 5. Left kidney and adrenal gland

Right lower quadrant: 1. Cecum 2. Appendix 3. Right ureter 4. Right ovary and tuba uterina

Left lower quadrant: 1. Sigmoid colon 2. Left ureter 3. Left ovary and tuba uterine

In this distribution, the abdominal aorta, inferior vena cava, bladder, uterus and rectum are located along the midline, while the small intestines are spread to all quadrants around the umbilicus. The second method is to divide the abdomen into nine zones with two horizontal and two vertical lines. The horizontal lines that provide this division unite the lowest points of the arch of the costae at the top and the anterior superior of the spina iliaca at the bottom. Vertical lines pass through the palpation points of the femoral arteries in the right and left groin. The main organs in the abdomen are distributed to these regions as follows:

Right hypochondrium: 1. Liver 2. Gallbladder and biliary tract 3. Duodenum 4. Right bend of the colon

Epigastrium: 1. Distal stomach 2. Pancreas 3. Transverse colon 4. Aorta and inferior vena cava

Left hypochondrium: 1. Proximal stomach 2. Spleen 3. Left bend of the colon

Right lumbar region: 1. Right kidney and adrenal gland 2. Proximal part of right ureter 3. ascending colon

Umbilical region: 1. Small intestines 2. Aorta and inferior vena cava

Left lumbar region: 1. Left kidney and adrenal gland 2. Proximal part of left ureter 3. Descending colon

Right inguinal region: 1. Cecum 2. Appendix 3. Distal part of right ureter 4. Right ovary and tuba uterina

Hypogastrium: 1. Bladder 2. Uterus 3. Rectum

Left inguinal region: 1. Sigmoid colon 2. Distal part of left ureter 3. Left ovary and tuba uterina (25)

Examination, palpation, percussion, and auscultation have become the 4 pillars of clinical bedside medicine (26).

2.1. Inspection

Whether the abdomen participates in breathing, scar tissue, hernia, and the presence of collateral formations are determined. The general appearance of the abdomen (diffuse swelling, asymmetry), skin color and lesions (icterus, hyperpigmentation, hair growth, skin lesions, etc.) are determined and recorded.

2.2. Auscultation

After inspection, auscultation should be performed before palpation to avoid increased bowel movements. The four quadrants should be listened to separately and each quadrant should be listened for at least one minute and the bowel sounds should be evaluated. Auscultation is performed by gently placing the diaphragm of the stethoscope on the abdomen. Abdominal aorta and renal artery auscultation should be performed and pathological findings (murmur) detected should be recorded.

2.3. Percussion

With percussion of the abdomen, pathologies can be distinguished by tympanic sound (coming from hollow organs) and dullness (solid organs or mass or presence of acid in the abdomen in appropriate matte distribution). The presence of ascites in the abdomen can be evaluated by percussion starting from the epigastric region and radiating the location of organs in the abdominal cavity (an enlarged uterus, liver or spleen) (27).

2.4. Superficial and Deep Palpations and Rebound tenderness

Palpation should be started by superficial palpation. With superficial palpation, localization of pain, muscle resistance, presence of mass and condition of superficial organs are determined. Deep palpation is combined with

percussion findings to determine the condition of the intra-abdominal organs and, if any, mass-masses. It is tried to obtain information about intra-abdominal pathologies (rebound tenderness is detected if inflammation occurs in the peritoneum above the diseased organ) by looking at rebound tenderness. While pressing the area where the patient feels pain in a slow but controlled way, the occurrence of pain with the sudden withdrawal of the hand gives information about rebound tenderness. This examination finding suggests inflammation in the parietal peritoneum. In acute abdominal pain; Involuntary muscular defense, direct and indirect rebound tenderness, is evaluated as an indicator of peritoneal stimulation by evaluating whether it is regional or widespread. If the patient is obese, then palpation can be performed by placing the other hand on the palpating hand during palpation.

2.5. Acid Examination

In the presence of acid, the navel and lateral grooves of the abdomen will be erased in direct proportion to the amount of acid, and the appearance of a frog's belly will appear. Depending on the cause of the ascites, additional findings will accompany it (such as the presence of collateral in liver cirrhosis). Starting from the xiphoid and extending to the lower abdominal regions, acid-mass separation is made with the radial percussion method (a matte line with the aperture facing upwards is obtained in acid). Detailed examination findings about ascites are noted by looking at the displaced dullness and fluctuation sensation (28).

2.6. Liver examination

Liver examination is started from the right inguinal region using the appropriate palpation technique. Palpation is done in accordance with the respiratory phases. During inspiration, the palpating hand is moved upwards and the lower edge of the liver is tried to be felt. After inspection; liver size, edge features, consistency, surface, and tenderness are recorded. By percussion from the midclavicular line, the upper border of the liver is determined and the total vertical liver size is decided by determining how much it has passed the rib curve in the same line with palpation. In addition, the presence of murmur is evaluated by auscultation of the liver. An increase in jugular vein engorgement (hepatojugular reflux) by pressing on the liver is a helpful physical examination method in detecting conditions that cause liver congestion such as heart failure.

2.7. Spleen examination

Examination is started from the left inguinal region using the appropriate palpation technique. Palpation is done in accordance with the respiratory phases. Percussion of the Traube area is performed. Thus, with percussion and palpation, information about the size of the spleen, if it is large, the detection of the notch, the spleen edge and surface properties, consistency, and sensitivity are obtained. Pathological findings found are recorded. (29).

2.8. Kidney examination

With the palpation of the kidney lodge, information about the condition and sensitivity of the kidneys is obtained. To palpate the right kidney, try to palpate the kidney between both hands from the lateral rectus muscle with the right hand while pushing the kidney upward from behind with the left hand parallel to the 12th rib and reaching the costovertebral angle. In the left kidney palpation, you can try to palpate by laying the patient on the left side or as in the spleen examination.

The bladder, ovaries, and uterus are normally not discernible by palpation and percussion. Globe vesical (full bladder due to inability to urinate) or tumors that will develop in all three organs can be detected by palpation or percussion. In such cases, they present with percussion as a downward facing matte line.

In the abdominal examination, special painful points are detected by palpation and their relationship with the complaints is determined (such as McBurney, Murphy's point) (30).

References

1- Dodd, M.J, Miaskowski, C. Paul. S.M. (2001 Symptom clusters and their effect on the functional status of patients with cancer. Oncol Nurs Forum, Apr;28(3):465-70.

2- Vakil N, van Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol 2006;101:1900-20; quiz 1943.

3- DeVault KR, Castell DO. Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. Am J Gastroenterol 2005;100:190-200.

4- Moloy PJ, Charter R. The globus symptom. Incidence, therapeutic response, and age and sex relationships. Arch Otolaryngol. 1982;108(11) :740-4.

5- Rasmussen ER, Schnack DT, Ravn AT. A prospective cohort study of 122 adult patients presenting to an otolaryngologist's office with globus pharyngeus. Clin Otolaryngol. 2018;43(3) : 854-60.

6- Kearney DJ. Approach to the patients with gastrointestinal disorders. In: Friedman SL, McQuaid KR, Grendell JH, (eds). 2nd ed. Current Diagnosis-Treatment in Gastroenterogy: McGraw-Hill; 2003:1-33.

7- Clouse RE. Approach to the patients with dysphagia or odynophagia. In: Yamada T, Alpers DH, Kaplowitz N, et al (eds)s. 4 nd ed. Textbook of Gastroenterogy. Philadelphia: Lippincott Williams-Wilkins. 2003;678-91.

8- Current Approach to Dyspepsia in Primary Care, https:// www.ttb.org.tr/ STED/ sted0603/ dispepsiye.pdf

9- Malagelade JR, Malagelade C. Nause and vomiting. Sleisenger and Fortran's Gastrointestinal and Liver Disease. 2006;143-58.

10- ADA Reports: Position of the American Dietetic Association: Nutrition intervention in the treatment of anorexia nervosa, bulimia nervosa, and eating disorders not otherwise specified (EDNOS). Journal of the American Dietetic Association 101(7):810-19, 2001.

11- Agrawal A, Whorwell PJ. Review article: abdominal bloating and distension in functional gastrointestinal disorders-epidemiology and exploration of possible mechanisms. Aliment Pharmacol Ther 2008; 27: 2-10.

12- Brandt LJ, Prather CM, Quigley EM, et al. Systematic review on the management of chronic constipation in North America. Am J Gastroenterol 2005;100(Suppl 1):S5-S21.

13- Juckett G, Trivedi R. Evaluation of Chronic Diarrhea" American Family Physician 84(10): 1119-1126, 2011.

14- Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on defnitions and terminology of clinical nutrition. Clin Nutr 2017;3: 49-64.

15- Higashi H. Pharmacological aspects of visceral sensory receptors. In Carvero F, Morrison JFB (Ed): Visceral sensation. Amsterdam, Elsevier, 1986;21.

16- Glaskow RE, Mulvihill SJ. Abdominal pain, including the acute abdomen. In: Feldman MH, Sleisenger BF, (Ed). Gastrointestinal and Liver Diseases. W.B. Saunders Company, Philadelphia, 1998;80-9.

17- Jarvis C. Physical examination and health assessment. 3rd ed. Philadelphia: W.B. Saunders Company; 2000. p. 581 - 611.

18- Zeybel M, Çolakoğlu Ö, Uğur F. Asit, In: Ünsal B. Editor. Portal Hypertension and Its Complications, 1st edition. İzmir . Meta Edition 2003;123-59.

19- Julien TY. Miscellaneous Discases of the Peritoneum and Mesentery, In: Friedman SL, McQuaid KR, Grendell JH, Editors. Current Dragnosis and Treatment in Gastroenterology. 2 nd ed. USA. McGraw-Hill Companies, Inc 2003; 166-76.

20- Yaris N. Causes of Abdominal Mass. J Curr Pediatr 2006;4.

21- Gilbert DA. Epidemiology of upper gastrointestinal bleeding. Gastrointest Endosc1990;36:8-13.

22- Edit: Feldman M, Friedman LS, Sleisenger MH. Sleisenger & Fordtran's Gastrointestinal and Liver Disease: pathophysiology, diagnosis, management.7th ed. : 211-243.

23- Özgür PIRGON. Süleyman Demirel University Physical Examination Book. S.D.Ü. Printing Promotion Services.2019; 207-215.

24- Aleksanyan V. Basic Information in Diagnosis (Propedeutics). Istanbul. 2nd Edition. FilizBookstore. 1982;352-483.

25- GÜVEN, M. Introduction to Clinical Diagnosis(2002). Ankara: Turgut pp.250.

26- Jagat Narula, Y Chandrashekhar, Eugene Braunwald. Time to Add a Fifth Pillar to Bedside Physical Examination: Inspection, Palpation, Percussion, Auscultation, and Insonation. JAMA Cardiol. 2018 Apr 1;3(4):346-350.

27- Ökten A. Abdominal Examination. In: Molvalılar Ş. (Ed). Semiology in Internal Medicine. Istanbul. Alpha Publishing House. 1997;325-59.

28- https://pubmed.ncbi.nlm.nih.gov/21250202/ (Access Date:10.12.2022)

29- https://guncel.tgv.org.tr/journal/30/pdf/322.pdf (Access Date:01.12.2022)

30- Memik F, Arınık A. Examination Methods and System Examination in Internal Diseases. In: Arinik A, (Ed). Symptom, Finding and Examination Methods in Internal Diseases, Bursa. Route Publishing. 2000;217-51.

CHAPTER III

ABDOMINOPELVIC PAIN & EMERGENCIES

Sinem Erfidan

(MD), Bornova Türkan Özilhan State Hospital, Department of Anesthesiology & Reanimation, Izmir, TURKEY
E – mail: sinem.erfidan@gmail.com
ORCID: 0000 – 0002 – 3849 – 6932

1. Introduction

The patient group with abdominal pain constitutes an important part of the admissions to both the emergency service and various outpatient clinics. It is important to take a good history, to know the causes and mechanisms of intra-abdominal and extra-abdominal pain in order to accurately evaluate abdominal pain and provide satisfactory care to the patient. If pain lasts less than a week then it is called acute pain. Such patients should be evaluated and diagnosed quickly. If all patients with acute abdominal pain are considered, 40% of the patients have abdominal pain that does not comply with the known forms of abdominal pain clinical features (1).

The main point to be considered when making the initial evaluation of the patient with abdominal pain in the emergency room is to decide whether the event is acute or not. Treatment of acute pain should be planned without delay according to the surgical or internal causes. The way to do this starts with a correct anamnesis and physical examination. After ensuring the hemodynamic stability of the patients with the available resources, advanced diagnostic methods and examinations should be used. Although the use of analgesics is not recommended in acute abdominal pain, since it prevents early diagnosis, eliminates symptoms and prolongs the event, painkillers can be administered after appropriate physical examination in order to ensure the comfort of patients who will wait in the emergency service for a long time and to prevent unnecessary agitation (2).

The term acute abdomen denotes a non-traumatic condition. In the literature, it is expressed as new abdominal pain that started within the last

week. Delays in the diagnosis and treatment of this syndrome, whose etiological factors are often related to an intra-abdominal disorder, adversely affect the prognosis. The diagnosis of acute abdomen is not always easy. It was determined that half of the patients who applied to the emergency services with acute abdominal pain were not related to acute abdomen but were based on reasons such as gastroenteritis and menstrual disorders. The most common causes of acute abdomen are acute appendicitis, acute cholecystitis, bowel obstruction, perforated ulcer and diverticulitis. Comparing the groups of patients presenting with acute abdominal pain who required or did not require surgery, it was seen that fever or leukocytosis were present in both groups (2).

These results suggest that the mentioned factors cannot be surgical criteria. As a co-factor, pain always precedes nausea in patients with surgical problems. The opposite situation is observed in patients who do not need surgery. No laboratory or X-ray finding of a pathognomonic clinical syndrome has been identified for acute abdominal pain. Therefore, if the patient has surgical treatment conditions, there is usually an indication for laparotomy (1, 2).

2. Types of Pain Caused by Abdominopelvic Diseases

2.1. Sudden Onset of Pain

In this presentation pain starts suddenly. The patient can tell the beginning of the event. The patient may go into shock due to etiological reasons. Abdominal tenderness may occur with the development of perforation and peritonitis. Radiological examination and paracentesis can detect disease. Angiography may reveal mesenteric vascular lesions. Fever and leukocytosis are not seen at the onset of sudden pain (3).

2.2. Rapid Pain

Rapid pain develops over an hour and is possibly related to obstruction and/or inflammation. Most common of these events are appendicitis, pancreatitis and ureteral stones. If the patient prefers to lie in bed, then peritonitis is present. If his movements are slow and tired, it is judged that he has visceral pains such as biliary colic and intestinal obstruction. Upper abdominal pain usually suggests acute cholecystitis, pancreatitis, or perforated peptic ulcer. Pain in the middle region of the abdomen indicates appendicitis, intestinal obstruction or mesenteric vascular lesions (3).

Lower abdominal pain can be caused by appendicitis, diverticulitis, ureteric colic, ectopic pregnancy, or torted ovarian cyst. Localized pain may result from appendicitis, cholecystitis, diverticulitis, or pancreatitis. If right lower quadrant pain is observed at Mc Burney point, appendicitis should be considered. Vomiting usually begins with pain. If vomiting is non-bilious, it indicates pyloric, and fecaloid, middle or upper intestinal obstruction. Surgical pain usually occurs before vomiting. All hernia orifices should be thoroughly examined on physical examination. This may be overlooked, especially in obese patients. A fever of 38°C may be observed in patients. Chills and fever above 39°C are unusual, except for diverticulitis, appendicitis, cholecystitis (3).

2.3. Gradual pain

Gradual pain reaches its peak in 12 – 24 hours. The slow development of symptoms may mislead the clinician. Therefore, it is necessary to repeat the examination in the first few hours for successful early diagnosis (3).

3. Origin of Abdominopelvic Pain

Two main types of afferent fibers are responsible for pain transmission to the brain. Type A delta fibers terminate in the thalamus. Therefore, the brain can perceive the localization of pain more precisely. This type of nerve fibers are found in the parietal peritoneum. Type C fibers terminate in the brain stem and because these fibers terminate before reaching the thalamus, the localization of pain in the central nervous system is much more difficult to perceive. Pain transmitted by these fibers is deeper, slower, and the character and localization cannot be accurately described by the patient. Abdominal visceral organs are innervated by these fibers. Abdominal pain is mainly of three types: visceral, parietal, and referred pain (4).

3.1. Visceral Pain:

3.1.1. Tension-type Pain:

Also known as colic pain, it is typically caused by increased forceful peristaltic contraction. This type of pain often occurs when trying to expel a bowel irritant (infectious agent, harmful food, foreign substance, etc.). Tension-type pain may occur as a result of strong contractions in the case of partial or total obstruction, adhesion and even constipation in the intestine. Acute stretching of an organ capsule also leads to this type of pain. Tension-type pain in

is typically vague and deep pain localization is not fully understood. Patients are in a constant effort to find a comfortable position. Gastroenteritis, constipation, acute pancreatitis pains are in this group (3, 4).

3.1.2. Inflammatory Pain:

Inflammatory pain begins as deep and uncertain localization as tension-type pain. Alternatively, its source is usually inflammation in the visceral peritoneum. The classic example is appendicitis. Initially, the patient describes the pain as midabdominal or periumbilical as the visceral peritoneum is affected. Hours later, when the inflammation reaches the parietal peritoneum, the patient localizes the pain more precisely to the right lower quadrant. Unlike tension-induced visceral pain, the patient with inflammatory pain tries to lie still (3, 4).

3.1.3. Ischemic pain:

Ischemic pain is the least common but most serious type of pain. It has sudden onset, intense, persistent and progressive. Unlike other types of abdominal pain, it is not relieved by analgesia (3, 4).

3.2. Parietal Pain:

Parietal pain is typically sharp and well localized. It results from direct irritation of the peritoneum, and since this innervation is unilateral, lateralization of pain can be done. Type a is transmitted by delta fibers (3).

3.3. Reflected Pain:

Reflected pain occurs when stimuli carried by visceral afferents from the patient organ enter the spinal cord at the same level as somatic fibers in distant anatomical localization. It is typically well localized. In inflammation of the gallbladder, the pain spreads to the right shoulder, back and right arm due to the stimulation of the spinal region between T5 – T9. Since pain due to pancreatic causes covers a wide area between T3 and T12, it is felt in the abdomen, back, waist and hips (3, 4).

4. Diagnosis in Abdominopelvic Diseases with Regards to Pain As Emergency

4.1. Anamnesis

Localization, shape and spread of abdominal pain are important. Pain in hollow organs such as gastrointestinal tract, urinary system, gallbladder and

ducts, salpinx is called colic pain. They are kind of pains that get worse from time to time and have intermittent relief periods. However, there is a stable, continuous sharp pain in gastric duodenal perforations, acute appendicitis rupture and acute pancreatitis. In addition, the patient should be asked whether he uses painkillers. The location of the pain, the onset time, the relationship between the onset time and nausea and vomiting should be clarified. Detailed bowel habits should be questioned, including episodes of diarrhea or constipation (5).

What needs to be learned in order to reveal the characteristics of pain can be elaborated as: time, localization, intensity and factors that increase and decrease pain. Co-existing fever, chills, heartburn, excessive flatulence and burping, weight loss, rectal bleeding and referred pain provide important clues to reveal the underlying cause of abdominal pain. The stool character should also be questioned, especially in terms of color and presence of blood. Bloody diarrhea indicates infectious enterocolitis or inflammatory bowel disease, while the classic 'currant gel' indicates fecal intussusception (6).

Previous medical history should include jaundice or liver disease, ulcer, previous abdominal surgery, and trauma. Hospitalization with previous diagnoses such as sickle cell anemia, porphyria or Familial Mediterranean Fever should be sought. Previous history of pelvic inflammatory disease (PID), intrauterine device use, tubal ligation should suggest the risk of ectopic pregnancy. In addition, symptoms accompanying abdominal pain are important and should be questioned (7).

Anorexia is an early symptom in all inflammatory diseases. Nausea and vomiting have no diagnostic value because they are non-specific. It suggests severe peritoneal irritation, distension of the mesentery and absorption of toxic substances from the intestines. The style, content and frequency of vomiting are important. A large amount of watery diarrhea is characteristic of gastroenteritis or other internal causes of acute abdomen. Bloody diarrhea occurs in ulcerative colitis, Crohn's disease, bacillary or amoebic dysentery. Constipation is not always a sure sign of intestinal obstruction. However, if progressive, painful abdominal distension or recurrent vomiting is present, it suggests mechanical intestinal obstruction (8).

4.2. Physical Examination

Physical examination creates excellent opportunities to detect the etiology of pain. The general appearance of the patient, sweating, fever, heart rate and rhythm should suggest sepsis, cholangitis, pyelonephritis, or bacterial small intestinal infections. In case of pain secondary to organs, the patient changes

positions frequently. However, if there is peritonitis, movement is avoided. Hernias should be carefully investigated. Increased bowel sounds may suggest enteritis or obstruction. In peritonitis, the decrease or disappearance of sounds suggests paralytic ileus. Hearing a murmur on auscultation is observed in an aortic aneurysm. Palpation of the abdomen should generally be started from the pain-free area. Otherwise, the patient's confidence will be lost and adequate examination may not be possible as a result of excessive defense. Abdominal wall stiffness suggests peritonitis (9).

Local defense findings are observed in conditions such as acute cholecystitis, appendicitis, and diverticulitis. The size of the organs and the presence of a mass should be carefully investigated. In acute appendicitis, tenderness of Mc Burney point and localization of pain to a few centimeters are important findings for the diagnosis of appendicitis. After slow and deep pressure on the sensitive area, "rebound" pain occurs when the hands are suddenly withdrawn. This process indicates that the parietal peritoneum is involved (10).

Genital, rectal, and pelvic examinations should be performed in every patient with abdominal pain. Thus, the diagnosis of acute pelvic inflammation, ovarian cyst, rectal tumor can be made. Rectal touche is recommended for patients with pelvic and lower abdominal pain. Pregnancy, salpingitis, tubaovarian abscess with signs of peritoneal irritation can be detected on rectal examination, along with findings such as fecalitis, melena, fresh blood, and retrocecal appendicitis should be considered in right-sided tenderness. Douglas should be investigated by rectal touche, and it should be checked for tenderness or mass. Prevalence of tenderness should primarily suggest irritation of the pelvic peritoneum, tenderness on the right side should suggest pelvic appendicitis, and tenderness on the left side should primarily suggest diverticulitis (11).

It is especially important in patients with mechanical intestinal obstruction whether there is a mass, petrified stool or foreign body in the rectum. In bedridden patients, the petrified stool, which is often the cause of obstruction, is manually restrained, and treatment is provided at the same time. In addition, the tone of the anus, whether the rectum is empty or filled with stool, the presence of melena and hematochezia are investigated during touche. Existing stomas, fistulas and wounds in patients should also be examined by touche (12 – 14).

4.3. Laboratory Tests

4.3.1. Blood Tests

Hemoglobin, hematocrit and white blood cell counts give very good information. An increase in the white blood cell count or marked leukocytosis,

with a left shift in the peripheral smear, indicates a serious infection. Moderate leukocytosis, seen in both medical and surgical inflammatory conditions, is usually nonspecific, and may not be seen in elderly and debilitated patients even if there is an infection. Serum electrolytes, urea and creatinine are very important, especially when hypovolemia is expected (shock, severe vomiting and diarrhea, abdominal distention or prolonged after onset of symptoms). Arterial blood gases should be determined in patients with hypotension, generalized peritonitis, pancreatitis, ischemic bowel disease and septicemia (15).

Metabolic acidosis that was not previously considered may be the first sign of a serious condition. In addition to the abdominal pain in aortic dissection, it should be kept in mind that the results of the dissected vascular structure in the relevant organ will be reflected in the blood picture and it is an emergency situation that should be considered in the differential diagnosis (16).

Elevated serum amylase level confirms the diagnosis of acute pancreatitis: Since elevation in amylase level is also seen in strangulated or ischemic bowel, ovarian cyst torsion or peptic ulcer perforation, care should be taken in the differential diagnosis. When a hepatobiliary disease is suspected, liver function tests (serum bilirubin, alkaline phosphatase, ALT, AST, albumin, globulin) serve to distinguish surgical diseases of the liver from internal ones and to understand the importance of the underlying parenchymal disease. If the patient has a history of a possible hematological disorder (cirrhosis, petechiae) in the anamnesis, coagulation tests (platelet count, prothrombin time and partial thromboplastin time) and peripheral smear should be requested. The sedimentation rate, which is often non-specific in acute abdomen, never excludes a serious condition (17).

4.3.2. Urine Examination

When patients have hyperbilirubinemia, foaming tea-colored urine occurs when shaken. Microscopic hematuria or pyuria seen in ureteral colic or urinary tract infections protects the patient from an unnecessary emergency operation. Urine analyzes (albumin, bilirubin) with sticks can also cause acute abdomen. It can distinguish a medical cause from surgical diseases (18).

4.3.3. Stool Analysis

Although gastrointestinal bleeding is not a common condition in acute abdomen, stool occult blood test should be performed routinely in every patient. A positive test result indicates a mucosal lesion or occult cancer that may cause chronic anemia. Stool smears to reveal bacteria, parasites and eggs in the stool may show amoeba trophozoites in patients with bloody and mucous diarrhea (18).

4.3.4. Paracentesis

Abdominal paracentesis provides very useful information in patients with free peritoneal fluid. Unlike blunt trauma, puncture can provide as much information as peritoneal lavage in the acute abdomen. The most valuable finding is free blood or turbid infected acid. Aspiration of blood, bile and intestinal contents is a definite indication for emergency laparotomy (18).

4.3.5. Endoscopy

Proctosigmoidoscopy is indicated in patients with suspected colonic obstruction, massive rectal bleeding, or rectal mass (18).

4.4. Radiologic Diagnostics

4.4.1. Direct Abdominal X-rays:

Chest X-ray should be requested from every patient presenting with acute abdomen. Depending on the situation, patients should have inpatient and standing direct abdominal radiographs (or lateral decubitus radiographs in thin patients). The sensitivity of direct X-ray in patients with acute abdominal pain is 64%, and the specificity is 68%. The sensitivity increases if the patient who will be taken with a direct abdominal X-ray (DKG) or decubitus position is kept in the standing or decubitus position for 5 – 10 minutes. Even 1 – 2 cm3 of air can be detected using this method (19). Gas accumulation in hollow organs in standing direct abdominal X – ray; Free or normal air outside the subdiaphragm, bile ducts and intestinal wall, contours of solid organs and peritoneal fat lines, radiopaque formations should be observed thoroughly. Abnormal gas accumulation in the intestines indicates paralytic ileus, mechanical intestinal obstruction or pseudo-obstruction, especially in the absence of bowel sounds, diffuse gas accumulation in the intestines with air limiting the ampulla recti indicates paralytic ileus (20).

As a rule, air-fluid levels are usually seen in intestinal obstruction, whereas a taut cecum and dilatation of the small intestines are seen in colonic obstruction. Fingerprint appearance on the colon wall is observed in half of patients with ischemic colitis. Free air under the hemidiaphragm can be overlooked unless it is sought. The presence of this condition in approximately 80% of perforated ulcers supports the clinical diagnosis (19 – 21).

4.4.2. Ultrasonography and CT Scan

Ultrasonography is a useful method to evaluate upper abdominal pain different from ulcer or intestinal obstruction pain and to investigate abdominal masses. The biggest advances in IT technology are spiral CT and Voyager programmed CTs. With spiral CT, inaccuracies caused by respiratory movements could be minimized (22).

4.4.3. Radionucleic Scans

Liver, spleen, HIDA and Gallium scans are very helpful in localizing intra-abdominal abscesses and in the diagnosis of acute cholecystitis (23).

4.4.4. Angiography

Performing angiography in cases of suspected intestinal ischemia or intra-abdominal bleeding must. Angiography should be performed beforehand, since the examination of the gastrointestinal tract with contrast material prevents the image. Selective visceral angiography is a reliable method in the diagnosis of mesenteric infarction (23).

5. Abdominopelvic Emergencies

5.1. Acute Appendicitis

Acute appendicitis is the inflammation of the appendix vermiformis. It requires abdominal surgery that frequently affects children and young adults. The classic presentation is pain that starts at the periumbilical level, then localizes to the right lower quadrant, accompanied by tenderness, defense, rebound, fever, nausea, and vomiting. It typically occurs due to obstruction in the lumen of the appendix. Causes of obstruction include lymphoid hyperplasia, appendicolith, foreign body and tumor (24).

Direct radiographs often do not provide sufficient information for diagnosis, but they may show free peritoneal air or appendicolith. Since ultrasonography does not contain radiation, it is preferred in children and young patients and is an effective method to show appendicitis in experienced hands. However, visualization of the normal appendix is more difficult and the diagnosis of appendicitis cannot be excluded by USG. Among the USG findings; dilated appendix that does not show peristalsis and cannot be compressed (external

diameter >6 mm), appendicolith, increased pericecal/periappendial echogenicity and periappendicular fluid can be counted. The described structure needs to be confirmed as an appendix by showing that it originates from the floor of the cecum and ends blindly (24, 25).

Computerized tomography is highly sensitive (94 – 98%) and specific (at a rate of up to 97%) for diagnosis, allowing the recognition of complications. The need for contrast material (intravenous, oral or both) is controversial and its use differs between centers. CT findings include; dilated appendix with thickening and contrast enhancement in its wall (diameter > 6 mm), periappendicular inflammation findings such as increased density in the adjacent adipose tissue, and appendicolith can be counted (24).

Complications include perforation, abscess formation, diffuse peritonitis, and gas in the portal system. Terminal ileitis, pelvic inflammatory disease, right-sided diverticulitis, Meckel's diverticulitis, acute epiploic appendigitis, and omental infarction can be considered in the differential diagnosis of appendicitis, whose clinical findings are frequently confused with mesenteric adenitis (25).

5.2. Acute Diverticulitis

Acute diverticulitis is one of the presentations of diverticular disease and is often asymptomatic. It is the most common complication of colonic diverticulosis. It is characterized by persistent pain accompanied by tenderness, often starting in the left iliac fossa due to obstruction of the neck of the diverticulum. As the disease progresses, signs of diffuse peritonitis occur (26).

CT is the preferred method for diagnosis and it also enables the evaluation of the extent of the disease and its complications. While segmental thickening and contrast enhancement is observed in the affected colon wall, there is an increase in density in the pericolic adipose tissue. Air and fluid monitoring in the pelvis or peritoneal cavity suggests perforation (26).

Complications are: bowel obstruction due to perforation, abscess or fistula and adhesions. It can be fistulized to the bladder, vagina, small intestine and skin. Gas monitoring in the bladder may suggest the presence of a fistula, as well as the fistula tract itself (26).

Its differential diagnosis includes colorectal carcinoma, epiploic appendagitis, ischemic colitis, pseudomembranous colitis, inflammatory bowel disease, and acute appendicitis in the presence of right-sided diverticulitis. In the presence of malignancy, short segment involvement is observed and

inflammatory changes are less. In cases of colitis, wall thickening is more pronounced than the increase in pericolic density (26).

5.3. Ovarian Torsion

Ovarian torsion refers to the rotation of the ovary and part of the fallopian tube. This rotation may cause necrosis as it causes vascular stasis in the ovary temporarily or permanently. Therefore, it is a condition that requires emergency surgery. Its clinical presentation is often nonspecific but tenderness accompanied by severe abdominal and pelvic pain. It is a pathology with a bimodal age distribution that frequently affects young and postmenopausal women, and 20% of cases occur during pregnancy. The two main causes are adnexal mass or ovarian hypermobility. The most common accompanying mass is dermoid cyst, and an increase in the size of the mass increases the risk of torsion (27).

USG is the preferred method for imaging, but CT and MRI can also be used for diagnosis. On USG, ovarian size has increased due to venous and lymphatic stasis in gray scale, and its echogenicity is variable. The follicles are displaced towards the periphery, and there may be rotational displacement in the ovary itself, and it is often in the midline. In chronic cases, cystic or hemorrhagic degeneration may be seen due to infarction (27).

Free fluid and ovarian mass may be seen. Doppler USG findings may vary. While low or absence of venous flow is common, absence of arterial flow is a rarer but poor prognostic finding. Normal flow due to intermittent torsion or dual blood flow from the ovarian and uterine arteries can be seen and does not exclude torsion. A swirl mark may be seen due to the rotated vascular pedicle. Sensitivity is expected when compressing the torsioned ovary with the probe (27).

Demonstration of the rotated ovarian pedicle, if visible, on computed tomography is helpful for diagnosis. A complex adnexal lesion is observed, and the enlarged ovary, distant pedicle, and underlying mass are often indistinguishable from each other. Hemorrhage and a decrease in contrast enhancement may be detected. Thickening of the surrounding adipose tissue, edema, and free fluid may be seen (28).

Since it is a condition that requires emergency surgery, MRI is often not preferred in the diagnosis, but it can be useful in cases in between. Because of its high soft tissue resolution, it shows adnexal mass-enlarged ovarian parenchyma, rotated pedicle and presence of bleeding better than CT. Acute bleeding appears

hyperintense in T1 and hypointense in T2. Polycystic ovary, ovarian edema, pelvic inflammatory disease and its complications may be included in the differential diagnosis, but it is easier to differentiate because the clinical findings are often different (28).

5.4. Ectopic Pregnancy

Ectopic pregnancy refers to the implantation of the fertilized ovum outside the uterine cavity. It constitutes 1 – 2% of all pregnancies and its incidence increases in cases of in vitro fertilization. The classic presentation is abdominal pain and bleeding. Symptoms are usually not severe. Mild pelvic pain and bleeding occur in early pregnancy. The hemodynamic status should be monitored, as bleeding can be life-threatening (29).

In the majority of cases, the localization is the fallopian tubes, while in the tubes, the bulbs occur most often in the region. In addition, interstitial/cornual, ovarian, cervical, cesarean scar, or abdominal ectopic pregnancy may also occur. The slower increase in serum β-hCG and progesterone levels compared to normal pregnancies is a marker. Knowing the β-hCG levels before imaging is important because normal pregnancies with values less than 2000 IU are not expected to be seen on USG (29).

The preferred method for imaging is USG, and it is appropriate to do it both transabdominal and transvaginally. While the transabdominal route is useful for evaluation of the abdomen, the transvaginal examination is important for diagnostic sensitivity. In the sonographic evaluation, an empty endometrial cavity in the uterus and an increase in echogenic material in the cavity can be seen. Simple adnexal cyst or non-adnexal complex cyst or mass may be seen. Although a solid mass is nonspecific, it can be seen. An echogenic ring around the extrauterine gestational sac and blood supply in this ring are observed on color Doppler USG and are called tubal ring and fire ring signs, respectively, but the latter can also be seen in the presence of the corpus luteum. Viable pregnancy in the extrauterine space is 100% specific, but is rare (29).

Severe abdominal pain, accompanied by impaired haemodynamics, should sonographically suggest a large amount of free fluid tubal rupture. The differential diagnosis is broad and in suspicious cases, ectopic pregnancy should be excluded with USG. It is necessary to separate the corpus luteum from the corpus luteum in the foreground on USG, and the presence of the corpus luteum as an intraadnexal cyst or mass is important in the differentiation (29).

5.5. Acute Cholecystitis

Acute cholecystitis, an acute inflammation of the gallbladder, is the primary complication of cholelithiasis and the most common cause of right upper quadrant pain. The pain may radiate to the right shoulder. Unlike biliary colic, the pain of cholecystitis typically persists for more than 6 hours. In addition, symptoms such as nausea, vomiting and fever may also be seen. Gallstones are the cause of 90 – 95% of cases (30).

Ultrasonography is the modality of choice for the evaluation of right upper quadrant pain. Its sensitivity in the diagnosis of acute cholecystitis is higher and more accessible than HIDA scintigraphy and CT. The most sensitive USG finding in acute cholecystitis is the sonographic Murphy sign accompanying the presence of cholelithiasis. The sonographic Murphy sign is the appearance of maximum abdominal tenderness by compression with the probe as soon as the gallbladder is visualized. Increased gallbladder wall thickness (>3 mm) and pericholecystic fluid are secondary findings (31).

Distension in the bladder, biliary sludge, stones in the bladder neck or cystic duct are other findings. In scintigraphy, which should be preferred in sonographically ambiguous cases because it is insufficient to show complications and alternative diagnoses, no sac is observed in the presence of acute cholecystitis (31).

Computerizwd tomography is less sensitive than USG for cholecystitis, and its findings are cholelithiasis, bladder distension, wall thickening, mural or mucosal enhancement, increased density in pericholecystic fluid and adipose tissue, and enhancement in the adjacent liver parenchyma due to reactive hyperemia. MRI is a sensitive method in the detection of acute cholecystitis, with findings similar to those in CT and USG (32).

Magnetic resonance cholangiopancreatography (MRCP) can show stones in the gallbladder neck or cystic duct. Complications include gangrenous cholecystitis, emphysematous cholecystitis, gallbladder perforation, pericholecystic abscess, and cholecystoenteric fistula. The differential diagnosis includes cholelithiasis or systemic causes of increased gallbladder wall thickness such as biliary colic due to choledocholithiasis, acute hepatitis, liver abscess, Fitz-Hugh-Curtis syndrome, acute pancreatitis, duodenal ulcer perforation and congestive heart failure, hypoalbuminemia (32).

5.6. Renal Colic

Urinary system stone disease refers to the presence of stones at any point in the urinary tract. Although the definition of renal colic actually describes the symptoms of pain, it is often used synonymously with ureteral stones. Stones outside the ureter are usually asymptomatic and when they cause pain, the symptoms are not usually acutely onset. Renal colic due to non-stone causes such as clots, detached papillae and papillary necrosis is extremely rare (33).

The prevalence of ureteral stones is quite high, with a rate of 7% in women and 12% in men. People with a positive family history are at higher risk. It is usually seen in people between the ages of 30 – 60, and the peak age range is 35 – 45. New-onset stone disease over the age of 50 is rare. Its clinical presentation is colic-like pain, hematuria, nausea and vomiting. The severity and location of the pain depend on the localization of the stone in the ureter. While a stone in the ureteropelvic junction causes deep flank pain, as it goes distally in the ureter, the pain can go down and hit the groin (33).

Large radiopaque stones can be seen on plain radiograph, but small or radiolucent stones will be missed. It also does not show signs of obstruction such as hydronephrosis. It may be useful for follow-up in cases where the diagnosis is known. CT is the gold standard method and can show almost all stones. Patients can be evaluated in the prone or supine position. Examination in the prone position allows to understand whether the stone is in the bladder if the stone is at the level of the ureterovesical (UV) junction. If a stone is detected at the UV junction in the supine position, the patient can be rotated and scanned again. CT also allows the visualization of secondary findings related to obstruction such as hydroureteronephrosis, increased perinephric density (34).

Although computed tomography is the gold standard, USG is particularly useful in pregnant women and children who are trying to avoid radiation. In USG, echogenic stone, acoustic shadow due to stone, twinkle artifact can be seen in color Doppler USG, as well as findings such as hydronephrosis or pyonephrosis (34).

Complications include acute renal failure and pyonephrosis. Although the family history is easily recognizable due to the colic nature of the pain, ureteropelvic junction stones can be clinically confused with acute pyelonephritis and distal ureteral stones with phleboliths on CT (35).

5.7. Acute Pancreatitis

Acute pancreatitis is the acute inflammation of the pancreas and can be life-threatening. For the diagnosis of acute pancreatitis; Two of the criteria must

be met: a) sudden onset, continuous and severe epigastric pain, b) lipase and amylase levels above three times the normal values, c) characteristic imaging findings in contrast-enhanced CT, MRI and USG. In the absence of the first two criteria, besides being necessary to confirm the diagnosis, imaging can also be used to guide treatment and evaluate complications (36).

Although gallstones are the main cause in its etiology, alcohol use, hypercalcemia, hyperlipidemia, and autoimmune causes are other common causes. Iatrogenic pancreatitis may also develop after ERCP. Classically, the clinical presentation is acute onset of severe epigastric and dorsal girdle pain, tenderness, and exacerbation of pain in the supine position. Amylase and lipase elevation are 90 – 95% specific for diagnosis (36).

The role of imaging in acute pancreatitis; to clarify the diagnosis, assess the severity of inflammation, determine the prognosis, and detect complications when clinically unclear. Typical findings include focal or diffuse parenchymal enlargement, density differences due to edema, blurred pancreatic borders due to inflammation, and increased density in the surrounding retroperitoneal adipose tissue. In the presence of necrosis, loss of parenchymal enhancement, which is often multifocal, is observed. Well-circumscribed fluid collection without necrosis indicates abscess formation. High-density fluid in the retroperitoneum or peripancreatic tissues indicates bleeding. USG is used to evaluate certain pathologies such as fluid collections and pseudocysts during follow-up (37).

Complications include pancreatic fluid collections, necrosis, abscess, bleeding, pseudoaneurysm, splenic or portal vein thrombosis, fistula, and pseudocyst formation. The differential diagnosis includes pancreatic adenocarcinoma, autoimmune pancreatitis, peptic ulcer disease and pancreatic lymphoma (37).

5.8. Bowel Obstruction

Small bowel obstructions constitute 80% of all mechanical obstructions and the remaining 20% are colon obstructions. The clinical presentation is cramping abdominal pain, abdominal distention, nausea and vomiting. The most common cause is fibrous adhesions due to previous surgeries, followed less frequently by abdominal hernias. Rare causes include endometriosis, masses, strictures due to Crohn's disease or radiotherapy, bezoars, and gallstone ileus (38).

The sensitivity of direct radiographs for small bowel obstruction is 50-60%. Observable findings; At least 3 intestinal loops that dilate over 3 cm are air-fluid levels with the valvula conniventes becoming visible (38).

Computerized tomography is more sensitive than radiographs and shows the cause and transition point in approximately 80% of cases. The use of

positive oral contrast is not preferred in CT scans to evaluate the obstruction, because it usually does not reach the transition zone when diluted and restricts the evaluation of the intestinal wall, making the diagnosis of ischemia difficult. CT findings include; enlargement of more than 2.5 cm between the outer walls of the dilated intestinal loops, collapse of the distal loops, and fecal sign in the small intestines (39).

Cases where a transition point is seen both proximal and distal to a certain bowel segment due to adhesions, herniations or rotation of the mesentery is called closed-loop obstruction. In long-lasting obstructions, arterial blood flow is impaired due to the increase in venous and lymphatic pressure in the intestinal wall and causes infarction. This situation is called strangulation and is the most important cause of mortality. The risk of strangulation is higher in closed-loop obstructions (39).

5.9. Colon Obstruction

Due to the high distention capacity of the colon, obstructions of the large intestine or colon are observed quite clearly on imaging. It is less common than small bowel obstructions. In its clinical presentation, abdominal pain and distension are accompanied by absence of gas and stool output. The appearance of symptoms associated with peritonitis indicates perforation (40).

The two most common causes are colorectal cancer and diverticulitis, respectively, and they together constitute 90% of colon obstructions. Other causes are cecal (1 – 3%) or sigmoid volvulus (3 – 8%), ischemic stricture, fecal impaction and hernias. Adhesions do not cause large bowel obstruction. It should be kept in mind that volvulus will cause closed-loop obstruction. Colon obstructions, pro-occlusion It is characterized by distension in the ximal and collapse in the distal. Although there is no definitively accepted dilatation limit, more than 6 cm for the colon and more than 9 cm for the cecum is considered in favor of dilatation (40).

On direct X-ray, distension in the colon and absence of gas in the distal colon are observed. In long-term obstructions, dilatation of the small intestines may be observed. CT is the most commonly used modality and besides confirming the diagnosis, it also shows the location of the obstruction and often the cause. The large bowel wall is distended, but wall contrast is normal except for ischemia. If the ileocecal valve is released, the small intestine is collapsed. Air in the colon wall and portal system due to prolonged ischemia, free air in case of perforation.

Differential diagnosis includes adynamic ileus, small bowel obstruction, toxic megacolon and ischemic colitis (40=.

5.10. Acute Mesenteric Ischemia

Acute mesenteric ischemia is a pathology that occurs due to sudden disruption of the vascular nutrition of the intestines and has a high mortality if not treated quickly. Although invasive angiography is the gold standard diagnostic method for diagnosis, the sensitivity of multislice CT has reached 90% with recent developments (41).

The clinical presentation is variable and often difficult to recognize at first. The most common finding is sudden onset, severe, and difficult to localize abdominal pain. Acute mesenteric ischemia is examined under four main headings with different predisposing factors, clinical presentations and prognosis for practical purposes. These; acute superior mesenteric artery (SMA) embolism (50%), acute SMA thrombosis (25%), nonocclusive mesenteric ischemia (20%), mesenteric venous thrombosis (10%) (42).

CT is the first-line imaging method, intravenous contrast and water should be used as neutral luminal contrast. In this way, bowel wall enhancement and thickening can be evaluated appropriately. When the HU value of the abdominal aorta exceeds 100, images of the arterial phase are taken, and 30 seconds after the completion of the arterial phase, images of the venous phase are taken (41).

Increase in wall thickness and loss of contrast enhancement in ischemic bowel are the most common findings and occur in varying degrees. In cases of arterial occlusion, loss of enhancement is observed in the SMA lumen or its branches. In thrombosis cases, occlusion is often close to the origin, whereas in embolism cases, it is often seen just distal to the middle colic artery origin. In venous thrombosis, there is a filling defect compatible with the thrombus in the superior mesenteric vein or its branches (41).

Pneumatosis intestinalis, air in the portal system, free peritoneal air due to perforation, and free peritoneal fluid can be seen in advanced ischemia, regardless of etiology. Especially in arterial occlusion, since mortality rates can reach 60-80% despite treatment, it is important to perform rapid and appropriate imaging at the slightest suspicion and to pay attention to arterial and venous structures in the evaluation of imaging. Although the conditions discussed above are the main causes of acute abdomen, it should not be forgotten that there are other rare and often confused causes (42).

6. Conclusion

Acute abdomen describes sudden onset, severe abdominal pain that has started within the last 24 hours. Many diseases are included in the differential diagnosis, from self-limiting pathologies to life-threatening conditions, and it may be difficult to diagnose pathologies that require specific medical or surgical treatment in cases where clinical signs and symptoms are ambiguous. Misdiagnosis may cause delays in treatment as well as unnecessary surgeries.

The importance of radiological imaging is increasing day by day in order to give the appropriate treatment quickly. Direct radiography, ultrasonography (USG), computed tomography (CT), and magnetic resonance imaging (MRI) are commonly used for imaging. Direct radiographs do not contribute much to the diagnosis, except in specific cases. CT; It is a diagnostic modality in most cases because it allows rapid imaging, evaluation of contrast material uptake, and 3D reconstruction. However, ionizing radiation is the main limitation in the use of CT. Although MRI is not frequently preferred due to the length of the examination period, it is used in specific pathologies due to its high soft tissue resolution.

The main causes of acute abdomen are specifically explored above. It should be kept in mind that there may be many reasons other than these, and that the frequently mentioned causes are included in the differential diagnosis. As a result, many patients come to emergency outpatient clinics with abdominal pain. Presenting with the diagnosis of acute abdominal pain and in case of emergency determining whether there is an abdominal urgency requiring surgery still remains a hot topic fort he clinician and surgeons.

Table 1: Abdominopelvic Emergency Causes

Acute appendicitis
Acute cholecystitis
Acute pancreatitis
Acute gastroenteritis
Biliary colic
Internal diseases
Other surgical diseases
Dysmenorrhea
FMF attack
Mechanical intestinal obstruction
Gynecological diseases
Choledocholithiasis
Chronic cholecystitis
Mesenteric lymphoadenopathy
Nephrolithiasis
Nonspecific abdominal pain
Perforated appendicitis
Peptic ulcer activation
Peptic ulcer perforation
Renal colic
Urinary infections

REFERENCES

1. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, The revised international association for the study of pain definition of pain: concepts, challenges, and compromises. Pain. 2020 Sep 1;161(9):1976–82.

2. Black CJ, Drossman DA, Talley NJ, Ruddy J, Ford AC. Functional gastrointestinal disorders: advances in understanding and management. Lancet. 2020 Nov 21;396(10263):1664–74.

3. Treede RD, Rief W, Barke A, Aziz Q, Bennett MI, Benoliel R, A classification of chronic pain for ICD-11. Pain. 2015;156(6):1003–7.

4. Aziz Q, Giamberardino MA, Barke A, Korwisi B, Baranowski AP, Wesselmann U, IASP taskforce for the classification of chronic pain. The IASP classification of chronic pain for ICD-11: chronic secondary visceral pain. Pain. 2019 Jan;160(1):69–76.

5. Sperber AD, Drossman DA. Review article: the functional abdominal pain syndrome. Aliment Pharmacol Ther. 2011;33(5):514–24.

6. Viniol A, Keunecke C, Biroga T, Stadje R, Dornieden K, Bösner S, et al. Studies of the symptom abdominal pain–a systematic review and meta-analysis. Fam Pract. 2014; 31(5):517–29.

7. Wallander MA, Johansson S, Ruigómez A, García Rodríguez LA. Unspecified abdominal pain in primary care: The role of gastrointestinal morbidity. Int J Clin Pract. 2007;61(10): 1663–70.

8. Bharucha AE, Chakraborty S, Sletten CD. Common functional gastroenterological disorders associated with abdominal pain. Mayo Clin Proc. 2016;91(8):1118–32.

9. Sandler RS, Stewart WF, Liberman JN, Ricci JA, Zorich NL. Abdominal pain, bloating, and diarrhea in the United States: prevalence and impact. Dig Dis Sci. 2000 Jun;45(6):1166–71.

10. El-Metwally A, Shaikh Q, Aldiab A, Al-Zahrani J, Al-Ghamdi S, Alrasheed AA, The prevalence of chronic pain and its associated factors among Saudi Al-Kharj population: a cross sectional study. BMC Musculoskelet Disord. 2019;20(1):177–9.

11. Jackson T, Thomas S, Stabile V, Shotwell M, Han X, McQueen K. A systematic review and meta-analysis of the global burden of chronic pain without clear etiology in low- and middle-income countries: trends in heterogeneous data and a proposal for new assessment methods. Anesth Analg. 2016;123(3):739–48.

12. Sperber AD, Bangdiwala SI, Drossman DA, Ghoshal UC, Simren M, Tack J, Worldwide prevalence and burden of functional gastrointestinal disorders, results of rome foundation global study. Gastroenterology. 2021 Jan;160(1):99–114.e3.

13. Koop H, Koprdova S, Schürmann C. Chronic abdominal wall pain. A poorly recognized clinical problem. Dtsch Arztebl Int. 2016; 113(4):51–7.

14. Lindsetmo RO, Stulberg J. Chronic abdominal wall pain–a diagnostic challenge for the surgeon. Am J Surg. 2009 Jul;198(1):129–34.

15. Camilleri M. Management options for irritable bowel syndrome. Mayo Clin Proc. 2018; 93(12):1858–72.

16. Pichetshote N, Pimentel M. An approach to the patient with chronic undiagnosed abdominal pain. Am J Gastroenterol. 2019 May; 114(5):726–32.

17. Srinivasan R, Greenbaum DS. Chronic abdominal wall pain: a frequently overlooked problem. Practical approach to diagnosis and management. Am J Gastroenterol. 2002; 97(4):824–30.

18. Farmer AD, Aziz Q. Mechanisms and management of functional abdominal pain. J R Soc Med. 2014;107(9):347–54.

19. Stoker J, van Randen A, Laméris W, Boermeester MA. Imaging patients with acute abdominal pain. Radiology 2009; 253: 31-46.

20. Miller SK, Alpert PT. Assesment and Differential Diagnosis of Abdominal Pain. The Nurse Practitioner 2006; 31: 38–47.

21. Schmulson MJ, Drossman DA. What is new in Rome IV. J Neurogastroenterol Motil. 2017;23(2):151–63.

22. Talley NJ. How to do and interpret a rectal examination in gastroenterology. Am J Gastroenterol. 2008;103(4):820–2.

23. Mendelson R. Imaging for chronic abdominal pain in adults. Aust Prescr. 2015 Apr;38(2): 49–54.

24. Hanbidge AE, Buckler PM, O'malley ME, Wilson SR. From the RSNA refresher courses: Imaging evaluation for acute pain in the right upper quadrant. Radiographics 2004; 24: 1117-3

25. Macaluso RC, McNamara RM. Evaluation and management of acute abdominal pain in the emergency department. Int J Gen Med 2012; 5: 789-97

26. Templeton AW, Strate LL. Updates in diverticular disease. Curr Gastroenterol Rep 2013; 15: 339.

27. Duigenan S, Oliva E, Lee SI. Ovarian torsion: diagnostic features on CT and MRI with pathologic correlation. AJR Am J Roentgenol 2012; 198: 122-31.

28. Chang HC, Bhatt S, Dogra VS. Pearls and pitfalls in diagnosis of ovarian torsion. Radiographics 2008; 28: 1355-68.

29. Lin EP, Bhatt S, Dogra VS. Diagnostic clues to ectopic pregnancy. Radiographics 2008; 28: 1661-71.

30. Harvey RT, Miller WT. Acute biliary disease: Initial CT and follow-up US versus initial US and follow-up CT. Radiology 1999; 213: 831-6.

31. Kiewiet JJ, Leeuwenburgh MM, Bipat S, Bossuyt PM, Stoker J, Boermeester MA. A systematic review and meta-analysis of diagnostic performance of imaging in acute cholecystitis. Radiology 2012; 264:708-20.

32. Akpinar A, Turkbey B, Karcaaltincaba M, Balli O, Akkapulu N, Balas S, Initial experience on utility of gadobenate dimeglumine (Gd-BOPTA) enhanced T1-weighted MR cholangiography in diagnosis of acute cholecystitis. J Magn Reson Imaging 2009;30:578-85.

33. Tamm EP, Silverman PM, Shuman WP. Evaluation of the patient with flank pain and possible ureteral calculus. Radiology 2003;228:319-29.

34. Türkbey B, Akpinar E, Özer C, Türkbey EB, Eken V, Karçaaltincaba M, Multidetector ct technique and imaging findings of urinary stone disease: An expanded review. Diagn Interv Radiol 2010;16:134-44.

35. Smith-Bindman R, Aubin C, Bailitz J, Bengiamin RN, Camargo CA Jr, Corbo J, Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med 2014;371:1100-10.

36. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2012;62:102-11.

37. Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology 2012;262:751-64.

38. Silva AC, Pimenta M, Guimaraes LS. Small bowel obstruction: what to look for. Radiographics 2009;29:423-39

39. Delabrousse E, Lubrano J, Jehl J, Morati P, Rouget C, Mantion GA, et al. Small-bowel obstruction from adhesive bands and matted adhesions: CT differentiation. AJR Am J Roentgenol 2009;192:693-7.

40. Khurana B, Ledbetter S, Mctavish J, Wiesner W, Ros PR. Bowel obstruction revealed by multidetector CT. AJR Am J Roentgenol 2002;178:1139-44.

41. Horton KM, Fishman EK. Multidetector CT angiography in the diagnosis of mesenteric ischemia. Radiol Clin North Am 2007;45:275-88.

42. Turkbey B, Akpinar E, Cil B, Karçaaltincaba M, Akhan O. Utility of multidetector CT in an emergency setting in acute mesenteric ischemia. Diagn Interv Radiol 2009;15:256-61.

CHAPTER IV

CIRRHOSIS OF THE LIVER

Akif Doğantekin

(MD), Private Gaziantep Emek Hospital, Department of Internal Diseases,
E- mail : akifdogantekin@gmail.com
ORCID : 0000-0001-6078-540X

1. Introduction

Liver cirrhosis is caused by various factors, especially chronic viral hepatitis and alcohol; It is a chronic liver disease characterized by parenchymal damage, fibrosis and nodule formation, and deterioration of lobular and vascular structure (1). Cirrhosis is a diffuse process of liver damage considered irreversible in its advanced stages. The natural course of cirrhosis is progression from the asymptomatic phase to the symptomatic decompensated phase with the development of ascites, bleeding, encephalopathy and jaundice, which are signs of decompensation. Once the patient enters the symptomatic decompensated phase, he progresses rapidly to liver transplant or death (2). Median survival is 12 years in asymptomatic compensated cirrhosis and 2 years in symptomatic decompensated cirrhosis. Approximately 5-7% of patients with compensated cirrhosis pass into the symptomatic decompensated phase per year (3). As soon as cirrhosis passes into the decompensated phase, it turns into a systemic disease, and multi-organ and system dysfunction develops. Two main strategies in the treatment approach in cirrhosis; They are treatments aimed at suppressing etiological causes and preventing decompensation and progression of the basic factors of pathogenesis. End-stage liver disease which is often automatically calculated according to Child-Pugh scoring (Table-1) and total bilirubin, creatinine and international normalized ratio (INR) values for staging of cirrhosis and based on cirrhotic nodule (CN) ranking [Model for end-stage liver disease (MELD)] score is used (4).

Table-1. Child-Pugh scoring (5)

• Encephalopathy: None = 1 point, Grade 1 and 2 = 2 points, Grade 3 and 4 = 3 points
• Ascites: None = 1 point, slight = 2 points, moderate = 3 points
• Bilirubin: under 2 mg/ml = 1 point, 2 to 3 mg/ml = 2 points, over 3 mg/ml = 3 points
• Albumin: greater than 3.5mg/ml = 1 point, 2.8 to 3.5mg/ml = 2 points, less than 2.8mg/ml = 3 points
• Prothrombin Time* (sec prolonged): less than 4 sec = 1 point, 4 to 6 sec = 2 points, over 6 sec = 3 points
• *Frequently INR will be used as a substitute for PT, with INR under 1.7 = 1 point, INR 1.7 to 2.2 = 2 points, INR above 2.2 = 3 points (The severity of cirrhosis: Child-Pugh A: 5 to 6 points Child-Pugh

2. Etiology

Early initiation of specific etiological treatments in any phase of cirrhosis prolongs the time to transition to the decompensatory phase and the occurrence of complications, and increases survival. In particular, cessation of alcohol in alcoholic cirrhosis, viral suppression in hepatitis B and hepatitis C, and immunosuppressive therapy in autoimmune hepatitis provide these benefits. While these effects are more pronounced in the compensated phase, they are variable in the decompensated phase as the pathogenesis is more complex (6). Therefore, when the patient is diagnosed with cirrhosis, the first thing to do is to investigate the etiology. The most common causes of cirrhosis in the United States are viral hepatitis (primarily hepatitis C virus [HCV] and hepatitis B virus [HBV]), alcoholic liver disease, and nonalcoholic steatohepatitis (table-2). HCV remains the leading cause of cirrhosis in patients awaiting liver transplant. With an increasing prevalence of nonalcoholic fatty liver disease (NAFLD) in the United States, estimates suggest that nonalcoholic steatohepatitis, a severe progression of NAFLD characterized by inflammatory steatohepatitis, will become the leading cause of cirrhosis in patients awaiting liver transplant sometime between 2025 and 2035 (7).

Table-2. Lists common etiologies of cirrhosis (8)

Viral hepatitis (hepatitis B, hepatitis C)
Alcoholic liver disease
Nonalcoholic fatty liver disease/nonalcoholic steatohepatitis
Storage diseases Hemochromatosis Wilson disease Alpha1-antitrypsin deficiency
Immune mediated Autoimmune hepatitis (types 1, 2, and 3) Primary biliary cholangitis Primary sclerosing cholangitis Immunoglobulin G4 cholangiopathy
Cardiovascular Veno-occlusive disease (Budd-Chiari syndrome) Congestive heart failure Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu disease)
Chronic biliary disease Recurrent bacterial cholangitis Bile duct stenosis
Other Medications (e.g., methotrexate, amiodarone) Erythropoietic protoporphyria Sarcoidosis Schistosomiasis
Note: Listed in order of generally decreasing prevalence.

3. Pathophysiology and Natural History of Cirrhosis

Chronic liver injury causes inflammation and hepatic fibrosis. Regardless of the cause, this can lead to the formation of fibrous septae and nodules, collapse of liver structures, and distortion of hepatic parenchyma and vascular architecture. Progressive fibrosis and cirrhosis subsequently result in decreased metabolic and synthetic hepatic function, causing a rise in bilirubin and decreased production of clotting factors and thrombopoietin, as well as splenic platelet sequestration, increased portal pressure, and the development of ascites and esophageal varices.

Cirrhosis can result from chronic liver damage of any cause. In patients with the three most common causes of liver disease, 10% to 20% will develop cirrhosis within 10 to 20 years. Factors associated with an increased risk of progression to cirrhosis include increased age, medical comorbidities (particularly patients coinfected with HIV and HCV), and male sex (except in alcoholic liver disease, where females progress more rapidly) (9). The point at which this process becomes irreversible, however, is not clear. Newer research has established that liver fibrosis is a dynamic process and that even early cirrhosis is reversible (10). Studies have demonstrated biopsy-proven fibrosis improvement rates as high as 88% after antiviral treatment in patients with HBV and HCV and as high as 85% after bariatric surgery in patients with nonalcoholic steatohepatitis (11). After cirrhosis is established, a patient may remain clinically stable, or compensated, for years. Patients with compensated cirrhosis caused by HBV, HCV, and alcoholic liver disease develop clinical signs of decompensation, which include ascites, hepatic encephalopathy, jaundice, or bleeding, at a rate of 4% to 10% per year (12). Variability of disease progression is influenced by the underlying cause and the presence or absence of treatment and ongoing liver injury. The median survival for those with compensated cirrhosis is 12 years, compared with two years once decompensation occurs (3).

4. Clinical Presentation

Most patients with compensated cirrhosis remain asymptomatic. When symptoms occur, they include fatigue, weakness, loss of appetite, right upper quadrant discomfort, and unexplained weight loss. With the onset of decompensation, patients may report symptoms of impaired liver function such as jaundice, portal hypertension (including ascites and peripheral edema), and hepatic encephalopathy (such as confusion and disordered sleep). Physical examination findings that may be present in patients with advanced liver disease (cirrhosis) are summarized in table-3 (13,14). In early compensated disease, laboratory findings may be normal. Incidentally elevated liver enzymes or evidence of hepatic disease on imaging may prompt the initial suspicion of chronic liver injury. Findings suggestive of cirrhosis include low albumin (less than 3.5 g per dL [35 g per L]), thrombocytopenia, aspartate transaminase (AST):alanine transaminase (ALT) ratio greater than 1, elevated bilirubin, and a prolonged prothrombin time (PT)/elevated international normalized ratio (INR) (15).

Table-3. Physical Examination Findings That May Be Present in Patients with Cirrhosis (13,14)

General	Muscle wasting
Central nervous system	Asterixis (tremor of the hand with wrist extension) Drowsiness, confusion
Head	Fetor hepaticus: sweet odor of the breath attributable to increased concentrations of dimethyl sulfide Jaundice: may see yellowing of mucous membranes beneath the tongue Parotid enlargement Scleral icterus Spider nevi
Chest	Gynecomastia Spider nevi Thinning axillary hair
Abdomen	Ascites Caput medusae (engorged superficial epigastric veins radiating from the umbilicus) Contracted or enlarged liver Hemorrhoids Splenomegaly
Hands and nails	Clubbing Dupuytren contracture (progressive fibrosis of palmar fascia, resulting in limited extension of the fingers) Palmar erythema Terry nails (whiteness of proximal half of nail plate)
Genitourinary (male)	Testicular atrophy
Lower extremities	Distal erythema Edema Petechiae

5. Complications of Cirrhosis

5.1. Ascites

Ascites, which is derived from the Greek word “askos” meaning bag or pouch, and defined as pathological free fluid collection in the peritoneal cavity, is

one of the three major complications of liver cirrhosis together with esophageal variceal bleeding and hepatic encephalopathy; It is the most common complication that patients with cirrhosis apply to the hospital (16). Ascites, with compensated cirrhosis; that is, such complications occur within 10 years in more than 50% of undeveloped cases. The development of ascites in patients with cirrhosis is an important turning point and indicates a poor prognosis; because after the development of ascites, the two-year survival rate is around 50% on average. In other words, with the development of ascites, 15% of the patients die in the first year and 44% die within 5 years. Therefore, every case of cirrhosis that develops ascites should be considered as a potential liver transplant candidate. More than 85% of patients with ascites have cirrhosis in their etiology; malignancy (10%), heart failure (3%), tuberculosis (2%), pancreatitis (1%) and other rare causes make up the rest, respectively (17). Therefore, every patient with ascites should be investigated first in terms of liver cirrhosis; however, even if cirrhosis is suspected, other possible causes, especially malignancy, should be investigated. Regardless of what the etiology is thought to be, in every newly detected ascites case, the ascitic fluid should be punctured and necessary investigations should be performed. On the other hand, possible spontaneous bacterial peritonitis (SBP) or malignancy should not be ruled out, especially if the clinical picture changes in patients with known cirrhotic acid (18).

5.2. Hepatic Hydrothorax

Hepatic hydrothorax is defined as the collection of fluid (usually>500 ml) in the pleural space in a cirrhotic patient without primary pulmonary or cardiac disease. Hepatic hydrothorax is diagnosed in 4%-10% of patients with cirrhosis. The pleural fluid accumulation associated with cirrhosis is usually right sided (66%), but may be bilateral (17%) or left sided (17%). Passage of ascitic fluid from the peritoneal cavity to the pleural space via lymphatic channels in the diaphragm or through congenital/acquired diaphragmatic defects have been reported to cause pleural effusion. Patients with hepatic hydrothorax may present with different pulmonary symptoms ranging from mild exercise intolerance to severe respiratory failure. The development of spontaneous bacterial peritonitis is a frequent complication in cirrhotic patients and communication between the abdominal ascitic fluid and pleural space may lead to thoracic bacterial pleuritis or spontaneous bacterial empyema (19).

5.3. Hyponatremia

Hyponatremia is common in decompensated cirrhotic patients due to abnormalities in body fluid homeostasis (20). Although the development of hyponatremia in patients with cirrhosis has been known for about 50 years, it has been used as a clinical marker in the last few years. Hyponatremia is an important prognostic factor in patients with cirrhosis. Vaptans cause an increase in serum Na levels by providing solute-free free fluid excretion with arginine vasopressin (AVP) antagonist effects. A serum Na level of 130 or less in patients with cirrhosis is defined as hyponatremia. However, it should be emphasized that; normal serum Na concentration is between 135-145 mmol/L. The prevalence of hyponatremia in patients with cirrhosis, Na <130 mmol/L, is 21.6%. If 135 mmol/L is used as the threshold value, this value increases up to 49.4% (21). Two types of hyponatremia develop in patients with cirrhosis. Hypovolemic hyponatremia develops in patients due to significant loss of extracellular fluid, especially from the kidney (overdiuresis due to excessive diuretic use) or from the gastrointestinal tract. This condition is known as hypovolemic hyponatremia and is characteristically associated with low serum Na concentration, plasma volume contraction, absence of edema and ascites, signs of dehydration, and prerenal azotemia. Hepatic encephalopathy develops frequently in these patients due to the rapid decrease in serum osmolarity affecting brain functions. In contrast to the hypovolemic hyponatremia seen in most patients with cirrhosis, hypervolemic hyponatremia is observed in cases where the extracellular fluid volume and plasma volume are enlarged and ascites/edema is added to the picture. This is due to significant renal solute-free water retention disproportionate to Na retention. Renal impairment is common, but not essential, in this type of hyponatremia. These two situations are distinctly different in terms of volume. In hypovolemic hyponatremia, the true plasma volume is decreased and at the same time, a decrease in the total extracellular fluid volume without ascites and edema has developed. In hypervolemic hyponatremia, plasma volume increases in absolute values, but lags behind marked vasodilation in the arterial circulation, which is known as effective arterial hypovolemia. Total extracellular fluid volume is increased here with ascites and/or edema (22).

5.4. Esophageal Variceal Bleeding

Esophageal varices develop in 30% of compensated cirrhosis and 60-70% of decompensated cirrhosis. It is responsible for 10% of upper gastrointestinal

system (GIS) bleeding. Veins at the gastroesophageal junction; are called intrinsic, extrinsic and communicantes. The intrinsic veins originate from the submucosal and subepithelial plexus of the gastric cardia and continue through the esophagus. Small varices consist of superficial venous plexus and large varices consist of deep intrinsic plexus. Varicose hemorrhages occur due to turbulent flow in the perforating veins at the lower end of the esophagus (23). Hepatic vein pressure gradient (HVPG > 12 mmHg, diameter of varicose, "red color sign" on endoscopy, Child classification (Child C), active alcohol intake in chronic alcoholic liver disease, local changes in distal esophagus are important in esophageal varices bleeding. There are 2 important clinical phases in the management of esophageal varices bleeding, as early phase and late phase. The risk of recurrent bleeding is quite high, especially in the late phase. In addition, HVPG >20 mmHg is an important risk factor for recurrent bleeding. While the rate of spontaneous stopping is 90% in upper gastrointestinal system bleeding, this rate is 50% in variceal bleeding. It is assumed that the bleedings stop spontaneously, especially in variceal bleeding secondary to hypotension. The risk of re-bleeding is quite high in the following 6-week period after active bleeding has stopped. The most risky period is especially in the first 48- It is a 72-hour period and re-bleeding can be seen at a rate of 50% in the first 10 days. is working. Being over 60 years old, chronic renal failure, large varicose veins, severe bleeding defined as hemoglobin value below 8 mg/dl at the time of admission are the main risk factors for early bleeding. The main factors affecting mortality are; Child-Pugh classification is age, BUN elevation, active bleeding, early rebleeding, HVPG > 20 mmHg (24).

5.5. Portal Hypertensive Gastropathy and Intestinopathy

The classic endoscopic finding of portal hypertension is varicose veins located in the esophagus and gastric fundus. Varicose veins located outside of these two regions are called ectopic varices. It is most commonly seen in the duodenum, anorectal region and anastomosis areas. They are difficult to detect endoscopically. In angiographic studies, the presence of duodenal varices has been reported up to 40%. Ectopic varices are responsible for approximately 5% of variceal bleeding. For this reason, their presence should be known and appropriate treatment should be planned urgently when they bleed (25). The most common lesion after esophageal varices in portal hypertensive patients is congestive or portal hypertensive gastropathy. Congestive gastropathy is

directly related to portal hypertension. It is seen in all cirrhotic and non-cirrhotic portal hypertension (26).

5.7. Hepatorenal Syndrome

Hepatorenal syndrome (HRS) is usually seen in patients with advanced liver disease and portal hypertension. It is characterized by the coexistence of circulatory and renal dysfunction. Blood pressure in the systemic circulation decreased due to the decrease in total systemic vascular resistance. Renal dysfunction is due to a decrease in renal blood flow. Renal failure is a common major complication in patients with advanced cirrhosis, and together with liver failure, it usually indicates a poor prognosis (27). However, when evaluated in terms of orthotopic liver transplantation, it emerges as an important risk factor because it increases mortality in the waiting list and the frequency of complications after transplantation. The Model for End-Stage Liver Disease (MELD) score, obtained with serum bilirubin and international normalized ratio values for prothrombin time, as well as serum creatinine, is used because it is a good predictor of 3-month mortality in cirrhotic patients who are candidates for liver transplantation and helps organ distribution. Thanks to this scoring system, the number of patients with kidney failure and liver transplantation has increased and mortality has decreased in patients awaiting liver transplantation. In addition, it is stated that pre-transplant kidney function is a predictor for survival after liver transplantation (28). Because of the close relationship between kidney and liver dysfunction, renal failure should be recognized, its pathogenesis should be understood and treated in patients with cirrhosis. The diagnosis of hepatorenal syndrome is based on exclusion of other diseases that cause acute kidney injury in cirrhosis, as there is no specific test. For the diagnosis of HRS, a serum creatinine value above 1.5 mg/dl despite a minimum of 2 days without albumin administration (1 g/kg) and diuretic therapy, absence of potential nephrotoxic drug use, absence of shock, and findings suggestive of renal parenchymal disease (protein excretion in the urine). Absence of >500 mg/day, >50 erythrocytes/ abnormal kidneys at high magnification or ultrasonography) is required. Major diagnostic criteria of HRS: 1. Liver failure and ascites 2. Creatinine >1.5 mg/ dl (133 μmol/L) 3. Absence of shock, ongoing bacterial infection, nephrotoxic agents, and fluid losses 4. After discontinuation of diuretic and no improvement following fluid resuscitation 5. Proteinuria (29).

5.8. Hepatopulmonary Syndrome

Pulmonary manifestations may be seen in patients with liver cirrhosis or portal hypertension. These changes are in the pleural space, pulmonary parenchyma, and or pulmonary circulation. It is mostly in the form of hepatic hydrothorax in the pleural area. Interstitial lung disease and expiratory airway obstruction are associated with parenchymal involvement. Changes in the pulmonary circulation may be observed in the form of impaired hypoxic vasoconstriction, hepatopulmonary syndrome, pulmonary hypertension, pulmonary varices and capillary insufficiency. Pulmonary symptoms of immune etiology such as pulmonary fibrosis, lymphocytic interstitial pneumonia, non-caseficial granulomas, bronchiolitis obliterans organizing pneumonia, lymphocytic bronchiolitis, pulmonary hemorrhage can be observed in primary biliary cirrhosis. Fluckiger and colleagues first described clubbing with cyanosis in a patient with syphilis-related liver failure in 1884 (30). In 1956, Rydell et al. reported hypoxemia in a 17-year-old boy with juvenile cirrhosis (31). Kennedy and Knutson reported a patient with alcoholic cirrhosis who developed orthodeoxy 4 years after the portacaval shunt (32).

5.9. Hepatocellular Cancer

Hepatocellular carcinoma (HSC) is the most common primary malignant tumor of the liver that originates from hepatocytes. Its incidence is between 20-200/100000. It is the 5th most common cancer. It ranks 3rd in cancer-related deaths. It causes 250,000 to 1 million deaths per year worldwide (33). The major risk factor for hepatocellular carcinoma is cirrhosis. The most common causes of cirrhosis in our country are viral hepatitis (HBV, HCV) and alcohol. Apart from these, other factors that increase the risk of hepatoma; male gender, nonalcoholic fatty liver, diabetes mellitus, smoking, hemochromatosis, alpha-1-antitrypsin deficiency. The most important event in the development of hepatocellular carcinoma is regeneration in the liver. Regardless of the cause, inflammation occurs first in the liver. After inflammation, necrosis, fibrosis, and regeneration develop, respectively. Fibrosis and regeneration are the most important pathophysiological indicators of cirrhosis. Dysplastic nodule, early hepatoma, and absolute hepatoma develop respectively from regeneration nodules. In the diagnosis of hepatocellular carcinoma; imaging methods, biomarkers and biopsy are used. Contrast ultrasonography (USG), computed tomography (CT) and magnetic resonance (MR) are used as imaging methods. Alpha feto protein

(AFP) value is checked as a biomarker. Biopsy is the method to be used if the diagnosis cannot be made despite all the examinations. Screening is for all patients with cirrhosis, whatever the cause. Apart from these, risk factors such as those with chronic HBV and HCV infection, those who use alcohol, and those with a family history of HCC are included in the screening. Screening is done with USG and AFP every 6 months. If a lesion is detected during scanning, diagnostic procedures are applied according to the size of the lesion (34).

5.10. Hepatic Encephalopathy

Hepatic encephalopathy refers to neuropsychiatric disorders observed in patients with chronic liver disease or portosystemic shunt. The terminology of HE is still confusing, and the terms may be used with different meanings among authors. Its classification can be made in accordance with the underlying disease or neuropsychiatric picture. Convened in Vienna in 1998, the IV. Hepatic encephalopathy clinical trials at the World Congress of Gastroenterology, by study group, hepatic encephalopathy: - Type A: encephalopathy due to acute liver failure - Type B: encephalopathy due to portosystemic shunts without hepatocellular disease - Type C: classification as encephalopathy observed in patients with cirrhosis and portal hypertension recommended (35). According to the character and duration of clinical findings, it can also be evaluated as acute episodic, chronic relapsing, chronic persistent and minimal hepatic encephalopathy (36). The main clinical features of hepatic encephalopathy are cognitive, motor and conscious disorders. The clinical picture can range from minimal personality and sleep pattern changes to deep coma. In minimal encephalopathy (in the early stages), changes in sleep patterns or personality changes are often observed, which is revealed by neuropsychiatric tests or neurophysiological measurements rather than routine clinical examination. Slowing of psychomotor speed, decrease in visual perception and attention are common. Such changes can be detected in 30-60% of cirrhotic patients without overt signs of encephalopathy. Calling this picture subclinical or latent encephalopathy - as it reduces its clinical significance - should not be used. In half of these cases, overt encephalopathy develops within 3 years. Therefore, it is recommended to treat minimal encephalopathy. When encephalopathy progresses, motor function defects and cognitive disorders become obvious, while changes in consciousness in accordance with this period attract attention (37).

5.11. Portal Vein Thrombosis

Portal vein thrombosis (PVT) is a medical problem that we rarely encounter in our gastroenterology practice and is an important cause of noncirrhotic portal hypertension. Many prothrombotic agents and local abdominal conditions can cause portal vein thrombosis (38). Portal vein thrombosis may also develop in patients with liver cirrhosis, associated with slowing or reversal of portal flow, especially in the presence of hepatocellular carcinoma (HCC). Transient PVT development may be observed in benign inflammatory conditions. Liver or pancreatic malignancies are responsible for 21-24% of all portal vein thrombosis. Direct vascular invasion, tumor compression, or hypercoagulation associated with a neoplastic event may cause portal vein thrombosis (39). Other less common causes of PVT include previous abdominal surgery, adenopathy, systemic inflammatory response syndrome, local ablation treatments for HCC, and biopsies of abdominal masses. Portal vein thrombosis is an important complication of cirrhosis and can be detected in 0.6–16% of compensated cirrhosis and 35% of decompensated cirrhosis. In one study, PVT was detected in 79 (11%) of 701 hospitalized patients with cirrhosis when routine ultrasonography was performed (40). Of these, 34 (43%) were asymptomatic, while 45 (57%) had intestinal infarction associated with portal hypertensive hemorrhage, abdominal pain, and mesenteric vein involvement. When PVT is detected in cirrhotic patients, the presence of overt or occult HCC should be considered and sought. PVT in this condition may be of malignant or benign origin (fibrin clot). Portal vein thrombosis can be clinically acute, subacute, or chronic, and may be symptomatic or asymptomatic. Acute PVT is usually clinically silent and is often found during radiological examination for other causes. PVT may be associated with abdominal pain and gastrointestinal bleeding in patients with cirrhosis. Improving the prognosis of patients with portal vein thrombosis and initiating the appropriate treatment method can be achieved by making the correct diagnosis as quickly as possible. In patients with suspected portal vein thrombosis, radiological examinations to reveal the presence of thrombosis should be performed. Abdominal ultrasonography (US) and Doppler studies, computed tomography (CT) and magnetic resonance (MR) angiography are often helpful in this situation. Venous phase angiography is the gold standard method when the diagnosis is still in doubt (41).

6. Treatment

It should be done according to the complications of cirrhosis and the patient’s symptoms. Moderate salt restriction, avoidance of long bed rest and

diuretics are recommended for treatment. Diuretics should be discontinued in case of gastrointestinal system (GI) bleeding, renal failure, hepatic encephalopathy (HE), hyponatremia (Na <125 meQ/lt), potassium level changes. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in the patient with ascites, as they may cause sodium (Na) retention, hyponatremia, and acute kidney injury. Angiotensin converting enzyme (ACE) inhibitors, angiotensin II agonists, alpha 1 blockers and aminoglycosides should not be used as they may cause kidney damage. Excretory paracentesis can be performed in Grade 3 acid. When more than 5 liters of acid is drained, albumin infusion (8 g/lt- depending on the amount of acid removed) is recommended (2). Liver transplantation should be considered in patients with serum Na levels below 130 mmol/L. In hypovolemic hyponatremia, the cause should be removed and normal saline given. In hypervolemic hyponatremia, fluid intake restriction of 1000 cc/day may prevent further deepening of hyponatremia. In hypervolemic hyponatremia, administration of hypertonic saline may be considered in the presence of life-threatening complications, may save time for liver transplantation. Slow administration (<8 mmol/L daily) prevents irreversible complications such as osmotic demyelination . When high-risk varices are detected (regardless of Child-Pugh stage, small varicose with red color or medium, large varices or Child C small varices are detected), primary prophylaxis should be performed because the risk of variceal bleeding increases. Primary prophylaxis with non-selective beta-blockers (NSBB) should be performed in small varicose veins with red color and Child-Pugh C patients. Variceal or non-variceal acute GI bleeding in patients with decompensated cirrhosis requires close follow-up because of the high risk of complications and mortality. Fluid replacement should be started immediately. Stabilization must be achieved and maintained. Colloids and/or crystalloids should be used (42). Empirical intravenous (IV) antibiotics should be started when spontaneous bacterial peritonitis is diagnosed. In the selection of empirical treatment, antibiotics are selected according to the environmental (nasocomial or community-based?), local resistance status and the severity of the infection.

References

1- Sherlock S, Dooley J (Eds). Diseases of the Liver and Biliary System. 11th ed. Oxford; Blackwell Science; 2002: p. 365-380.

2- European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69:406-60.

3- D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognosticindicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol 2006;44:217-31.

4- Peng Y, Qi X, Guo X. Child-Pugh versus MELD score for the assessment of prognosis in liver cirrhosis: A systematic review and meta-analysis ofobservational studies. Medicine (Baltimore) 2016;95:e2877.

5- Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973 Aug;60(8):646-9.

6- European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol 2018;69:406-60.

7- Wong RJ, Aguilar M, Cheung R, et al. Nonalcoholic steatohepatitis is the second leading etiology of liver disease among adults awaiting liver transplantation in the United States. gastroenterology. 2015;148(3):547-555.

8- Wiegand J, Berg T. The etiology, diagnosis and prevention of liver cirrhosis: part 1 of a series on liver cirrhosis. Dtsch Arztebl Int. 2013;110(6):85-91.

9- Poynard T, Mathurin P, Lai CL, et al.; PANFIBROSIS Group. A comparison of fibrosis progression in chronic liver diseases. J Hepatol. 2003;38(3): 257-265.

10- Bonis PA, Friedman SL, Kaplan MM. Is liver fibrosis reversible? N Engl J Med. 2001;344(6):452-454.

11- Jung YK, Yim HJ. Reversal of liver cirrhosis: current evidence and expectations. Korean J Intern Med. 2017;32(2):213-228.

12- Asrani SK, Kamath PS. Natural history of cirrhosis. Curr Gastroenterol Rep. 2013;15(2):308.

13- Smith, A., Baumgartner, K., & Bositis, C. (2019). Cirrhosis: diagnosis and management. American family physician, 100(12), 759-770.

14- https://stanfordmedicine25.stanford.edu/the25/liverdisease.html. Access Date(11.12.2022)

15- Udell JA, Wang CS, Tinmouth J, et al. Does this patient with liver disease have cirrhosis? JAMA. 2012;307(8):832-842.

16- Reynolds TB. ascites Clin Liver Dis 2000; 4: 151-168.

17- Moore KP, Wong F, Gines P, et al. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. Hepatology 2003; 38: 258-266.

18- Runyon BA. Management of adult patients with ascites due to cirrhosis: an update. Hepatology 2009; 49: 2087-21.

19- Gur C, Ilan Y, Shibolet O. Hepatic hydrothorax--pathophysiology, diagnosis and treatment--review of the literature. Liver Int 2004;24(4):281-4.

20- Gines P, Cardenas A, Schrier RW. Liver disease and the kidney. In: Schrier RW, ed. Disease of the Kidney & Urinary tract. Vol 3.8th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2006:2179-205.

21- Heuman DM, Abou-Assi SG, Habib A, et al. Persistent ascites and low serum sodium identify patients with cirrhosis and low MELD scores who are at high risk for early death. Hepatology 2004;40:802-10.

22- Gines P, Berl T, Bernrdi M, et al. Hyponatremia in cirrhosis; from pathogenesis to treatment. Hepatology 1998;28:851-64.

23- Moitinho E, Escorsell A, Bandi JC, et al. Prognostic value of early measurements of portal pressure in acute variceal bleeding. Gastroenterology 1999; 117: 626-31.

24- De Franchis R, Primignani M. Why do varices bleed? Gastroenterol Clin North Am 1992; 21:85-101.

25- Helmy A, Al Kahtani K, Al Fadda M. Updates in the pathogenesis, diagnosis and management of ectopic varices. Hepatol Int. 2008; 2:322-34.

26- McCormack TT, Sims J, Eyre-Brook I, et al. Gastric lesions in portal hypertension: inflammatory gastritis or congestive gastropathy. gout 1985; 26:1226-32.

27- Gines, P. et al., Hepatorenal syndrome. Lancet, 2003. 362(9398): p. 1819-27.

28- Weismüller TJ, Prokein J, Becker T, Barg-Hock H, Klempnauer J, Manns MP, et al. Prediction of survival after liver transplantation by pre-transplant parameters. Scand J Gastroenterol 2008;43:736-46.

29- Meltzer J, Brentjens TE. Renal failure in patients with cirrhosis: hepatorenal syndrome and renal support strategies. Curr Opin Anaesthesiol 2001;23:139-44.

30- Fulickiger M. Vorkommen von trommelschlagelformigen finger und phalanger ohne chrnische verdiderunger an den Lungen oder am Herzen. Wien Med Wochenschr 1884; 34: 1457.

31- Rydell R, Hofbauer FW. Multiple pulmonary arteriovenous fistulas in juvenile cirrhosis. Am J Med 1956; 21: 450–460.1977.

32- Kennedy TC, Knudson RJ. Exercise aggravated hypoxemia and orthodeoxia in cirrhosis. Chest 1997; 72:305–309.

33- Bosch, F. X. (1991). Hepatocellular carcinoma in the world: epidemiologic questions in etiology, pathology, and treatment of hepatocellular carcinoma in North America. Advances in applied biotechnology series, 35-54.

34- Bosch FX, Ribes J, Diaz M, et al. Primary liver cancer: worldwide incidence and trends. gastroenterology. Nov 2004;127.

35- Ferenci, P., Lockwood, A., Mullen, K., Tarter, R., Weissenborn, K., & Blei, A. T. (2002). Hepatic encephalopathy—definition, nomenclature, diagnosis, and quantification: final report of the working party at the 11th World Congresses of Gastroenterology, Vienna, 1998. Hepatology, 35(3), 716-721.

36- Cordoba J, Blei AT. hepatic encephalopathy. In: Schiff's diseases of the liver. Ed. Schiff ER, Sorrell MF, Maddrey WC. 10th ed. Lippincort Williams & Wilkins, Philedelphia, 2007;569-599.

37- O'Carroll R. E. Neuropsychological Aspects of Liver Disease and its Treatment Neurochem Res 2008;33:683-690.

38- Ogren M, Bergqvist D, Björck M, et al. Portal vein thrombosis: prevalence, patient characteristics and lifetime risk: a population study based on 23,796 consecutive autopsies. World J Gastroenterol 2006;12:2115-9.

39- Valla DC, Condat B. Portal vein thrombosis in adults: pathophysiology, pathogenesis and management. J Hepatol 2000;32:865-71.

40- Amitrano L, Guardascione MA, Brancaccio V, et al. Risk factors and clinical presentation of portal vein thrombosis in patients with liver cirrhosis. J Hepatol 2004;40:736.

41- Rossi S, Rosa L, Ravetta Vet al. Contrast-enhanced versus conventional and color Doppler sonography for the detection of thrombosis of the portal and hepatic venous systems. AJR Am J Roentgenol 2006;186:1-11.

42- Kim WR, Biggins SW, Kremers WK, et al. Hyponatremia and mortality among patients on the liver transplant waiting list. N Engl J Med 2008;359:1018-26.

CHAPTER V

HEMOCHROMATOSIS

Hasan Açık

(Asst. Prof. Dr.), Istanbul Okan University, Faculty of Medicine, Department of Internal Medicine
E-mail: hasan.acik@hotmail.com
ORCID: 0000-0002-7247-8164

Hemochromatosis is a disease characterized by the accumulation of iron in the body (1). It causes multiorgan dysfunction. Liver, pancreas, heart, thyroid, joints, skin, gonads and pituitary are the most affected organs. Iron metabolism in our body is by regulation of absorption rather than excretion. It is also known as bronze diabetes.

1. Iron Metabolısm

A large amount (63%) of iron in the body is found in the structure of hemoglobin. About 10% is found in myoglobin and other tissues. The remaining iron is stored in the reticuloendothelial system, liver and bone marrow. Iron overload causes free radical formation and cell death by lipid peroxidation. Controlling the absorption of iron in the diet plays an important role in iron metabolism, since iron cannot be actively eliminated from the body (5).

Iron is absorbed into mature erythrocytes via the divalent metal transporter 1 (DMT1). It then passes from the enterocytes to the circulation via ferroportin. It passes from circulation to hepatocytes via transferrin receptor 2 and HFE protein complex. Hepcidin is secreted by the uptake of iron into hepatocytes. Hepcidin combines with ferroportin, leading to loss of ferroportin from the membrane. Thus, the passage of iron into the circulation is prevented and the iron metabolism in the body is regulated (1,7,8).

Etiologically, it is divided into two groups as hereditary hemochromatosis and secondary hemochromatosis (2).

2. Hereditary Hemochromatosis

Hereditary hemochromatosis (HH) is caused by inherited mutations in the HFE gene, which regulates gastrointestinal iron absorption by hepcidin protein. It is an autosomal recessive disease. In most HH, hepcidin protein binds to ferroportin, the iron transport protein in erythrocytes, and prevents absorbed iron from entering the circulation. It also prevents the release of iron from lysed erythrocytes. Due to the decreased hepcidin protein in HH, both the addition of iron to the systemic circulation increases and the recycling of erythrocyte-derived iron increases (3). Then, it is transported to the tissues with the iron transferrin protein and accumulates as hemosiderin. This results in cell death and organ failure in the organs. The most common mutations in the HFE gene are C282Y and H63D. The HFE gene is located on the short arm of chromosome 6 (6p21.3).

There are four different types of HH:

Type-1a: It is inherited autosomal recessively and is the most common of the HH strains. It is caused by a mutation in the C282Y gene. It is more common in the white race (2).

Type1b: It is the type in which C282Y and H63D gene mutations are seen together (14,15,16). Iron overload is rare in these patients unless additional factors such as alcohol or hepatitis C are included (17,18).

Type1c: It is the type of HH that occurs as a result of the S65C mutation. Serum iron and ferritin levels are high; but excessive iron storage is not observed. Therefore, it is considered a clinically insignificant polymorphism (19,20).

Type 2a: It occurs as a result of hemojuvelin gene mutation. It is inherited autosomal recessively.

Type 2b: It occurs as a result of hepcidin (HAMP) gene mutation. It is inherited autosomal recessively. Type 2a and type 2b usually begin between the ages of 15-20.

Type 3: It is an autosomal recessive type of HH that usually occurs between the ages of 30-40. It is caused by a mutation in the transferrin receptor-2 gene.

Type-4: It is caused by ferroportin gene mutation. It is inherited autosomal dominant.

1.1 Epidemiology

Men are affected about 3 times more often than women in HH. Affected women become symptomatic at a older age than men due to iron loss in the

menstrual cycle (2). Although the C282Y gene mutation is common in society, a small proportion of individuals have iron accumulation. And this; suggests that environmental factors, such as lifestyle, also contribute to the development of the disease (4).

Clinical Manifestations

Patients may present to the clinic at different stages of iron overload. While iron accumulates in the liver and synovial tissue in the early period, it accumulates in the pancreas, skin, heart and pituitary in the late period. This can result in cirrhosis, pancreatic insufficiency, heart failure, arthritis, adrenal insufficiency, hypothyroidism, hypogonadism, and skin hyperpigmentation (3). Systolic and diastolic dysfunction due to myocardial iron accumulation may develop especially in advanced disease, and this situation is often at a level that may prevent liver transplantation in end-stage patients (12). Despite these organ damage, the diagnosis of HH is often made by coincidental hyperferritinemia (3). In a study, it was found that only 2.1% of patients diagnosed with HH had diabetes, heart failure, and skin hyperpigmentation at the time of admission (6).

2.3 Laboratory Findings

The research should be started by looking at the serum ferritin level and transferrin saturation. Further investigation should be initiated when the ferritin level is greater than 200 mcg/l in women, 300 mcg/l in men, or the transferrin saturation is greater than 40% in women and 50% in men. C282Y and H163D HFE gene mutations should be investigated, especially in the white race, due to their high prevalence. However, increased ferritin levels do not always indicate hemochromatosis. Elevated ferritin levels can also be seen in metabolic syndrome, alcoholism, or inflammation. Aminotransferases are found to be high in most patients; but not more than twice as high. Since hypogonadism may accompany, other tests such as hormone tests and thyroid function tests should also be done.

First-degree relatives of patients with HH should also be examined for HH genetic mutations.

2.4 Radiological Findings

Chondrocalcinosis seen on X-ray of wrists or knees or low T2-weighted signal in liver, spleen and pancreas on MRI support the diagnosis of

hemochromatosis. Chest radiography may show cardiomegaly and increased pulmonary vascular traces, and echocardiography may show cardiomyopathy.

2.5 Liver Biopsy

Liver biopsy; It is the most sensitive and specific test that can detect iron storage and liver damage. The classical pathological finding of hemochromatosis is iron accumulation in biliary epithelial cells and Kupfer cells, primarily in hepatocytes (2,4).

3. Secondary Hemochromatosıs

Iron accumulation in the body and related organ damage can develop even without the genetic mutations that cause HH. It usually develops due to thalassemia major, sickle cell anemia, hemolytic anemia, intensive blood transfusion or other liver diseases (21,22). Hemochromatosis may develop with increased intestinal iron absorption in patients with chronic alcohol use. Serum ferritin and transferrin saturations are also found to be high in these patients (23). In addition, alcohol-dependent hepcidin expression is also reduced. This is one of the major causes of iron accumulation in chronic alcohol use (24,25). Secondary hemochromatosis causes are shown in Table-1.

Table-1: Secondary Hemochromatosis causes

Anemias that cause iron overload
• Thalassemia major
• In the chronic phase of hemolytic anemia
• Sickle cell anemia
• Hereditary spherocytosis
• Aplastic anemia
Parenteral iron overdose
• Blood transfusion
Chronic liver diseases
• Porphyria cutanea tarda
• Hepatitis B and C
• Alcoholic liver disease
• Non-alcoholic fatty liver disease
Other reasons
• Malignancies (HCC, breast cancer)
• Chronic inflammatory processes (SLE etc.)

4. Treatment

Phlebotomy is the most effective treatment method for reducing morbidity and mortality, which has been used in the treatment of HH for many years. Each 500 ml phlebotomy removes 250 mg of iron from the body. A weekly or biweekly phlebotomy is recommended. The aim here is to keep the ferritin level at 50 lg/L without anemia. Ferritin level should be checked monthly until it reaches the upper abnormal limits, and then every 2 weeks until it reaches the target level. Patients with a diagnosis of HH should be followed for life and phlebotomy should be performed every 1-4 months, depending on their ferritin level (9). Although phlebotomy is recommended especially in the treatment of ferroportin deficiency patients, it should be performed less frequently due to the risk of anemia due to decreased iron recycling (2).

Patients should eat healthy foods by avoiding foods with high iron content. High consumption of alcohol should be avoided.

Iron chelation is recommended in patients with secondary hemochromatosis and in patients in whom phlebotomy is contraindicated, in cases where iron cannot be removed effectively with felbotomies or is impossible due to poor vascular conditions (9). Deferoxamine, deferiprone and deferasirox are the most commonly used iron chelators. Deferoxamine is used intravenously (iv). Deferiprone and deferasirox are oral iron chelators.(10).

Erythropoietin can be used in patients whose phlebotomy is difficult due to anemia (2).

Erythrocytopheresis is a treatment method that selectively removes erythrocytes with the help of a special device. It returns waste products such as plasma proteins and platelets back to the patient. It can be used as an alternative method to phlebotomy (26). In phlebotomy, 250-500 ml of blood can be removed from the body in one session, while 1000 ml of erythrocytes can be removed in one session with erythrocytopheresis.

Treatment improves insulin sensitivity, skin hyperpigmentation, and fatigue. Cirrhosis, hypogonadism and arthropathy persist even with effective treatment (2).

Studies have shown that the survival of liver transplantation in hepatic failure due to HH is lower than that of transplantation for non-HH diseases. However, transplantation can still be considered in patients with end-stage liver failure (11).

Hepatocellular carcinoma (HCC) accounts for 30% of mortality in HH patients. For this reason, patients should be followed up with alpha fetoprotein (AFP) levels and liver ultrasonography twice a year (2).

In addition, the incidence of infections due to Listeria monocytogenes, Yersinia enterocolitica and Vibrio vulnificus is increasing in these patients (13).

Hepcidin-based treatments may be used in addition to or instead of phlebotomy in future treatment, due to the decreasing hepcidin level in HH patients in the future (9).

REFERENCES

1. Balaban Y H, Şimsek H. Hemokromatozis. İç Hastalıkları, 3. Baskı. Güneş Tıp Kitabevi. Editörler: İliçin G, Biberoğlu K, Süleymanlar G, Ünal S. Ankara, Türkiye: 2012; 1570-1573.

2. Porter JL, Rawla P. Hemochromatosis. 2022 Oct 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 28613612.

3. Murphree C, Nguyen N, Raghunathan V et al. Diagnosis and management of hereditary haemochromatosis. Vox Sang. 2020 May;115(4):255-262

4. Brissot P, Pietrangelo A, Adams P C et al. Haemochromatosis. Nat Rev Dis Primers. ; 4: 18016.

5. Munoz M, Garcia-Erce J A, Remacha A F. Disorders of iron metabolism. Part 1: Molecular basis of iron homoeostasis. J Clin Pathol 2011;64:281-6.

6. Gasser B, Courtois F, Hojjat-Assari S et al. Hereditary Hemochromatosis: presenting manifestations and diagnostic delay. Rev Med Interne 2014;35:160–165

7. Gürsel O, Eker İ, Kürekçi A E. Demir Metabolizması ve Bozuklukları. Türkiye Çocuk Hastalıkları Dergisi. 2015; 1: 71-77

8. Nemeth E, Ganz T. Hepcidin-Ferroportin Interaction Controls Systemic Iron Homeostasis. Int J Mol Sci 2021 Jun 17;22(12):6493.

9. Adams P, Altes A, Brissot P et al. Contributors and Hemochromatosis International Taskforce. Therapeutic recommendations in HFE hemochromatosis for p.Cys282Tyr (C282Y/C282Y) homozygous genotype. Hepatol Int. 2018 Mar;12(2):83-86. doi: 10.1007/s12072-018-9855-0. Epub 2018 Mar 27. PMID: 29589198; PMCID: PMC5904234.

10. Brissot P, Butzeck B, Cabantchik I et al. Therapeutic recommendations in HFE hemochromatosis for p.Cys282Tyr (C282Y/C282Y) homozygous genotype. Hepatology International (2018) 12:83–86

11. Mobarra N, Shanaki M, Ehteram H et al. A Review on Iron Chelators in Treatment of Iron Overload Syndromes. Int J Hematol Oncol Stem Cell Res. 2016 Oct 01;10(4):239-247.

12. Kowdley KV, Brandhagen DJ, Gish RG et al. National Hemochromatosis Transplant Registry. Survival after liver transplantation in patients with hepatic iron overload: the national hemochromatosis transplant registry. Gastroenterology. 2005 Aug;129(2):494-503.

13. Daniłowicz-Szymanowicz, L, Swi atczak, M. Sikorska K et al. Pathogenesis, Diagnosis, and Clinical Implications of Hereditary Hemochromatosis—The Cardiological Point of View. Diagnostics 2021, 11, 1279

14. Khan FA, Fisher MA, Khakoo RA. Association of hemochromatosis with infectious diseases: expanding spectrum. Int J Infect Dis. 2007 Nov;11(6):482-7.

15. Adams PC, Reboussin DM, Barton JC, et al. Hemochromatosis and ironoverload screening in a racially diverse population. N Engl J Med 2005; 352(17):1769–78.

16. Allen KJ, Gurrin LC, Constantine CC, et al. Iron-overload-related disease in HFE hereditary hemochromatosis. N Engl J Med 2008;358(3): 221–30.

17. Girouard J, Giguere Y, Delage R, et al. Prevalence of HFE gene C282Y and H63D mutations in a French-Canadian population of neonates and in referred patients. Hum Mol Genet 2002;11(2):185–9

18. Walsh A, Dixon JL, Ramm GA, et al. The clinical relevance of compound heterozygosity for the C282Y and H63D substitutions in hemochromatosis. Clin Gastroenterol Hepatol 2006;4(11):1403–10.

19. Cheng R, Barton JC, Morrison ED, et al. Differences in hepatic phenotype between hemochromatosis patients with HFE C282Y homozygosity and other HFE genotypes. J Clin Gastroenterol 2009; 43(6):569–73

20. Aranda N, Viteri FE, Montserrat C, et al. Effects of C282Y, H63D, and S65C HFE gene mutations, diet, and life-style factors on iron status in a general Mediterranean population from Tarragona, Spain. Ann Hematol 2010;89(8):767–73.

21. Asberg A, Thorstensen K, Hveem K, et al. Hereditary hemochromatosis: The clinical significance of the S65C mutation. Genet Test 2002;6(1):59–62

22. Kowdley KV, Brown KE, Ahn J et al. ACG Clinical Guideline: Hereditary Hemochromatosis. Am J Gastroenterol 2019 Aug;114(8): 1202-1218.

23. Bottomley SS. Secondary iron overload disorders. Semin Hematol 1998; 35(1):77–86.

24. Mueller S, Rausch V. The role of iron in alcohol-mediated hepatocarcinogenesis. Adv Exp Med Biol 2015;815:89–112.

25. Harrison-Findik DD, Schafer D, Klein E, et al. Alcohol metabolismmediated oxidative stress down-regulates hepcidin transcription and leads to increased duodenal iron transporter expression. J Biol Chem 2006;281(32):22974–82.

26. Dostalikova-Cimburova M, Balusikova K, Kratka K, et al. Role of duodenal iron transporters and hepcidin in patients with alcoholic liver disease. J Cell Mol Med 2014;18(9):1840–50

27. Rombout-Sestrienkova E, van Kraaij MG, Koek GH. How we manage patients with hereditary haemochromatosis. Br J Haematol 2016;175(5): 759–70

CHAPTER VI

DIAGNOTIC APPROACH AND TREATMENT OF CHOLODOCHOLITHIASIS

Bora Aktaş,

(MD.), Ankara Atatürk Sanatory Training and Research Hospital , Gastroenterology
boraktas@hotmail.com
ORCID: 0000-0002-2523-7560

The presence of stones in the common bile duct (CBD) is called choledocholithiasis. Choledocholithiasis most commonly occurs with the displacement of gallstones into the CBD (85%). The development of primary gallstones in the CBD is less common (10%). After cholecystectomy, stones can be seen in the CBD in 2-4% (1). The majority of choledochal stones are cholesterol and bilirubin stones (2). 15% of patients with symptomatic cholelithiasis have choledochal stones (3).

1. Clinical Findings

Choledocholithiasis is frequently symptomatic, rarely asymptomatic. Abdominal pain and jaundice are the most common symptoms. Abdominal pain as seen a bilier colic form occurs in the right upper quadrant and epigastric region. It has a sudden onset and long duration. Jaundice occurs due to the mechanical barrier of the bile tree (2). Cholangitis may develop due to biliary stasis resulting from obstruction. In this case, high fever accompanies the process. In severe cases, bacteremia and sepsis may develop. In cases where choledocholithiasis blocks the flow of the pancreatic duct, pancreatitis may develop (4).

2. Diagnosis

Laboratory examination reveals elevated liver enzymes and bilirubin, characterized by a cholestatic pattern. Mild leukocytosis is frequently observed. When accompanied by cholangitis, leukocytosis is prominent. In the case of pancreatitis, elevated pancreatic enzymes are observed (2,5).

The methods used for imaging the biliary tract are ultrasonography, computed tomography, percutaneous transhepatic cholangiography (PTC), endoscopic retrograde cholangiopancreatography (ERCP), endoscopic ultrasonography (EUS), and magnetic resonance cholangiopancreatography (MRCP). Direct X-rays are not used because of their low diagnostic efficiency, but opaque stones and pneumobilia can be seen on direct X-rays (6).

Ultrasonography (US) is the first-choice, non-invasive, non-ionizing radiation-free and easily accessible method for choledochal stones (7). At least 8 hours of fasting is required before the US procedure. In postprandial US examinations, the lumen and wall structure cannot be evaluated optimally because the gallbladder is contracted. In addition, due to the gas created by the stomach-duodenum contents, the bile ducts cannot be displayed optimally. Choledocholithiasis is characterized by dilatation of the CBD and intrahepatic bile ducts on US (6-8). Choledoch stone is seen as echogenicity with posterior acoustic shadowing (Figure 1). US is not very successful in showing the stone in the common bile duct. On the other hand, when stones are detected in the common bile duct on US, its diagnostic accuracy is high (6). The normal diameter of the common bile duct is between 5-11mm (8,9). Intrahepatic bile ducts are normally difficult to distinguish because they are very thin (1-2mm). In 25-35% of patients with choledocholithiasis, the common bile duct is normal width. The presence of many stones smaller than 1 cm in the gallbladder may cause suspicion of choledochal Stones (6-8). Choledocholithiasis is found in 8-18% of those with symptomatic cholelithiasis (10).

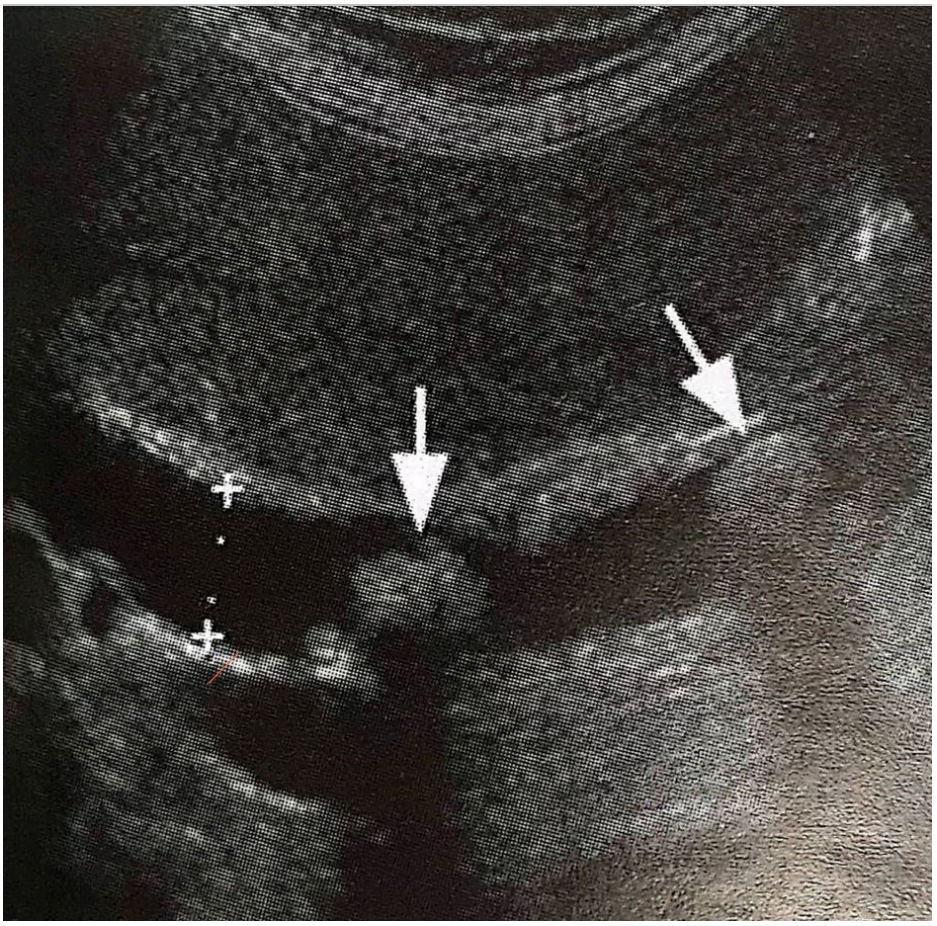


Figure 1: Two echogenic foci with posterior shadowing are seen in the dilated common bile duct.

Computed tomography (CT) is the method of choice in the second step in most patients who come to the emergency department with abdominal pain (11). However, bile duct stones are often difficult to see on CT because they are poor in calcium (Figure 2). Because the sensitivity and specificity of CT is lower than MRCP and it contains ionizing radiation, it is often not preferred in the demonstration of CBD stones (12,13). However, it is quite successful in demonstrating acute pancreatitis, which is a complication of CBD stones (11-13).

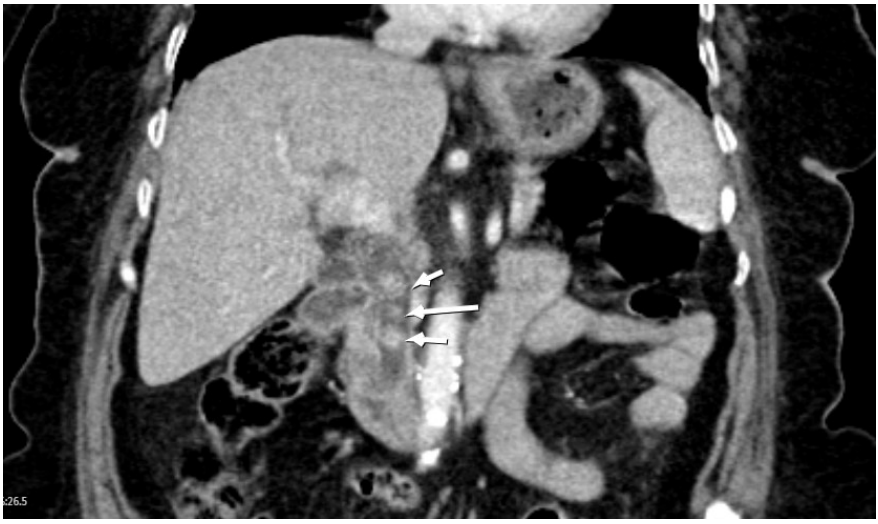


Figure 2: Coranal abdomen CT images show hyperdens stones (arrows) in dilated common bile duct

High soft tissue contrast resolution and efficient evaluation of peripheral bile ducts are the main advantages of MR imaging (Figure 3). MRCP is a noninvasive method, does not contain ionizing radiation, contrast agent and premedication are not required. Complications are not observed. It can be applied during attacks of pancreatitis and cholangitis. MRCP can visualize the ducts proximal and distal of the obstruction. Biliary duct pathology as well as adjacent organ damage can be visualized with MRCP (14,15). In one study, the sensitivity and specificity of MRCP were 93% and 96% in detecting CBD stones (16). MRCP has some disadvantages; spatial resolution is low, it does not show small ductal pathologies. MRCP can only be used for diagnostics and cannot be used for interventional treatment. It is not suitable for imaging in patients with obesity and claustrophobia. Optimal evaluation may not be possible due to artifact in the presence of metallic stent and operating materials. Bile ducts cannot be visualized in cases where there is massive acid in the abdomen. The success in imaging stones smaller than 5 mm is low (14-17). Heavy T2 images are obtained for MRCP. Six hours of fasting is required for MRCP examination. The examination is obtained in the supine position using a phased array coil. No contrast material is used. Bile duct stones are seen as multiple filling defects with angular contours on MRCP (Figure 4). Air bubbles, vascular compression, surgical clip artifacts, biliary flow artifacts, blood clot and concentrated bile can mimic choledocholithiasis in MRCP (15).

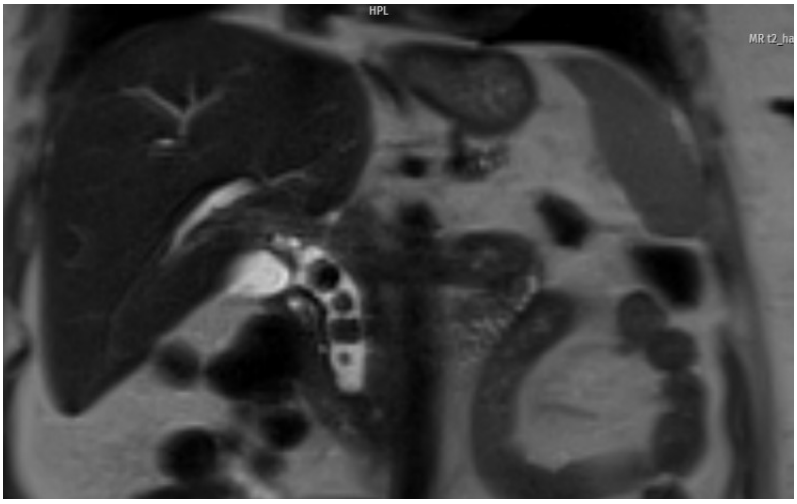


Figure 3. Coranal T2 weighted image shows multiple filling defects in dilated common bile duct.

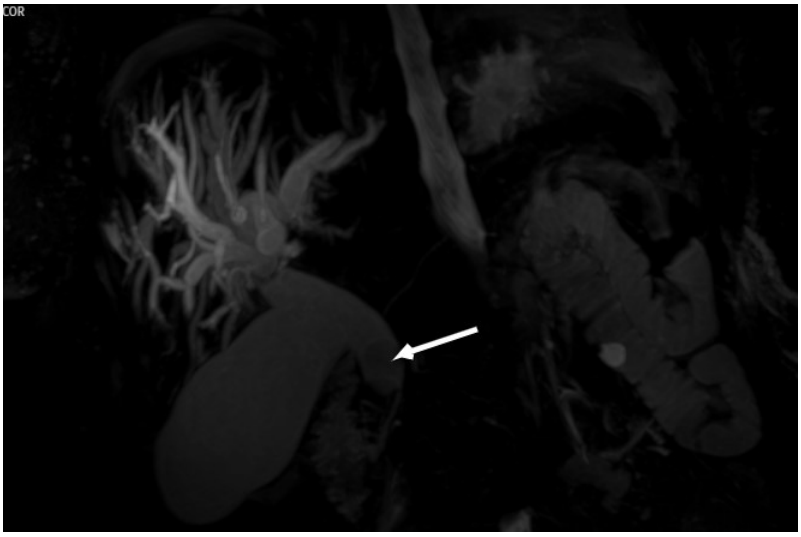


Figure 4. In MRCP, a filling defect is seen in dilated common bile duct (arrow) and intrahepatic and extrahepatic bile duct dilatation is visualised .

EUS is highly sensitive and specific in demonstrating bile duct dilatation and calculi. It has not been shown to be superior to diagnostic MRCP (15,16). Meeralam et al reported the sensitivity of EUS and MRCP as 97% and 90% and specificity as 87% and 92%. The higher sensitivity of EUS is because it is more successful in detecting small Stones (17). PTC is an invasive method that

is successful in showing biliary anatomy, the number and diameter of stones, and requires contrast material. The diagnostic sensitivity of ERCP is similar to MRCP, PTC and ERCP are not preferred as initial diagnostic methods (18).

Mirizzi syndrome, benign and malignant biliary tract strictures, and duck cysts should be considered in the differential diagnosis of choledocholithiasis (19).

3. Treatment

Supportive care includes improvement of fluid deficit and electrolyte imbalance, and broad-spectrum antibiotic therapy in case of cholangitis. Conservative treatment is successful in 85% of patients. Therefore, biliary drainage can be delayed for up to 48 hours. Earlier drainage is indicated in patients with clinical detoriation who do not respond to conservative treatment (20).

3.1. Endoscopic Treatment

The standard treatment for choledocholithiasis is removal of the choledochal stone by endoscopic sphincterotomy. ERCP is a minimally invasive treatment used for this purpose (Figure 5). Treatment techniques of ERCP include papillotomy, biliary sphincterotomy, pancreatic sphincterotomy, stone removal, lithotripsy, plastic and metal stent placement (21).

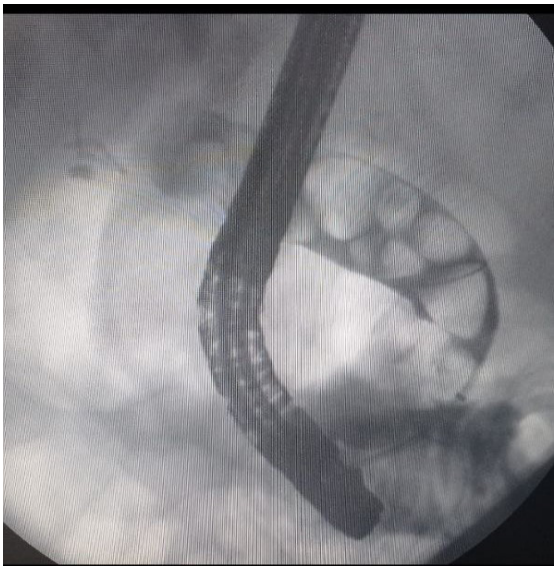


Figure 5. ERCP imaging shows multiple filling defects in dilated common bile duct.

The endoscopic treatment procedure of choledocholithiasis consists of bile duct drainage, stone localization by colongiography, biliary sphincterotomy. Balloon catheter and metal wire basket are frequently used additional instruments for stone removal, the standard approach is 90 percent successful in stone removal. Advanced techniques such as mechanical, electrohydraulic, laser lithotripsy and stent placement are required in 10 percent of cases (22). Stent and lithotripsy may be required, especially in patients with stones larger than 15 mm. The plastic stent is indicated for drainage of large stones that cannot be removed. Endoscopic balloon dilatation of the papilla may be preferred as an alternative to sphincterotomy in patients who use anticoagulants and have comorbidities such as cirrhosis. The risk of pancreatitis in the endoscopic balloon dilatation procedure is higher than in sphincterotomy (7.4%). In addition, this procedure requires more mechanical lithotripsy (23). If choledocholithiasis is accompanied by biliary pancreatitis, the treatment should be stone removal with ERCP after stabilization of the patient, if biliary pancreatitis is accompanied by cholangitis, early ERCP is recommended within the first 48 after stabilization of the patient (24). The advantage of urgent ERCP has not been demonstrated in the absence of obstructive jaundice. Urgent ERCP is not recommended in biliary pancreatitis without cholangitis. In the case of biliary pancreatitis in patients with cholecystectomy, sphincterotomy is the standard to prevent recurrent attacks. After biliary pancreatitis, 25% recurrent episodes can be observed within 6 weeks, therefore early cholecystectomy is recommended (20,24,25). Complications due to ERCP are pancreatitis (4%) hemorrhage (1%) cholangitis (1%) perforation (0.5%) (26)

If it is not possible to access the biliary system with the endoscopic method, radiographic Percutaneous transhepatic cholangiography (PTC) may be preferred for drainage (27). In cases where visualization of the papilla is difficult, such as Roux-en-y anastomosis or billroth 2 gastrectomy, papillary drainage can be performed with special endoscopies such as single balloon endoscopy, double balloon endoscopy, or PTC may be preferred (27,28).

References

1. Abboud PA, Malet PF, Berlin JA, et al. Predictors of common bile duct stones prior to cholecystectomy: a meta-analysis. Gastrointest Endosc. 1996 ; 44: 450-5.

2. Frossard JL, Morel PM. Detection and management of bile duct stones. Gastrointest Endosc. 2010; 72: 808-16.

3. Onken JE, Brazer SR, Eisen GM, et al. Predicting the presence of choledocholithiasis in patients with symptomatic cholelithiasis. Am J Gastroenterol. 1996; 91: 762-7.

4. Kimura Y, Takada T, Kawarada Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg. 2007; 14: 15-26.

5. Peng WK, Sheikh Z, Paterson-Brown S, Nixon SJ. Role of liver function tests in predicting common bile duct stones in acute calculous cholecystitis. Br J Surg. 2005; 92: 1241-7.

6. Cianci P, Restini E. Management of cholelithiasis with choledocholithiasis: Endoscopic and surgical approaches. World J Gastroenterol. 2021; 27: 4536-4554.

7. Costi R, Sarli L, Caruso G, et al. Preoperative ultrasonographic assessment of the number and size of gallbladder stones: is it a useful predictor of asymptomatic choledochal lithiasis? J Ultrasound Med. 2002; 21: 971–976.

8. Stott MA, Farrands PA, Guyer PB, Dewbury KC, Browning JJ, Sutton R. Ultrasound of the common bile duct in patients undergoing cholecystectomy. J Clin Ultrasound. 1991;19:73–76.

9 Einstein DM, Lapin SA, Ralls PW, Halls JM. The insensitivity of sonography in the detection of choledocholithiasis. AJR Am J Roentgenol. 1984;142:25–728.

10. Ko CW, Lee SP. Epidemiology and natural history of common bile duct stones and prediction of disease. Gastrointest Endosc. 2002;56:165-9.

11. Mitchell SE, Clark RA. A comparison of computed tomography and sonography in choledocholithiasis. AJR Am J Roentgenol. 1984;142:729–733.

12. Soto JA, Alvarez O, Múnera F, Velez SM, Valencia J, Ramírez N. Diagnosing bile duct stones: comparison of unenhanced helical CT, oral contrast-enhanced CT cholangiography, and MR cholangiography. AJR Am J Roentgenol. 2000;175:1127–1134.

13. Anderson SW, Rho E, Soto JA. Detection of biliary duct narrowing and choledocholithiasis: accuracy of portal venous phase multidetector CT. Radiology. 2008;247:418–427

14. Polistina FA, Frego M, Bisello M, Manzi E, Vardanega A, Perin B. Accuracy of magnetic resonance cholangiography compared to operative endoscopy in detecting biliary stones, a single center experience and review of literature. World J Radiol. 2015;7:70–78

15. Shanmugam V, Beattie GC, Yule SR, Reid W, Loudon MA. Is magnetic resonance cholangiopancreatography the new gold standard in biliary imaging? Br J Radiol. 2005;78:888-93.

16. Lammert F, Gurusamy K, Ko CW,et al. Gallstones. Nat Rev Dis Primers. 2016;2:16024.

17. Meeralam Y, Al-Shammari K, Yaghoobi M. Diagnostic accuracy of EUS compared with MRCP in detecting choledocholithiasis: a meta-analysis of diagnostic test accuracy in head-to-head studies. Gastrointest Endosc. 2017;86:986–93.

18. Scheiman JM, Carlos RC, Barnett JL, et al. Can endoscopic ultrasound or magnetic resonance cholangiopancreatography replace ERCP in patients with suspected biliary disease? A prospective trial and cost analysis. Am J Gastroenterol. 2001;96:2900-4.

19. Kulkarni SS, Hotta M, Sher L, et al. Complicated gallstone disease: diagnosis and management of Mirizzi syndrome. Surg Endosc. 2017;31:2215-22.

20. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. Gastroenterology. 2018;154:1096-1101.

21. Park CH, Jung JH, Nam E, et al. Comparative efficacy of various endoscopic techniques for the treatment of common bile duct stones: a network meta-analysis. Gastrointest Endosc. 2018;87:43-57.

22. Magalhães J, Rosa B, Cotter J. Endoscopic retrograde cholangiopancreatography for suspected choledocholithiasis: From guidelines to clinical practice. World J Gastrointest Endosc. 2015;7:128-34.

23. Teoh AYB, Cheung FKY, Hu B, et al. Randomized trial of endoscopic sphincterotomy with balloon dilation versus endoscopic sphincterotomy alone for removal of bile duct stones. Gastroenterology. 2013;144:341-345.

24. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13:1-15.

25. Aboulian A, Chan T, Yaghoubian A, et al. Early cholecystectomy safely decreases hospital stay in patients with mild gallstone pancreatitis: a randomized prospective study. Ann Surg. 2010;251:615-9.

26. Chandrasekhara V, Khashab MA, Muthusamy VR, et al. Adverse events associated with ERCP. Gastrointest Endosc. 2017;85:32-47.

27 Jeong EJ, Kang DH, Kim DU,et al. Percutaneous transhepatic choledochoscopic lithotomy as a rescue therapy for removal of bile duct stones in Billroth II gastrectomy patients who are difficult to perform ERCP. Eur J Gastroenterol Hepatol. 2009;21:1358-62.

28. Itoi T, Ishii K, Sofuni A, et al. Long- and short-type double- balloon enteroscopy-assisted therapeutic ERCP for intact papilla in patients with a Roux-en-Y anastomosis. Surg Endosc. 2011;25: 713-21.

CHAPTER VII

ACUTE MESENTERIC ISCHEMIA

Sinan Göçer

(MD.), Institution: Department of Cardiovascular Surgery,
Bahcesehir University, Istanbul, Turkey
E-mail: drsinangocer@gmail.com
ORCID: 0000-0002-7873-769X

1. Objectives

- *To describe the etiology and clinical presentation of acute mesenteric ischemia.*
- *Management of acute mesenteric ischemia in emergency situations.*
- *To discuss the current management and diagnostic options of acute colonic ischemia.*
- *To improve disease management via surgery and medication.*
- *Utilizing modern technologies.*

2. Introduction

Ischemic intestinal events continue to be the leading cause of death in the aging population. Acute mesenteric ischemia is a significant problem for emergency medical services. This chapter highlights the therapeutic developments in the treatment of acute mesenteric ischemia while it also covers some of the areas that are still open for debate.

Any interruption of blood flow in the mesenteric arteries causes acute mesenteric ischemia (AMI). Small and large intestines are intensely vulnerable to sepsis and may progress to mortality unless effective treatments are initiated. Since symptoms are non-specific, the diagnosis of acute mesenteric ischemia may be quite challenging and fatal outcomes are frequently observed if not treated in the early window of opportunity. The total incidence is of AMI is between 0.09% and 0.2% of all acute patients admitted to emergency service. On the contrary the mortality of AMI rate exceeds 60% (1, 2).

The evolution of interventional procedures on endovascular surgery has made this method a significant option for patients who have ischemia of the superior mesenteric artery (SMA). In previous literature it was reported that endovascular therapy had lower mortality and colon resection rates compared to conventional surgery methods (3, 4).

The diagnosis of acute mesenteric ischemia should be performed by a multi-disciplinary team. Additionally, the damage of interrupted circulation should be minimized as soon as possible. Individuals with colon resection usually have better outcomes and medical care can both improve survival, long-term outcomes, and quality of life (5, 6). According to some investigators, the aggressive "endovascular first" method has reduced overall AMI mortality by about 40% in absolute terms (7).

Within the last two decades, utilization of warfarin, lipid-lowering drugs, and antithrombotic medications has substantially increased in the treatment of atrial fibrillation and atheromatous diseases. Additionally, elevated use of interventional stenting has also been considered as an alternative for the treatment of acute vascular ischemia (8, 9).

3. Mechanism of Acute Mesenteric Ischemia

3.1. Etiology

All acute occlusive or non-occlusive mesenteric ischemia cases typically have one or more of the following underlying causes: myocardial infarction, atrial fibrillation, congestive heart failure, hyperlipidaemia atherosclerosis, smoking, diabetes, hypertension, aortic aneurysm, aortic dissection, vasopressors, chronic heart failure, kidney failure, sepsis, cardiac or abdominal surgery, vasculitis, dehydration and aging (10, 11). The etiology of AMI has altered due to up to high percentages of acute arterial thrombosis caused by plaques, which may be adequately characterized by contemporary anticoagulant medications used to treat atrial fibrillation.

The underlying pathologies of acute mesenteric ischemia could be elaborated as vascular thrombosis in 40 – 50% of cases, acute arterial thrombosis in 25 – 30% of cases, and non-occlusive mesenteric ischemia accounts for 20% of cases. AMI has been observed more common in females, elderly, and individuals with severe comorbidities.

The most frequent reason of AMI is acute obstruction of left mesenteric artery in 50% of the cases. Atrial fibrillation (in the left atrium), ventricle dysfunction accompanied by low ejection fraction, or the cardiac valve

endocarditis could be the source of mesenteric embolism. Hypertension may accelerate atherosclerosis in a certain period thus, producing embolism. Aforementioned, cardiac problems such as arrhythmias, myocardial infarction, cardiomyopathy, or mitral/aortic valvular diseases and mural thrombo-embolism have also the potential to embolize mesenteric arteries.

3.2. Epidemiology

Left mesenteric artery is directly exposed to anterior aorta wall just making it susceptible to embolism. Most of the cases are observed in the 3 – 10 cm proximal region, preventing small intestinal and colorectal ischemia. In a similar manner, left mesenteric artery emboli may disseminate to other arterial lumens, such as the kidney and spleen. Due to the large luminal structure of left mesenteric artery, blood clot may readily pass through it and depending on the size of the thrombosis, various circulatory structures could be partially or completely affected resulting in bowel infarction, congestion, necrosis, and perforation (12).

In previous literature it was reported that intestines can be endurable to ischemia up to 12 hours without causing any serious damage (13). Individuals' mean age in a retrospective study was 68.43 years in investigations that have been documented (14).

In a recent prospective study; ventricular dysfunction, lactate levels, and intestinal loop dilatation on computerized tomography were found to be three predictors of persistent transmural intestinal necrosis in AMI. Regarding the results of this research, the rate of irreversible colon necrosis had increased from 3 – 38% to 89 – 100% of (15).

3.3. Pathophysiology

During ischemia gastrointestinal mucosal membranes are the first to be affected by metabolic reactions compared to serosa. Congestion, swelling, and haemorrhage occur in the affected bowel surface. Arteriolar vascular relaxation, protection of splanchnic tissue perfusion, and a biochemical response to adenosine and other mucosal infarct compounds are the suggested mechanisms. Additionally, under ischemic injury, the colon membrane can spare higher levels of oxygen to protect the mucosal structures during metabolic shock. Prolonged ischemia damages the intestinal epithelium as a result of reactive oxygen radicals and polymorphonuclear neutrophil activity. This may trigger intestinal haemorrhage within 1 to 4 days, lead to necrosis, perforation, systemic infection, or serious adverse events (16,17).

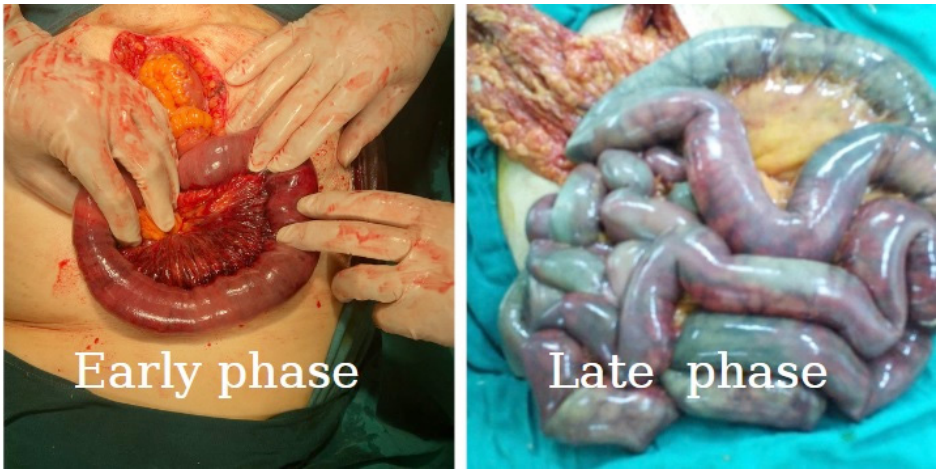


Figure 1: *Early and late injury in the colon after acute mesenteric ischemia*

4. Clinical presentation

Although AMI may manifest itself with acute intestinal ischemia and infarction of colon, patients often come with postprandial pain and anxiety. Considering the variety of intestinal symptoms such as weight loss, abdominal pain and substantial mesenteric arterial ischemic diseases, the diagnosis may be delayed. However, it is necessary to correlate the clinical symptoms with these two conditions. The objectives of treatment include relieving the acute symptoms, limiting the occurrence of acute mesenteric ischemia, and ameliorating general condition of life (18).

It is crucial to evaluate the risk of cardiovascular events in suspicion of embolism/thrombosis origins in patients with acute gastrointestinal symptoms. Abdominal pain, vomiting, rapid satiety, diarrhea, post-prandial pain, nausea, constipation, and weight loss are just a few of the symptoms that patients may experience. Intra-abdominal procedures, biliary disease, gastric ulcer, pancreatitis, ulcerative colitis, gastroesophageal leakage, and digestive problems, can also cause postprandial pain. A comprehensive examination and patient history might be helpful in the diagnosis. Recurrent nausea and vomiting also occur in severe cases of food intolerance, dietary phobia leading to weight loss.

5. Laboratory Paramete

The analysis of electrolytes, fluid, and acid-base balance and infectious parameters should be processed in possible acute intestinal infarction cases. Patients and especially the elderly emerge with acidosis, especially as a result of dehydration and limited nutritional intake. Lactic acidosis is a sign of severe ischemia or permanently damaged colon.

In order to prevent complete necrosis, surgical intervention should be conducted before acute visceral infarction. Albumin, transferrin, C-reactive protein and transthyretin should be obtained in cases of prolonged intestinal infarction.

6. Diagnostic Imagi

Duplex ultrasound imaging has a high degree of consistency and accuracy in the diagnostic of intestinal arterial ischemia, with a sensitivity and specificity of 85 – 90% (19). It should not be forgotten that although it has favourable aspects and is cost-effective, duplex ultrasonography may fail to visualize distal visceral abdominal branches.

Computerized tomographic angiography (CTA) has a 95–100% accuracy rate, and is now the first choice radiological technique for the identification of abdominal vascular syndromes (20). Contrast enhancement records the early arterial phase of a CT scan, which lasts for nearly 30 seconds. The mesenteric arterial vascular anatomy and any collaterals are denoted in the arterial phase. Specific findings, such as: oval-shaped embolism, left mesenteric arterial thrombosis, mesenteric edema, intestine pneumatosis, and mesenteric venous gas, may be utilized to diagnose AMI via CTA. Additionally, it provides information on the perfusion of other abdominal organs.

7. Manageme

All individuals who have a suspicion of AMI should be hospitalized in the intensive care unit. The primary goal of treating AMI is to improve their hemodynamic condition. Considering that these individuals have substantial volume gap, they should receive fluid replacement using crystalloids and

blood products. Especially, acid-base balance should be achieved as soon as possible in elderly patients as hyperkalaemia and metabolic acidosis are common. The risk of sepsis increases as the acidosis progresses and leads to severe decline in systemic inflammatory response syndrome. Another side effect of acidosis, deteriorating cardiac hemodynamic parameters. In individuals with ischemia, vasopressors should be avoided as they aggravate mesenteric obstruction.

Patients with acute mesenteric ischemia should be administered broad-spectrum antibacterial drugs for anaerobic protection in order to prevent significant colonic bacterial translocation. Even if there is no clinical sign of severe infection such as sepsis, antibiotics should be initiated. Additionally, a nasogastric tube should be placed to achieve continuous drainage.

Intravenous unfractionated heparin infusion should can be initiated if systemic anticoagulation is not contraindicated. Heparin is the preferred medication due to its short half-life, ease of APTT monitoring, and accessible antidote regimen.

8. Invasive Treatment

8.1. Endovascular interventions

The upside of endovascular treatment could be elaborated as reduced rate of morbidity. Unless peritonitis and colonic perforation are obvious, open surgery should only be performed as a last option. Every measure must be taken to establish mesenteric arterial revascularization if endovascular surgery is available in the institution. In a previous study, while mortality was reduced in the endovascular group by 23 – 26% it was published as 36 – 56% in the open surgery group (21).

The preferred option for endovascular interventions is selective thrombectomy with the use of thrombolytic medication. If an underlying stenosis is confirmed, stenting may be attempted. Depending on the localisation of stenosis, either self-expandable stents or balloon-expandable stents are preferred.

8.2. Open surgery

Open surgery should be recommended if there are signs of peritonitis, intestinal perforation, or if vascular intervention has failed. The laparotomy facilitates the return of circulation to the intact colon while enabling direct visualization of the ischemic area and the removal of non-viable tissue. The clinicians sometimes prefer to create a stoma from the healthy intestine and let the distal end recover. Individuals that are eligible for intestinal transplantation should be considered unless the patient will not suffer from short bowel syndrome in the post-operative period. Some individuals with extensive intestinal injury may be considered inoperable, and palliative care is applied (21, 22, 23).

Patients may develop acute respiratory distress syndrome (ARDS), sepsis and multiorgan failure following open surgery. To achieve the best possible hemodynamics, they should be recovered in the intensive care unit with high-quality hemodynamic monitoring, intensive fluid replacement, and sympathomimetic medication.

Despite benefits of surgical or vascular intervention, 30-day survival is relatively poor and significant mortality is observed due to aging, delayed diagnosis, lactic acidosis, disseminated small intestinal insufficiency, and arterial embolism (24).

References

1. Yıldırım MA, Kocabaş R, Kılınç İ, Şimşek G, Şentürk M, Çakır M, Belviranlı M. Role of thiol-disulfide hemostasis in early diagnosis of acute mesentery ischemia: An experimental Ulus Travma Acil Cerrahi Derg.2022 Apr;28(4):403-410.

2. Bala M, Catena F, Kashuk J, De Simone B, Gomes CA, Weber D, vd. Acute mesenteric ischemia: updated guidelines of the World Society of Emergency Surgery. World J Emerg Surg.2022;17(1):54.

3. Acosta-Mérida MA, Marchena-Gómez J, Saavedra-Santana P, Silvestre-Rodríguez J, Artiles-Armas M, Callejón-Cara MM. Surgical Outcomes in Acute Mesenteric Ischemia: Has Anything Changed Over the Years? World J Surg.2020;44(1):100-7.

4. Arthurs ZM, Titus J, Bannazadeh M, Eagleton MJ, Srivastava S, Sarac TP, vd. A comparison of endovascular revascularization with traditional therapy for the treatment of acute mesenteric ischemia. J Vasc Surg.2011;53(3):698-704.

5. Mizushima T, Udagawa E, Hasegawa M, Tazuke Y, Okuyama H, Fernandez J, vd. Etiologies and treatments of chronic intestinal failure-short bowel syndrome (SBS) in Japanese adults: a real-world observational study. Surg Today.2022;52(9):1350-7.

6. Harpain F, Schlager L, Hütterer E, Dawoud C, Kirchnawy S, Stift J, vd. Teduglutide in short bowel syndrome patients: A way back to normal life? JPEN J Parenter Enteral Nutr.2022;46(2):300-9.

7. Sungho Lim, Pegge M Halandras, Carlos Bechara, Bernadette Aulivola, Paul Crisostomo. Contemporary Management of Acute Mesenteric Ischemia in the Endovascular Era. Vasc Endovascular Surg.2019 ;53(1):42-50.

8. Zettervall SL, Lo RC, Soden PA, Deery SE, Ultee KH, Pinto DS, vd. Trends in Treatment and Mortality for Mesenteric Ischemia in the United States from 2000–2012. Ann Vasc Surg.2017; 42:111-9.

9. Schwinger RHG. Cardiovascular Medication in Elderly Patients. Dtsch Med Wochenschr.2018 Feb;143(4):236-243.

10. Somarajan S, Muszynski ND, Olson JD, Bradshaw LA, Richards WO. Magnetoenterography for the Detection of Partial Mesenteric Ischemia. J Surg Res.2019;239:31-7.

11. Expert Panels on Vascular Imaging and Gastrointestinal Imaging, Ginsburg M, Obara P, Lambert DL, Hanley M, Steigner ML, vd. ACR Appropriateness Criteria® Imaging of Mesenteric Ischemia. J Am Coll Radiol.2018;15(11S):S332-40.

12. Liao G, Chen S, Cao H, Wang W, Gao Q. Review: Acute superior mesenteric artery embolism: A vascular emergency cannot be ignored by physicians. Medicine (Baltimore).2019;98(6):e14446.

13. Ha C, Magowan S, Accortt NA, Chen J, Stone CD. Risk of arterial thrombotic events in inflammatory bowel disease. Am J Gastroenterol.2009;104(6):1445-51.

14. Tanrıkulu Y, Şen Tanrıkulu C, Sabuncuoğlu MZ, Temiz A, Köktürk F, Yalçın B. Diagnostic utility of the neutrophil-lymphocyte ratio in patients with acute mesenteric ischemia: A retrospective cohort study. Ulus Travma Acil Cerrahi Derg.2016;22(4):344-9.

15. Nuzzo A, Maggiori L, Ronot M, Becq A, Plessier A, Gault N, vd. Predictive Factors of Intestinal Necrosis in Acute Mesenteric Ischemia: Prospective Study from an Intestinal Stroke Center. Am J Gastroenterol.2017;112(4):597-605.

16. van den Heijkant TC, Aerts BAC, Teijink JA, Buurman WA, Luyer MDP. Challenges in diagnosing mesenteric ischemia. World J Gastroenterol.2013;19(9):1338-41.

17. Acosta S. Surgical management of peritonitis secondary to acute superior mesenteric artery occlusion. World J Gastroenterol.2014;20(29):9936-41.

18. Huber TS, Björck M, Chandra A, Clouse WD, Dalsing MC, Oderich GS, vd. Chronic mesenteric ischemia: Clinical practice guidelines from the Society for Vascular Surgery. J Vasc. Surg.2021;73(1S):87S-115S.

19. AbuRahma AF, Stone PA, Srivastava M, Dean LS, Keiffer T, Hass SM, vd. Mesenteric/celiac duplex ultrasound interpretation criteria revisited. J Vasc Surg.2012;55(2):428-436.

20. Coulier B. Multidetector Computed Tomographic Angiography for Optimal Cartography of the Visceral Abdominal Arterial Network: An Extensive Pictorial Review with Emphasis on Common and Uncommon Collateral Pathways, Complications and some Specific Syndromes. J Belg Soc Radiol. 2017;101(1):6.

21. Gupta S, Tomar DS. Ischemic Gut in Critically Ill (Mesenteric Ischemia and Nonocclusive Mesenteric Ischemia). Indian J Crit Care Med.2020;24(Suppl 4):S157-61.

22. Lauro A, Lacaille F. Short bowel syndrome in children and adults: from rehabilitation to transplantation. Expert Rev Gastroenterol Hepatol.2019;13(1):55-70.

23. Roussel A, Castier Y, Nuzzo A, Pellenc Q, Sibert A, Panis Y, vd. Revascularization of acute mesenteric ischemia after creation of a dedicated multidisciplinary center. J Vasc Surg.2015;62(5):1251-6.

24. Atkins MD, Kwolek CJ, LaMuraglia GM, Brewster DC, Chung TK, Cambria RP. Surgical revascularization versus endovascular therapy for chronic mesenteric ischemia: a comparative experience. J Vasc Surg.2007;45(6):1162-71.

CHAPTER VIII

UROLOGICAL APPROACH TO HEMATURIA

İrfan Şafak Barlas

(MD.), Ankara Acıbadem Hospital, Urology Department
isbarlas89@gmail.com
ORCID: 0000-0001-7894-9118

Hematuria is the presence of red blood cells in the urine. Hematuria could be a symptom of a disease affecting any part of the genitourinary system or a non-urological systemic disease, but it may also occur in the absence of pathology. Excessive exercise, vaginal bleeding, systemic infections, acute appendicitis, acute diverticulitis, decompensated heart and respiratory system diseases, vaccinations, and serum administrations can cause or be confused with hematuria in the absence of urinary tract pathology. Therefore, patients with hematuria must be thoroughly examined. Hematuria is more prevalent than expected, especially among men. There are studies demostrating that random tests detect between 2,5-5,4% hematuria in men. In some instances, hematuria is a pathology that causes severe blood loss, but it is usually an indicator of a pathology. Until proven otherwise, patients with hematuria should be assumed to have a malignant disease. Some of the studies report that neoplasia is the major cause of hematuria and the most prevalent benign disease is benign prostatic hypertrophy. Infection was the second most common diagnosis after neoplasia, followed by nephrolithiasis. (1,2).

The patient may recognize haematuria, often known as visible or macroscopic haematuria. Red urine is observed in patients with macroscopic hematuria (1,2). Otherwise, it may be discovered only upon analysis of urine, most often as a positive urinalysis test for blood (chemical dipstick) or as more than three red cells per high-power field on microscopy or in a Coulter counter (3,4). Urological pathology can not be detected in all cases of hematuria, but hematuria should be investigated under the presumption that it is malignancy until proven otherwise. The elderly and men with hematuria are more likely to have a malignancy. Although those with microscopic hematuria are less likely

to have urological pathology than those with macroscopic hematuria, this does not necessarily mean that those with microscopic hematuria have less severe urological pathology (5).

That whenever a patient presents with the complaint of hematuria, a thorough anamnesis should be conducted. Urine samples for the patient's urine analysis and culture, and also kidney function tests in blood serum, should then be examined. Ultrasound imaging of the urinary system is necessary. If the patient with hematuria is being monitored because of advanced age, male gender, smoking, a history of pelvic radiotherapy and exposure to chemicals that increase the risk of bladder cancer such as cyclophosphamide, or a urological disease, cystoscopic examination should be performed (5-7).

1. APPROACH TO THE PATIENT WITH HEMATURIA

1.1. Anamnesis

The most important and first step in treating a patient with hematuria is to obtain an anamnesis in order to plan the treatment by identifying the cause. At this step, it is important to determine whether the hematuria is microscopic or macroscopic, at what stage of the urine it is observed, if it is accompanied by dysuria, and if there is a clot in the urine. The presence of hematuria only at the beginning of the urine and the absence of hematuria in the latter part of the urine are indicative of urethral pathologies; the presence of hematuria only at the terminal of the urine is indicative of bladder neck and prostate pathologies. Most cases of widespread hematuria in the urine are caused by problems with the bladder and upper urinary tract. Many drugs may induce either hematuria or coloration of the urine; consequently, a full history of the patient's prescription and consumed medications is very beneficial. Analgesic nephropathy, which may be linked with hematuria and papillary necrosis, may be related to heavy or hidden use of analgesics. The use of oral contraceptives has been linked to the syndrome of loin pain hematuria. As with cyclophosphamide-treated individuals, smokers have a greater risk of developing bladder cancer. Inquire about a family history of hematuria, sickle cell disease, polycystic kidney disease, or other renal illnesses, as well as travel to malaria or schistosomiasis endemic regions. Hematuria accompanied by dysuria suggests that it is primarily caused by an inflammatory condition; malignant hematuria is typically not accompanied by pain. But sometimes, hematuria may be accompanied by pain for a variety of reasons, even in

malignant cases. Malignancy may also be accompanied by non-malignant urinary tract pathologies, such as infection, urolithiasis, etc. It is critical to determine whether a woman with hematuria is menstruating at the time of examination so that extra precautions can be taken to obtain an uncontaminated urine specimen for testing. Also in hematuria caused by upper urinary tract pathologies, renal colic can be observed regardless of the underlying cause. Clots typically occur in the bladder or prostate and are highly suspicious of being malignancy. However, worm-shaped vermiform clots can be observed in diseases of the upper urinary tract. Additionally, weight loss should be questioned.Weight loss, extrarenal signs (rash), arthritis, arthralgia, and pulmonary symptoms are indicative of a number of systemic diseases, such as vasculitic syndromes, malignancy, tuberculosis and recent pharyngitis or skin infection are indicative of poststreptococcal glomerulonephritis. (1,5,8,9).

1.2. Physical Examination

Renal disease may arise with hypertension, particularly if it is recent. Petechiae, arthritis, multiplex mononeuritis, and rash may be signs of coagulopathy, an immunologic illness, or vasculitis. If Alport syndrome is suspected, a hearing evaluation is required. The prostate and urethral meatus are examined as part of a comprehensive examination (1).

1.3. Laboratory Analysis

1.3.1. Urinalysis

The first stage in the laboratory evaluation is a urine examination with a dipstick test. Whether the dipstick test is positive for heme, the next step is to assess if urine protein excretion is elevated and if red blood cells, white blood cells, casts, or crystals are seen on microscopic inspection of the urine. Urine analysis is crucial, especially in patients with microhematuria. In individuals with more prominent pyuria than hematuria, infectious or inflammatory diseases should be examined more often. In addition, the presence of isomorphic erythrocytes, mainly in individuals with microscopic hematuria, implies urological pathology; but dysmorphic erythrocytes imply mainly glomerular disorders. Since microscopic hematuria of glomerular origin may be present, it is crucial to examine the urine sediment, especially in individuals at low risk for malignancy. In addition, red urine can be observed in the absence of blood cells; this phenomenon is known as pseudohematuria. Due to the fact

that certain antibiotics and anti-inflammatory drugs; also the presence of red pigments such as bilirubin, myoglobin, and hemoglobin in the urine; and the presence of coloring chemicals in some foods could even cause the urine to appear red without blood cells, urine analysis should be performed on patients with red urine to determine the presence of true hematuria. (1,5,10).

1.3.2. Blood and Serum Analysis

If a patient has a positive dipstick test, erythrocytes in the sediment, and no protein in the urine, the next step is to test for a bleeding disorder by analyzing a platelet count, prothrombin time, and partial thromboplastin time, as well as, if the patient is black, a sickle cell trait test and also blood serum values suggesting kidney function should be analyzed because they may help in the evaluation of patients with pathologies of the upper urinary tract. (1).

1.3.3. Urine Cytology

Cystoscopy may be delayed in low-risk individuals, such as those under 40 years old with no risk factors for bladder cancer. However, these patients should have a voiding urine cytology test performed. Urine cytology is a cost-effective test that is advised in situations where cystoscopy is not needed. Patients at high risk for uroepithelial malignancies, such as smokers, those who overuse analgesics, those over the age of 40, those exposed to chemicals or dyes, and those with irritative voiding symptoms, may benefit most from urine cytology (1).

1.4. Imagining Methods

1.4.1. Ultrasound Imaging

Although ultrasound is insufficient for visualizing the upper urinary tract, it is considered the first imaging modality for the diagnosis of hematuria because upper urinary tract cancer is a low percentage of kidney cancers and ultrasound has a very high sensitivity for detecting bladder cancer and renal cell cancer. Ultrasound imaging has the advantages of being inexpensive, simple, and noninvasive. In cases where ultrasound alone is insufficient to diagnose hematuria, conventional urography imaging with intravenous contrast, computed tomography, and magnetic resonance imaging can also be performed. Also in instances when ultrasound imaging and cystoscopy reveal no pathology but

hematuria persists and abnormal cells are found at urine cytology, conventional urography imaging with intravenous contrast should be preferred (11).

1.4.2. Intravenous Pyelography

This imaging technique was the most commonly used to examine the urinary tract before the widespread usage of ultrasonography and the accumulation of expertise, because it produces detailed images of the collecting structures, is inexpensive, and is standardized. However, it is insensitive to masses smaller than 3 centimeters in diameter and has limited use in evaluating the bladder and urethra. Also, contrast material is needed, which increases the risk of nephrotoxicity in people who don't have enough kidney function (1).

1.4.3.Computed Tomography

Small renal parenchymal masses, urolithiasis, and renal infectious lesions are most effectively detected by computed tomography (CT). It is cheaper than magnetic resonance imaging (MRI) and detects small parenchymal masses as well. Nevertheless, it is more expensive than ultrasonography or intravenous pyelography. CT's lack of sensitivity in identifying uroepithelial cancers is its weakness. CT urography, which is the combination of CT and radiography after contrast-enhanced CT, increases detection rates. The combination of ultrasonography and retrograde pyelography should be examined in patients who can't undergo CT urography because of underlying renal failure, contrast allergy, or both (1).

1.5. Cystoscopy

Bladder cancer is the most important factor that should not be overlooked in hematuria. Moreover, the possibility of bladder cancer cannot be ruled out without a cystoscopy. In cases of hematuria originating from the urethra, prostatic urethra, bladder, and upper urinary tract, the cause of hematuria can be determined by observing the flow of hematuric urine from the ureteral orifices using cystoscopy. Therefore, cystoscopy is a crucial step in determining the cause of hematuria, especially in patients with a high risk of bladder cancer. However, its sensitivity in diagnosing hematuria from the upper urinary tract is low. On cystoscopy, the absence of hematuric urine coming from the ureteral orifice does not rule out the presence of hematuria sourced from the upper

urinary tract. Therefore, a cystoscopy alone is insufficient to rule out hematuria originating from the upper urinary tract (5).

1.6. Angiography

If the previous tests come back negative and the hematuria continues, angiography can be used to look for a minor arteriovenous malformation. (1).

2. CONTROL OF MASSIVE HEMATURIA

Massive hematuria may be described as either acute or chronic widespread venous hemorrhage. The most common cause of massive bladder bleeding in the absence of trauma is hemorrhagic cystitis. There are infectious and non-infectious causes of hemorrhagic cystitis. The target of treatment for infectious hemorrhagic cystitis is the underlying infectious agent. Hemorrhagic cystit may manifest with significant irritative voiding symptoms, such as urine retention, suprapubic discomfort, and hemodynamic impact (12,13).

Radiotherapy of the prostate, bladder, and pelvic organs may result in hemorrhagic cystitis. Radiation causes submucosal hemorrhage and mucosal edema initially, followed by obstructive endarteritis and ischemia. Steroid, vitamin E, and trypsin administration were ineffective in the treatment of radiotherapy-induced hemorrhagic cystitis; however, hyperbaric oxygen therapy and coating the bladder mucosa with synthetic agents such as pentosan polysulfate sodium were beneficial (12).

One of the leading causes of hemorrhagic cystitis is chemotherapy medications. Patients who take thiotepa and alkalized drugs such as busulfan, cyclophosphamide, and ifosfamide frequently causes hemorrhagic cystitis. Especially, the hepatic metabolite of cyclophosphamide, acrolein, directly affects the bladder mucosa and causes bleeding. These chemicals can cause possibly fatal hemorrhagic cystitis. Hemorrhagic cystitis is more prevalent in people receiving high doses, dehydrated patients and intravenous administration of chemotherapy. It causes changes in the bladder simillar with the secondary to radiation, such as edema, ulceration, neovascularization, necrosis, and hemorrhage. Prophylactically, it is advised to consume large amounts of fluids and preventative agents like N-acetyl cysteine and 2 mercapto-ethane sulfate (mesna). However, caution should be used while utilizing N-acetyl cysteine, since it may diminish the anti-neoplastic activity of cyclophosphamide and increase busulfone-induced bleeding (12).

Chemical poisons, unique and immune-mediated medication responses are capable of causing hemorrhagic cystitis. In the majority of cases, conservative measures, such as avoiding the substance that causes bleeding, consuming enough fluids, and irrigating the bladder, significantly reduce the bleeding (12).

In most instances, endoscopic resection of the tumor and fulguration can control bladder bleeding caused by urothelial malignancy. Patients with a metastatic or unresectable bladder tumor and severe bleeding are candidates for radiotherapy as palliative therapy. In certain instances where bleeding cannot be controlled, cystectomy, urinary diversion, or percutaneous nephrostomy could be used to stop the bleeding (12).

In addition to malignancies other possible causes of bladder bleeding include atypical manifestations of underlying disease, and idiopathic etiologies. Also occasionally, renal transplant recipients and people with weakened immune systems have been reported with acute hemorrhagic cystitis caused by viral infections. Hemorrhagic cystitis may be difficult to diagnose, and its different forms can create challenging therapeutic challenges. Severe instances usually need several blood transfusions for anemia caused by urinary blood loss, in addition repeated cystoscopies to remove blood clots and treat urine retention. The condition is accompanied with substantial morbidity and might sometimes demand invasive surgery (12).

Mild hematuria is treatable with a large amount of fluid intake. Clots in the bladder should be irrigated by placing a urethral catheter and, if necessary, intravesical irrigation fluid should be supplied for continuous bladder washing in instances with more resistant bleeding. Several approaches have been proposed for the control of bleeding in massive hematuria, such as light fulguration, systemic management of aminocaproic acid and intravesical instillation of cold water, potassium and ammonium aluminum sulfate cause vasoconstriction of superficial vessels in the mucosa but patients with kidney failure should pay particular attention to their aluminum levels. In addition, elevated aluminum levels can cause encephalopathy and severe acidosis in individuals. Also prostaglandins (PGE_2, $PGF_{2\alpha}$) and their analogues (karboprost) administered intravesically or intravenously. Prostaglandins can be utilized as a prophylactic or therapeutic agent due to their anti-inflammatory and anti-hemorrhagic effects.Under general anesthesia, intravesical phenol and formalin can be administered to patients who do not respond to all of these treatments. Patients with vesicoureteral reflux (VUR) would develop ureteral and renal fibrosis if phenol and formalin were applied; VUR must be ruled out before this treatment

is administered to patients. Furthermore, petroleum jelly should be applied to the external genitalia to prevent skin damage. Additionally, intravesical administration of silver nitrate solution, infusion of systemic vasopressin, external compression devices, hydrostatic tamponade, cryosurgery, vascular embolization, and surgical intervention are other techniques for the local control of bleeding. Also, it has been proposed that conjugated estrogen medication may have an impact on the capillary wall, resulting in reduced vascular fragility, based on the appearance of the bladder mucosa between the first period and remission following treatment. Generally, non-aggressive local approaches are recommended but they are often ineffective, whereas more aggressive therapies are linked with severe morbidity and death. (12,13).

REFERENCES

1-Mazhari R, Kimmel PL. Hematuria: an algorithmic approach to finding the cause. Cleve Clin J Med. 2002 Nov;69(11):870, 872-4.

2-Rodgers M, Nixon J, Hempel S, et al. Diagnostic tests and algorithms used in the investigation of haematuria: systematic reviews and economic evaluation. Health Technol Assess. 2006;10(18):iii-259.

3-Barocas DA, Boorjian SA, Alvarez RD, et al. Microhematuria: AUA/SUFU Guideline. J Urol. 2020;204(4):778-786.

4-Kelly JD, Fawcett DP, Goldberg LC. Assessment and management of non-visible haematuria in primary care. BMJ. 2009;338:a3021. Published 2009 Jan 16.

5-Boorjian SA, Raman JD, Barocas DA. Evaluation and management of hematuria. Campbell-Walsh Urology. 11th ed. Philadelphia, PA: Elsevier. 2016;183-194.

6-van der Molen AJ, Hovius MC. Hematuria: a problem-based imaging algorithm illustrating the recent Dutch guidelines on hematuria. American Journal of Roentgenology. 2012;198(6):1256-1265.

7-Grosfeld, GD, Litwin MS, Wolf JS. Evaluation of asymptomatic microscopic hematuria in adults: the American Urological Association best practice policy-part I: definition, detection, prevalence and etiology. Urology 57. 2001;599-603.

8-Brendler CB, Gerber GS. Evaluation of the urologic patient: history, physical examination and urinalysis. Campbell MF, Walsh PC. Campbell's Urology. 7th ed. Philadelphia: Saunders 1998;144-56.

9-Mariani AJ, Mariani MC, Macchioni C, et al. The significance of adult hematuria: 1,000 hematuria evaluations including a risk-benefit and cost-effectiveness analysis. The Journal of urology. 1989;141(2):350-355.

10-Sayer J, McCarthy MP, and Schmidt JD. Identification and significance of dysmorphic versus isomorphic hematuria. The Journal of urology. 1990;143(3):545-548.

11-Cochlin DL, Dubbins PA, Alexander AA. Urogenital ultrasound: a text atlas. CRC Press; 1994.

12-Pohar KS, Bahnson RR. Vesical trauma and hemorrhage. Glenn's urologic surgery, Seventh Edition. Editor: Graham SD, Keane TE & Glenn JF. Lippincott Williams & Wilkins, Philadelphia, USA; 2010:143-149.

13-Luna JR, Teruel JL, Vallejo J, et al. Control of massive hematuria in idiopathic hemorrhagic cystitis after administration of conjugated estrogen. The Journal of urology. 1992;148(5):1524-1525.

CHAPTER IX

INTRA-ABDOMINAL HYPERTENSION AND ABDOMINAL COMPARTMENT SYNDROME: EVALUATION AND MANAGEMENT

Selman Karadayi[1] & Onur Küçük[2]

[1]Kırklareli Education and Research Hospital, Kırklareli, Turkey

ORCID: 0000-0001-9321-075X,

[2]Ankara Atatürk Sanatory Education and Research Hospital, Ankara, Turkey

ORCID: 0000-0001-5534-7579

Introduction

Intra-abdominal pressure (IAP) is defined as the pressure measured within the abdominal cavity. Although the abdomen is a closed cavity, the intra-abdominal pressure is determined with the aid of using abdominal contents such as gas, liquid, fat, organs and the compliance of the abdominal wall (1). Intra-abdominal hypertension (IAH) is a process that continues with a progressive boost in IAP and can not be recompensed by abdominal compliance. Abdominal compartment syndrome (ACS) is the most hazardous shape of IAH and is basically the condition of adding organ failure to the increase in IAP. If IAH is not intervened in time, it causes physiological consequences in many organs and systems and evolves into ACS and this situation is associated with high mortality (2).

After Richard Volkmann described compartment syndrome in the extremity in 1811; In 1863, Etienne-Jules Marey reported a link between the respiratory system and IAP (3). Then, in the 20th century, studies on organ damage due to IAP were carried out on animal models. Studies on gastrointestinal, cardiac, pulmonary complications and abdominal decompression followed these (3).

IAP, which was previously measured intrauterine and rectal with a manometer, gained a practical use in 1875 when Odebrecht first measured it from inside the bladder (3,4). Sir Heneage Oglivie put forth abdominal decompression and open abdomen management for seriously wounded soldiers in World War II (5). In 1984, the subject started to gain interest again after Kron's case series report on high IAP after abdominal surgery (6). The World Society of the Abdominal Compartment Syndrome (WSACS) was established in 2004 and the issue was evaluated from a multidisciplinary perspective. Thus, information about IAP, IAH and ACS became clear (7, 8).

The definition of IAH is IAP ≥ 12 mmHg. ACS is the condition in which IAP is above 20 mmHg with new-onset organ failure (SOFA score >3) (9). In the critically ill, the normal IAP is 5-7 mmHg. When the IAP rises above 12 mmHg, pathological changes are observed in the patient. IAH is divided into four categories for clinical practice and research purposes (I: 12-15 mmHg, II: 16-20 mmHg, III: 21-25 mmHg, IV: >25 mmHg) (10). In Grade II and above it, respiratory, cardiovascular and renal organ failures develop (10).

IAH and ACS are divided into three groups as primary, secondary, and refractory based on their etiology and recurrence. Primary IAH/ACS is caused by damaging of the abdominopelvic region and there is usually a chance to be treated with interventional procedures such as drainage and decompression. Secondary IAH/ACS etiology is non-abdominopelvic causes including fluid overload, ventilator, burns, shock and sepsis (9).

Epidemiology

IAH and ACS, commonly observed in critically ill patients, are independent markers of mortality (11). The incidence of IAH increases in intensive care unit (ICU). This situation is related with being thought more as in the pre-diagnosis and recognition of the syndrome (5). The prevalence levels in critically ill patients are ACS 2-6%, IAH Grade III-IV 2-10%, IAH Grade II 10-20%, IAH Grade I 20-30%. ACS is the group which becomes the highest mortality with 75-90%. Mortality rates of IAH are Grade III-IV 50-60%, Grade II 15-45%, Grade I 10-25% (5). While 90-day mortality in intensive care patients is 7.1% in patients with normal IAP, it is 15.2% in IAH and 38.9% in ACS (12).

IAH and ACS are associated with prolonged ICU stay, organ, kidney, and respiratory failure (13). It prolongs the duration of mechanical ventilation and kidney replacement therapy (12). IAH is one of the mechanisms that cause

acute kidney injury in critically ill patients and increases the risk of acute kidney injury by 2.6 times (14, 15). In kidney transplant patients, high IAP is associated with a high resistance index and low urine output. The average IAP in the first 72 hours is a significant predictor of postoperative complications and delayed graft function (16).

As long as ACS is recognized and managed, its incidence is observed to decrease in ICU (12). However, it still remains a serious problem in obese and acute pancreatitis patients. The highest prevalence of ACS is seen in acute pancreatitis with 57% (12). Organ failure develops more frequently in patients with acute pancreatitis who develop IAH and ACS. Patients with ACS accompanied by acute pancreatitis are at higher risk for surgery, pancreatic necrosis, mechanical ventilator, Systemic Inflammatory Response Syndrome (SIRS), GI intolerance, kidney replacement therapy, and long hospital stay. In addition, mortality in these patients has been shown to be 28% (17, 18). Mortality is 50% in acute pancreatitis patients with ACS who have undergone decompressive laparotomy (19). Emergency laparotomy is required in 13% of acute pancreatitis patients (20). In patients with critical cirrhosis, the rate of IAH is 82% and the rate of ACS is 23% (21). While IAH develops in half of orthotropic liver transplant patients, ACS develops in 15% (13). The prevalence of IAH in patients with a burn surface area over than 20% is between 57.8 - 82.6% (22).

Pathophysiology

Although the pathophysiology of IAH and ACS is not fully understood, multiple organ failure develops by developing a vicious circle with a chain of events that affect each other (23). Increased IAP mimics a sepsis-like condition. Loss of vasomotor tone occurs with disruption of endothelial intracellular connections. Fluid loading is usually the first choice to provide hemodynamic stability. However, excessive fluid overload may paradoxically cause ACS (22). IAH / ACS generally has the characteristics of compartment syndrome. When the pressure increases in an anatomical compartment, the perfusion pressure decreases and tissue hypoxia develops (1). The pressure that ensures adequate blood flow to the abdominal organs is called abdominal perfusion pressure. It is calculated by subtracting the IAP from the mean arterial pressure (MAP) (4). Abdominal compliance is defined as the unit volume change (ml/mmHg) corresponding to a unit pressure change and is determined by the elasticity of the abdominal wall and diaphragm. Normal compliance is in the range of 250–450 mL/mmHg. Because the abdominal pressure/volume curve is curvilinear,

even a small volume increase may cause an excessive pressure increase in case of decreased compliance (24).

To briefly talk about the chain of events that developed due to the increase in intra-abdominal pressure; with the increase in IAP, compression of the inferior vena cava develops and venous return (preload) to the heart decreases. Due to the decrease in preload, cardiac output decreases and organ perfusion decreases. Diaphragm elevation occurs due to high IAP, and thoracic volume decreases and intrathoracic pressure increases. This situation causes an increase in airway pressure and respiratory workload, reducing thoracic compliance. Increased intrathoracic pressure is another reason for decreased preload and cardiac output (25). Increased intrathoracic pressure impairs ventricular compliance and increases afterload by pressing on the systemic/pulmonary arteries (26). Due to the compression of the pulmonary parenchyma, the rate of intrapulmonary shunting increases and respiratory failure deepens. While the tidal volume and residual lung volume are declining; elevated pleural pressure, inspiratory pressure and peak pressure are observed (27). At the same time, cerebral venous return decreases due to increased intrathoracic pressure, resulting in increased intracranial pressure (ICP) and decreased cerebral blood flow (28).

Renal perfusion is reduced due to decreased cardiac output and renal vein compression caused by IAH. In this way, acute kidney injury (AKI) develops. Vasoconstriction occurs when the renin-angiotensin aldosterone system is activated and this situation results in fluid storage in the extracellular space. Inflammatory response develops due to IAH and accelerates the development of acute kidney injury (4). If the IAP level is above 15 mmHg, it causes oliguria, and if it is above 30 mmHg, it causes anuria (28). Oliguria is one of the early markers of ACS (29).

Splanchnic perfusion is also impaired due to decreased cardiac output and IAH. Mucosal blood flow in the intestine decreases due to decreased splanchnic perfusion. This situation causes the development of malabsorption syndrome and bacterial translocation (4). Intestinal edema develops due to hypo perfusion and the volume of the intestine increases, which further increases the IAP and contributes to the vicious circle. Hepatic venous and arterial blood flows decrease due to increased IAP and hepatocellular damage develops. Since lactate clearance cannot be performed effectively due to hepatic insufficiency, hyperlactatemia develops and causes metabolic acidosis (4).

The systemic effects of IAH and the conditions that contribute to the development of IAH are summarized in Tables 1 and 2.

Table-1: Systemic Effects of Intra-abdominal Hypertension (4)

• Intracranial Pressure ↑	• Cerebral Perfusion Pressure ↓
• Cerebral Venous Return ↓	• Intrathoracic Pressure ↑
• Preload ↓	• Afterload ↑
• Cardiac Output ↓	• Cardiac Contractility ↓
• Central Venous Pressure↑	• Pulmonary Artery Wedge Pressure ↑
• Lung Compliance ↓	• Atelectasis ↑
• Airway Pressures ↑	• Dead Space ↑
• PaCO2 ↑	• PaO2 ↓
• Abdominal Wall Compliance ↓	• Mesenteric Blood Flow ↓
• GIS Intolerance ↑	• Lactate Clearance ↓
• Liver Blood Flow ↓	• Renal Blood Flow ↓
• Glomerular Filtration Rate ↓	• Diuresis ↓
• Renin-Angiotensin-Aldosterone System ↑	

Table-2: Conditions that contribute to the development of intra-abdominal hypertension (30, 31)

Impaired Abdominal Wall Compliance: Pain, Abdominal Wall Edema, Obesity
Increased Abdominal Content: Gastroparesis, Ileus, Fluid Collection, Ascites, Hemoperitoneum, Retroperitoneal Bleeding, Intestinal Distention, Tumors
Capillary Leakage, Fluid Loading: SIRS, MODS

Risk Factors

Although there have been many studies on risk factors for IAH and ACS, significant scientific data could not be obtained due to clinical heterogeneity. Abdominal trauma, infections, severe burns, aortic aneurysm surgery, ARDS, liver transplantation, septic shock, massive fluid overload, obesity, and severe acute pancreatitis are major risk factors. Fluid overload is the highest risk factor for ACS in patients with a history of surgery and trauma (2, 32).

In studies conducted with critically ill patients in the ICU, transfusion of more than 3 liters of fluid in 24 hours is a risk factor for the development of IAH (33). In addition, administration of more than 250 ml/kg of fluid in the first 24 hours is a risk factor for ACS in patients who require excess fluid resuscitation, such as burn patients (34). Fluid loading that is aggressive, which is defined as 3-5 mL/kg/h in the first 24 hours in patients with acute pancreatitis, increases the risk of developing pulmonary edema and acute kidney injury by 2 times more (35). Mao and colleagues observed that patients diagnosed with acute

pancreatitis had a 72% incidence of ACS when fluid was infused at a rate of 10-15 mL/kg (36).

Although patients who have abdominal surgery are naturally at risk, the surgical risk is higher in patients who have orthotropic liver transplants, damage control surgery, abdominal aortic surgery, and massive incisional hernia (12). The application of noninvasive ventilation (even under pressure supports above 10 cm-H2O) is associated with the development of IAH (37).

Risk factors for IAH and ACS are summarized in Table 3.

Table-3: Risk Factors (22, 31)

• Obesity	• Age
• Abdominal Surgery	• Prone Positioning
• ARDS	• Mechanical Ventilation
• PEEP >10 mmHg	• Ventilator Dyssynchrony
• Gastric Distention	• Gastroparesis
• Ileus	• Volvulus
• Abdominal Tumor	• Damage Control Surgery
• Enteral Feeding	• Ascites
• Hemoperitoneum	• Pneumoperitoneum
• Major Trauma	• Laparoscopy with excessive inflation pressures
• Peritoneal Dialysis	
• Oliguria (<150 mL/24h)	• Abdominal Inflammation / Infection (Peritonitis)
• Pancreatitis	
• Hepatic Failure	• Abdominal abscess
• Acidosis	• Cirrhosis
• Hb <8 g/dL,	• Hypothermia (<34 ^{o}C)
• Coagulopathy	• Cardiac Index <2.6 L/min/m2
• >3 Units of Erythrocyte Transfusion	• Gastrointestinal Bleeding
• Sepsis / Shock	• Trauma
• >3L Crystalloid Resuscitation	• Hypotension (SBP <86 mmHg)
• Major Burns	

Diagnosis

Since the pressure will be evenly distributed to each area of the abdomen, theoretically measurements can be made from anywhere in the cavity. IAP can be measured directly with the help of catheters placed in the peritoneal cavity, as well as indirectly through hollow organs such as the bladder, stomach, rectum, and vagina (38). Although new and non-invasive IAP measurement methods are

being developed, transvesical measurement is seen as the gold standard (39). IAP measurement by palpation is unreliable. Even in the absence of abdominal distension, there may be a clinically significant IAH condition (40).

Transvesical IAP measurement is done as follows as standard (7):

1) Lay the patient in supine position
2) Reset transducer at mid-axillary line at iliac crest level
3) Make sure there are no abdominal contractions
4) Inject 25 mL of sterile saline into the empty bladder
5) Measure in mmHg at the end of the breath

If the measurement is made with a standpipe, the cm-H2O value should be converted to mmHg. Basal IAP have to be measured in sufferers with 2 or extra risk factors, and if there is an upward trend, the measurement should be repeated every 4-6 hours (9). In the critically ill patient, the normal IAP is 5-7 mmHg (7). However, normal IAP values in morbidly obese patients are between 9-14 mmHg (41). By elevating the patient's head by 30° and 45°, the IAP may increase by 4-9 mmHg compared to the supine position (41). Transvesical IAP measurement is contraindicated in sufferers with cystectomy or traumatic bladder injury (1).

Another measurement method of intraabdominal pressure is intragastric pressure measurement, but it is not common in practice (10). Noninvasive measurement of IAP is valuable, but the reliability of this method has not been proven by current studies (42). Methods such as transient radar method and microwave reflectometry are still under study (43, 44). In the Accuryn urinary catheter method, continuous IAP measurement can be made through a small balloon placed on the foley catheter tip, as well as urine output can be followed (45). Abdominal wall tension (AWT) is an important application and diagnostic ability in abdominal complications is higher than IAP (46). Although IAP measurement is seen as the main strategy in the detection of IAH and ACS, the search for biomarkers still continues. Urinary and plasma fatty acid binding protein have been investigated for intra-abdominal hypertension-related complications, but there is no a clear conclusion (47).

When viewed the abdominal tomography findings, a ratio of peritoneum to abdomen >0.52 is an indication of intra-abdominal hypertension, and a "round belly" finding (ratio of anteroposterior diameter to transverse abdominal diameter >0.8) is an indication of ACS (48). In addition, increased bowel thickness (>3 mm), elevation of the diaphragm, narrowing of the inferior vena

cava, and presence of intra-abdominal fluid are useful in diagnosis (48). Biliary dilatation and pleural effusion due to ACS are seen in patients with severe acute pancreatitis (10).

Treatment/Management

Treatment of IAH and ACS is divided into two as non-operative and operative. The treatment strategy should be directed towards the cause of IAH (10). Non-operative treatment options basically consist of improving wall compliance, reducing intraluminal contents, and maintaining fluid balance (Table 4) (30).

Table-4: Non-operative treatment options (10, 30)

Improving Abdominal Wall Compliance:	• Sedation • Analgesia • Neuromuscular blocking agents • Supine position • Removal of abdominal eschar and compressive clothing
Evacuate Intra-luminal contents:	• Nasogastric and colonic decompression • Promotility agents • Laxatives
Evacuate Abdominal Fluid Collections:	• Percutaneous drainage • Paracentesis
Maintaining Fluid Balance and Hemodynamics:	• Fluid restriction • Negative fluid balance • Diuretic • Colloids / hypertonic fluids (Albumin) • Hemodialysis • Ultrafiltration • Vasopressors
Organ Support:	• Optimize ventilation, alveolar recruitment • Use transmural (tm) airway pressures o $Pplat_{tm}$=Plat - 0.5 x IAP • Consider using volumetric preload indices • If using PAOP/CVP, use transmural pressures o $PAOP_{tm}$ = PAOP - 0,5 x IAP o CVP_{tm} = CVP - 0,5 x IAP

WSACS has published algorithms for medical management of IAH and ACS (Figures 1 and 2), but it should not be forgotten that the overall quality of evidence is low (9). The algorithm evaluates the quality of evidence for each endpoint on a 4-point scale, and each level of evidence is represented by a letter from D to A: very low (D), low (C), moderate (B) and high (A) (9). Medical management strategy in IAH/ACS is shaped according to both etiology and clinical situation. Interventions are applied gradually until the patient's IAP decreases. Treatment is escalated to the next step in the algorithm if there is no response to the intervention (9).

In case of gastroparesis, metoclopramide and erythromycin are used and enteral access is reduced (5). Neostigmine can be used with enemas as a colon prokinetic (9). Deepening sedation in mechanically ventilated patients has a limited effect on IAH (49). Neuromuscular blockers provide temporary decreases in IAP (50). Postoperative epidural and intravenous pain management strategies can reduce IAP (51).

In fluid management, resuscitation, optimization, stabilization and evacuation methods should be applied, respectively, with individualized treatment. Patients are considered hypovolemic at the start of treatment and normovolaemia or fluid overload may develop after fluid resuscitation. De-resuscitation is achieved with conservative fluid therapy and fluid withdrawal therapies (52).

Enteral nutrition increases intestinal blood flow, motility, and decreases bacterial translocation, but information on the initiation time of enteral nutrition in the presence of IAH / ACS is not sufficient. In the studies carried out, the incidence of abdominal distension increased in patients who started feeding within 24 hours, but IAP did not increase. It has been shown that GIS intolerance is less in cases where the IAP is <15 mmHg (53).

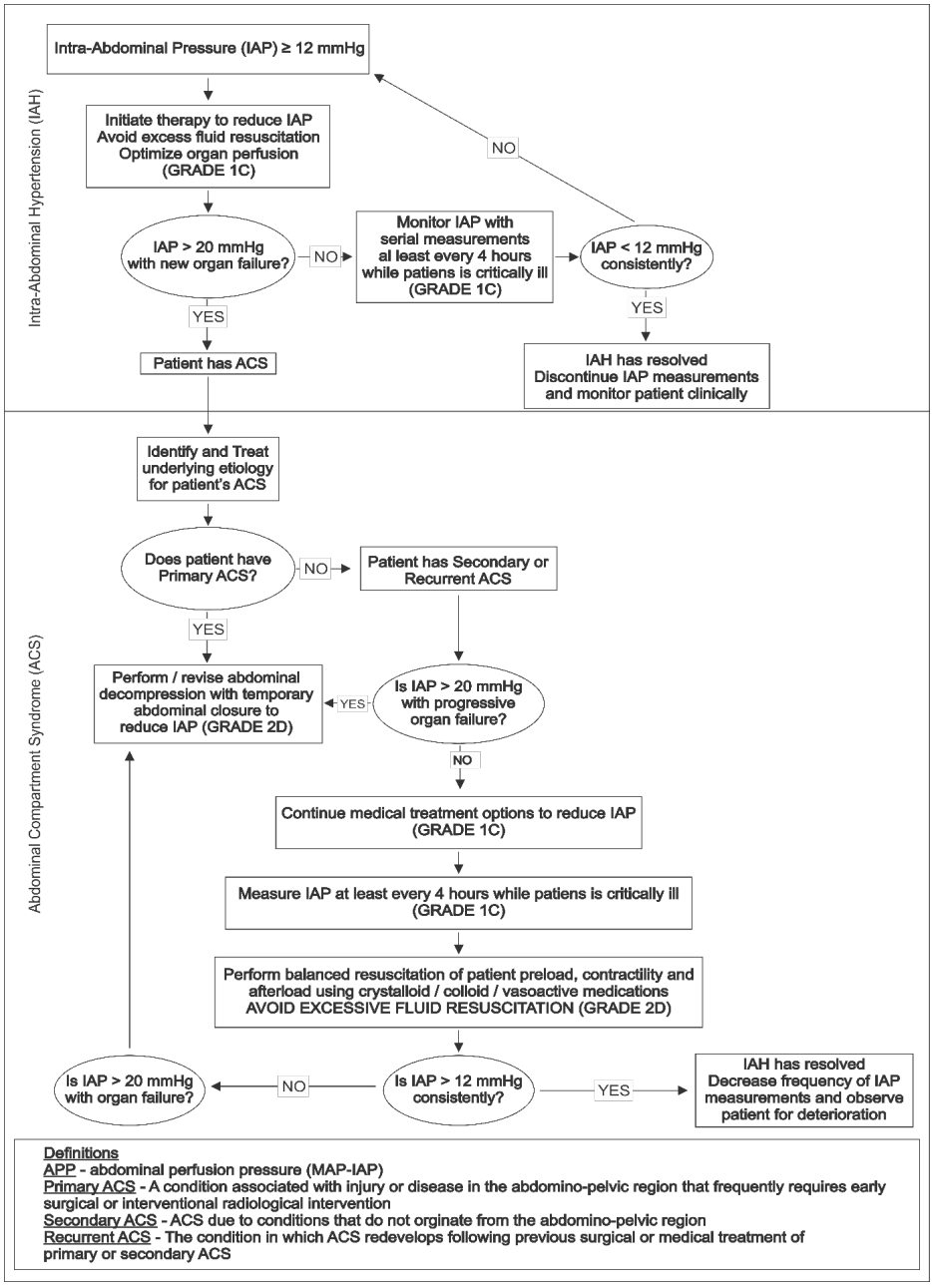


Figure-1: Intra-abdominal Hypertension / Abdominal Compartment Syndrome Management Algorithm (9)

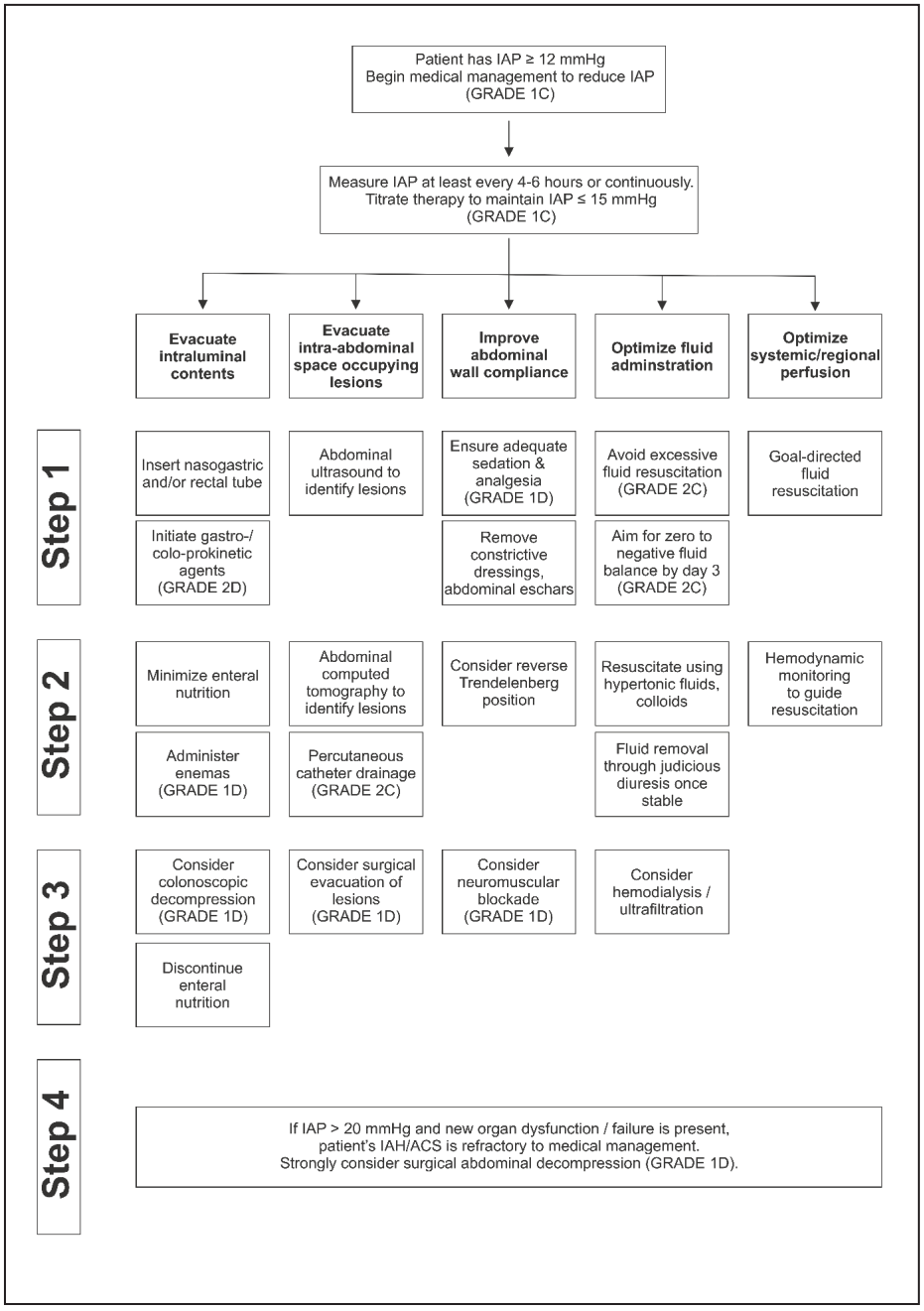


Figure-2: Intra-abdominal Hypertension / Abdominal Compartment Syndrome Medical Management Algorithm (9)

Decompressive Laparotomy and Open Abdomen

There is no consensus on the timing of decompressive surgery due to the lack of interventional studies (54). However, abdominal decompression surgery should be considered in case of development of organ failures and grade III-IV IAH for which non-operative options are useless (55). It has been shown that decompressive laparotomy provides significantly lower IAP and improvement in hemodynamic, respiratory and renal parameters. However, postoperative mortality is still high with 49.7% (55). Ischemia-reperfusion syndrome may develop after decompressive laparotomy and supportive treatment may be required together with fluid balance (56). Primary facial closure should be performed 4-7 days after decompressive laparotomy. If the fascia is not closed in the first 8 days, fistula and dull abdomen may develop. These patients have an indication of open abdomen (57).

Open Abdomen is the procedure of leaving the abdomen open by using temporary abdominal closure methods in order to prevent progression to recurrent ACS in patients requiring decompressive laparotomy (58). Abdominal contents are open to atmospheric pressure and protected by a temporary cover (59). Although open abdomen has complications such as infection risk, hypercatabolic state, fluid loss, enteroatmospheric fistula, abdominal wall loss, large hernias, it reduces the risk of recurrent ACS (60, 61).

Among the surgical techniques of laparotomy, median laparotomy is preferred, but bilateral transverse subcostal laparotomy and subcutaneous linea alba fasciotomy are also preferred (62). Various techniques such as skin closure only, Bogota bag, Opsite sandwich technique, absorbable mesh technique, non-absorbable (Wittmann patch) zipper, negative pressure wound therapy (NPWT) are used for temporary abdominal closure (63). 80% closure can be achieved using NPWT or a combination of vacuum therapy and mesh-mediated fascial traction (64). Although NPWT has no effect on facial closure time, morbidity and complication development, it contributes to the reduction of postoperative mortality and the length of stay in the ICU (65). Although NPWT is the preferred method for temporary abdominal closure, only skin closure can be performed when limited resources are available (66).

In acute pancreatitis patients who underwent decompressive laparotomy, the complication rate is 35% and the mortality is 8.5% (67). While the rate of enteroatmospheric fistula was found to be 8.9%, a correlation was found between the time from open abdomen to feeding and fistula formation (68). The recommended mean open time of the open abdomen is 19 days (69).

REFERENCES

1. Maluso P, Sarani B. Abdominal compartment hypertension and abdominal compartment syndrome. Principles of Adult Surgical Critical Care. 2016:233-40.

2. Rogers WK, Garcia L. Intraabdominal hypertension, abdominal compartment syndrome, and the open abdomen. Chest. 2018;153(1):238-50.

3. Papavramidis TS, Marinis AD, Pliakos I, Kesisoglou I, Papavramidou N. Abdominal compartment syndrome–Intra-abdominal hypertension: Defining, diagnosing, and managing. Journal of emergencies, trauma and shock. 2011;4(2):279.

4. Łagosz P, Sokolski M, Biegus J, Tycinska A, Zymlinski R. Elevated intra-abdominal pressure: A review of current knowledge. World journal of clinical cases. 2022;10(10):3005-13.

5. Padar M, Reintam Blaser A, Talving P, Lipping E, Starkopf J. Abdominal compartment syndrome: improving outcomes with a multidisciplinary approach–a narrative review. Journal of Multidisciplinary Healthcare. 2019:1061-74.

6. Kron IL, Harman PK, Nolan SP. The measurement of intra-abdominal pressure as a criterion for abdominal re-exploration. Annals of surgery. 1984;199(1):28.

7. Malbrain ML, Cheatham ML, Kirkpatrick A, Sugrue M, Parr M, De Waele J, et al. Results from the international conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. I. Definitions. Intensive care medicine. 2006;32(11):1722-32.

8. Cheatham ML, Malbrain ML, Kirkpatrick A, Sugrue M, Parr M, De Waele J, et al. Results from the international conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. II. Recommendations. Intensive care medicine. 2007;33(6):951-62.

9. Kirkpatrick AW, Roberts DJ, De Waele J, Jaeschke R, Malbrain ML, De Keulenaer B, et al. Intra-abdominal hypertension and the abdominal compartment syndrome: updated consensus definitions and clinical practice guidelines from the World Society of the Abdominal Compartment Syndrome. Intensive care medicine. 2013;39(7):1190-206.

10. De Waele JJ. Intra-abdominal hypertension and abdominal compartment syndrome. Current Opinion in Critical Care. 2022;28(6):695-701.

11. Malbrain M, Chiumello D, Cesana BM, Blaser AR, Starkopf J, Sugrue M, et al. A systematic review and individual patient data meta-analysis on

intra-abdominal hypertension in critically ill patients: the wake-up project. World initiative on Abdominal Hypertension Epidemiology, a Unifying Project (WAKE-Up!). Minerva anestesiologica. 2014;80(3):293-306.

12. Smit M, Koopman B, Dieperink W, Hulscher JB, Hofker HS, van Meurs M, et al. Intra-abdominal hypertension and abdominal compartment syndrome in patients admitted to the ICU. Annals of intensive care. 2020;10(1):1-10.

13. Freitas MS, Nacul FE, Malbrain ML, Silva RC, Lobo FR, Oliveira NE, et al. Intra-abdominal hypertension, fluid balance, and adverse outcomes after orthotopic liver transplantation. Journal of Critical Care. 2021;62:271-5.

14. Copur S, Berkkan M, Hasbal NB, Basile C, Kanbay M. Abdominal compartment syndrome: an often overlooked cause of acute kidney injury. Journal of Nephrology. 2022:1-9.

15. Sun J, Sun H, Sun Z, Yang X, Zhou S, Wei J. Intra-abdominal hypertension and increased acute kidney injury risk: a systematic review and meta-analysis. Journal of International Medical Research. 2021;49(5):03000605211016627.

16. Regli A, Blaser AR, De Keulenaer B, Starkopf J, Kimball E, Malbrain ML, et al. Intra-abdominal hypertension and hypoxic respiratory failure together predict adverse outcome–A sub-analysis of a prospective cohort. Journal of Critical Care. 2021;64:165-72.

17. Marcos-Neira P, Zubia-Olaskoaga F, López-Cuenca S, Bordejé-Laguna L. Epidemiology of Acute Pancreatitis in Intensive Care Medicine study g. Relationship between intra-abdominal hypertension, outcome and the revised Atlanta and determinant-based classifications in acute pancreatitis BJS Open. 2017;1:175e81.

18. Bhandari V, Jaipuria J, Singh M, Chawla AS. Intra-abdominal pressure in the early phase of severe acute pancreatitis: canary in a coal mine? Results from a rigorous validation protocol. Gut and Liver. 2013;7(6):731.

19. Boone B, Zureikat A, Hughes SJ, Moser AJ, Yadav D, Zeh HJ, et al. Abdominal compartment syndrome is an early, lethal complication of acute pancreatitis. The American Surgeon. 2013;79(6):601-7.

20. Henn J, Lingohr P, Branchi V, Semaan A, Von Websky MW, Glowka TR, et al. Open Abdomen Treatment in Acute Pancreatitis. Frontiers in Surgery. 2021;7:588228.

21. Pereira R, Buglevski M, Perdigoto R, Marcelino P, Saliba F, Blot S, et al. Intra-abdominal hypertension and abdominal compartment syndrome in the critically ill liver cirrhotic patient–prevalence and clinical outcomes.

A multicentric retrospective cohort study in intensive care. PloS one. 2021;16(5):e0251498.

22. Jacobs R, Wise RD, Myatchin I, Vanhonacker D, Minini A, Mekeirele M, et al. Fluid Management, Intra-Abdominal Hypertension and the Abdominal Compartment Syndrome: A Narrative Review. Life. 2022;12(9):1390.

23. Villa G, Samoni S, De Rosa S, Ronco C. The pathophysiological hypothesis of kidney damage during intra-abdominal hypertension. Frontiers Media SA; 2016. p. 55.

24. Malbrain ML, Peeters Y, Wise R. The neglected role of abdominal compliance in organ-organ interactions. Critical Care. 2016;20(1):1-10.

25. Luca A, Cirera I, García-Pagán JC, Feu F, Pizcueta P, Bosch J, et al. Hemodynamic effects of acute changes in intra-abdominal pressure in patients with cirrhosis. Gastroenterology. 1993;104(1):222-7.

26. Ridings PC, Bloomfield GL, Blocher CR, Sugerman HJ. Cardiopulmonary effects of raised intra-abdominal pressure before and after intravascular volume expansion. LWW; 1995. p. 1071-5.

27. Obeid F, Saba A, Fath J, Guslits B, Chung R, Sorensen V, et al. Increases in intra-abdominal pressure affect pulmonary compliance. Archives of Surgery. 1995;130(5):544-8.

28. Richards WO, Scovill W, Shin B, Reed W. Acute renal failure associated with increased intra-abdominal pressure. Annals of surgery. 1983;197(2):183.

29. Mohmand H, Goldfarb S. Renal dysfunction associated with intra-abdominal hypertension and the abdominal compartment syndrome. Journal of the American Society of Nephrology. 2011;22(4):615-21.

30. Mancilla Asencio C, Berger Fleiszig Z. Intra-Abdominal Hypertension: A Systemic Complication of Severe Acute Pancreatitis. Medicina (Kaunas, Lithuania). 2022;58(6).

31. Rajasurya V, Surani S. Abdominal compartment syndrome: Often overlooked conditions in medical intensive care units. World Journal of Gastroenterology. 2020;26(3):266.

32. Holodinsky JK, Roberts DJ, Ball CG, Blaser AR, Starkopf J, Zygun DA, et al. Risk factors for intra-abdominal hypertension and abdominal compartment syndrome among adult intensive care unit patients: a systematic review and meta-analysis. Critical Care. 2013;17(5):1-15.

33. Blaser AR, Regli A, De Keulenaer B, Kimball EJ, Starkopf L, Davis WA, et al. Incidence, risk factors, and outcomes of intra-abdominal hypertension

in critically ill patients—a prospective multicenter study (IROI study). Critical care medicine. 2019;47(4):535.

34. Ivy ME, Atweh NA, Palmer J, Possenti PP, Pineau M, D'Aiuto M. Intra-abdominal hypertension and abdominal compartment syndrome in burn patients. Journal of Trauma and Acute Care Surgery. 2000;49(3):387-91.

35. Gad MM, Simons-Linares CR. Is aggressive intravenous fluid resuscitation beneficial in acute pancreatitis? A meta-analysis of randomized control trials and cohort studies. World journal of gastroenterology. 2020;26(10):1098.

36. Mao E-q, Tang Y-q, Fei J, Qin S, Wu J, Li L, et al. Fluid therapy for severe acute pancreatitis in acute response stage. Chinese medical journal. 2009;122(02):169-73.

37. Regli A, Nanda R, Braun J, Girardis M, Max M, Malbrain ML, et al. The effect of non-invasive ventilation on intra-abdominal pressure. Anaesthesiology Intensive Therapy. 2022;54(1).

38. Malbrain ML. Different techniques to measure intra-abdominal pressure (IAP): time for a critical re-appraisal. Applied physiology in intensive care medicine. 2006:105-19.

39. Sugrue M, De Waele JJ, De Keulenaer BL, Roberts DJ, Malbrain ML. A user's guide to intra-abdominal pressure measurement. Anaesthesiology intensive therapy. 2015;47(3):241-51.

40. Kirkpatrick AW, Brenneman FD, McLean RF, Rapanos T, Boulanger BR. Is clinical examination an accurate indicator of raised intra-abdominal pressure in critically injured patients? Canadian Journal of Surgery. 2000;43(3):207.

41. De Keulenaer B, De Waele J, Powell B, Malbrain M. What is normal intra-abdominal pressure and how is it affected by positioning, body mass and positive end-expiratory pressure? Intensive care medicine. 2009;35(6):969-76.

42. Tayebi S, Gutierrez A, Mohout I, Smets E, Wise R, Stiens J, et al. A concise overview of non-invasive intra-abdominal pressure measurement techniques: from bench to bedside. Journal of Clinical Monitoring and Computing. 2021;35(1):51-70.

43. Tayebi S, Pourkazemi A, Malbrain ML, Stiens J. Non-Invasive Intra-Abdominal Pressure Measurement by Means of Transient Radar Method: In Vitro Validation of a Novel Radar-Based Sensor. Sensors. 2021;21(18):5999.

44. David M, Raviv A, Guttel A, García Reyes V, Simini F, Pracca F. Non-invasive indirect monitoring of intra-abdominal pressure using microwave

reflectometry: system design and proof-of-concept clinical trial. Journal of Clinical Monitoring and Computing. 2021;35(6):1437-43.

45. Kramer GC, Luxon E, Wolf J, Burnett DR, Nanduri D, Friedman BC. Inaccuracy of urine output measurements due to urinary retention in catheterized patients in the burn ICU. Journal of Burn Care & Research. 2017;38(1):e409-e17.

46. Tang H, Liu D, Guo Y, Zhang H, Li Y, Peng X, et al. A New Device for Measuring Abdominal Wall Tension and Its Value in Screening Abdominal Infection. Medical Devices (Auckland, NZ). 2021;14:119.

47. Strang SG, Habes QLM, Van der Hoven B, Tuinebreijer WE, Verhofstad MHJ, Pickkers P, et al. Intestinal fatty acid binding protein as a predictor for intra-abdominal pressure-related complications in patients admitted to the intensive care unit; a prospective cohort study (I-Fabulous study). J Crit Care. 2021;63:211-7.

48. Bouveresse S, Piton G, Badet N, Besch G, Pili-Floury S, Delabrousse E. Abdominal compartment syndrome and intra-abdominal hypertension in critically ill patients: diagnostic value of computed tomography. European radiology. 2019;29(7):3839-46.

49. Padar M, Starkopf J, Blaser AR. Deepening of sedation with propofol has limited effect on intra-abdominal pressure–An interventional study in mechanically ventilated adult patients with intra-abdominal hypertension. Journal of Critical Care. 2021;65:98-103.

50. Hoste E, Verholen E, De Waele JJ. The effect of neuromuscular blockers in patients with intra-abdominal hypertension. Intensive care medicine. 2007;33(10):1811-4.

51. Varosyan A, Mkhoyan G, Harutyunyan G, Hakobyan R. Epidural analgesia decreases intraabdominal pressure in postoperative patients with intraabdominal hypertension: 8AP1-8. European Journal of Anaesthesiology| EJA. 2007;24:87.

52. Malbrain ML, Van Regenmortel N, Saugel B, De Tavernier B, Van Gaal P-J, Joannes-Boyau O, et al. Principles of fluid management and stewardship in septic shock: it is time to consider the four D's and the four phases of fluid therapy. Annals of intensive care. 2018;8(1):1-16.

53. Sun J-k, Li W-q, Ke L, Tong Z-h, Ni H-b, Li G, et al. Early enteral nutrition prevents intra-abdominal hypertension and reduces the severity of severe acute pancreatitis compared with delayed enteral nutrition: a prospective pilot study. World Journal of Surgery. 2013;37(9):2053-60.

54. De Waele JJ, Hoste EA, Malbrain ML. Decompressive laparotomy for abdominal compartment syndrome–a critical analysis. Critical Care. 2006;10(2):1-9.

55. Van Damme L, De Waele JJ. Effect of decompressive laparotomy on organ function in patients with abdominal compartment syndrome: a systematic review and meta-analysis. Critical Care. 2018;22(1):1-11.

56. De Laet IE, Malbrain ML, De Waele JJ. A clinician's guide to management of intra-abdominal hypertension and abdominal compartment syndrome in critically ill patients. Critical care. 2020;24(1):1-9.

57. Chiara O, Cimbanassi S, Biffl W, Leppaniemi A, Henry S, Scalea TM, et al. International consensus conference on open abdomen in trauma. Journal of Trauma and Acute Care Surgery. 2016;80(1):173-83.

58. Björck M, Kirkpatrick A, Cheatham M, Kaplan M, Leppäniemi A, De Waele J. Amended classification of the open abdomen. Scandinavian journal of surgery. 2016;105(1):5-10.

59. Mentula P, Hienonen P, Kemppainen E, Puolakkainen P, Leppäniemi A. Surgical decompression for abdominal compartment syndrome in severe acute pancreatitis. Archives of surgery. 2010;145(8):764-9.

60. Padar M, Blaser AR, Talving P, Lipping E, Starkopf J. Abdominal compartment syndrome: improving outcomes with a multidisciplinary approach–a narrative review. Journal of Multidisciplinary Healthcare. 2019;12:1061.

61. Sartelli M, Abu-Zidan FM, Ansaloni L, Bala M, Beltrán MA, Biffl WL, et al. The role of the open abdomen procedure in managing severe abdominal sepsis: WSES position paper. World Journal of Emergency Surgery. 2015;10(1):1-11.

62. Smit M, van Meurs M, Zijlstra JG. Intra-abdominal hypertension and abdominal compartment syndrome in critically ill patients: A narrative review of past, present, and future steps. Scandinavian journal of surgery : SJS : official organ for the Finnish Surgical Society and the Scandinavian Surgical Society. 2022;111(1):14574969211030128.

63. Montalvo-Jave EE, Espejel-Deloiza M, Chernitzky-Camaño J, Peña-Pérez CA, Rivero-Sigarroa E, Ortega-León LH. Abdominal compartment syndrome: Current concepts and management. Revista de gastroenterologia de Mexico (English). 2020;85(4):443-51.

64. Berrevoet F, Lampaert S, Singh K, Jakipbayeva K, Van Cleven S, Vanlander A. Early initiation of a standardized open abdomen treatment with

vacuum assisted mesh-mediated fascial traction achieves best results. Frontiers in Surgery. 2021;7:606539.

65. Cirocchi R, Birindelli A, Biffl WL, Mutafchiyski V, Popivanov G, Chiara O, et al. What is the effectiveness of the negative pressure wound therapy (NPWT) in patients treated with open abdomen technique? A systematic review and meta-analysis. Journal of Trauma and Acute Care Surgery. 2016;81(3):575-84.

66. Kruger H, Couch D, Oosthuizen G. Skin-only closure as a temporary abdominal closure technique in a rural setting-exploring role and safety profile. South African Journal of Surgery. 2021;59(1):20-4.

67. Kao S-Y, Chen T-H, Wang C-Y, Hsiao C-Y, Chiang C-S, Chou S-C, et al. Surgical Intervention Strategies of Necrotizing Pancreatitis With Abdominal Compartment Syndrome. Pancreas. 2021;50(10):1415-21.

68. Coccolini F, Ceresoli M, Kluger Y, Kirkpatrick A, Montori G, Salvetti F, et al. Open abdomen and entero-atmospheric fistulae: An interim analysis from the International Register of Open Abdomen (IROA). Injury. 2019;50(1):160-6.

69. Willms A, Muysoms F, Güsgen C, Schwab R, Lock J, Schaaf S, et al. The Open Abdomen Route by EuraHS: introduction of the data set and initial results of procedures and procedure-related complications. Hernia. 2017;21(2):279-89.

CHAPTER X

EMERGENCY PRIMARY DISORDERS OF THE OMENTUM

Fatih Dal

(MD.), Department of General Surgery, Health Sciences University Turkish Ministry of Health İstanbul Research and Training Hospital, İstanbul, Turkey
E-mail: fatihdal07@gmail.com
ORCID: 0000-0002-9768-8125

1. History of the Omentum:

The term omentum derives from the word "Omen" that assesses and categorizes human cadavers by examining variations during embalming process in ancient Egypt. **Galen**, who lived between 128 and 199 A.D., believed that omentum was responsible for keeping the intraabdominal organs warms. His idea was based upon his observation that a gladiator, who had his omentum resection after being stabbed, had pain when it is cold (1). Today, we understand that the omentum is a special organ with the unique characteristic of limiting or controlling foreign masses and lesions as well as the inflammatory processes. Due to this characteristic, in the early 20th century, Rutherford Morrison named the omentum as the "abdominal policeman". Moreover, flaps prepared from the omentum, which has a rich vascular network, are used for healing and regeneration in all anatomical regions including the thorax, intra-abdominal, lower extremities and upper extremities (2,3).

2. The Omentum in Different Species:

The yolk sac was considered a source of stem cells in subgroup vertebrates. Today, however, the yolk sac is seen as a loose layer of mesothelial tissue and a rudimentary effector organ that performs simple immune functions such as allorecognition, innate cytotoxic reaction, and generation of chemokines. This area is located within a region bounded by the forelimbs, foregut, and

mesonephros. In mammals, the peritoneal fold determines the boundaries of this region (4). The immune system in humans is, on the other hand, more developed and complex. Omentum plays a defensive role in this complex immune system within the intraperitoneal area (1).

3. Embryology of the Omentum:

At the embryological stage, the lesser omentum develops from the dorsal mesoderm and the greater omentum develops from the ventral mesoderm. Around the 5th week of gestation, after the stomach rotates 90 degrees clockwise, the lesser and greater peritoneal sacs are formed. The lesser peritoneal sac grows behind the lesser curvature of the stomach towards the left, forming the cavity known as the omental bursa. The omental foramen (which is also known as the epiploic foramen or the foramen Winslow) provides the only natural communication between the greater and lesser peritoneal sacs. The greater omentum is formed from the ventral mesentery, which is involved in the rotations of the stomach. The greater omentum grows more quickly than the lesser omentum does. It fuses with the transverse mesocolon at the 8th to 9th weeks of gestation and develops in the large peritoneal sac. The development of the greater omentum continues till the age of eleven. When developed, the greater omentum can be viewed with ultrasonography (US) both before and after birth (5-8). These lymphoid tissue units, called "milky spots" in the omentum, were described in 1874 by Louis-Antoine Ranvier, who investigated the omentum in rabbits (8). The number of the milky spots (MS) developing in the omentum from the 20th to 35th weeks of gestation peaks during infancy. The size of MS varies from 0.3 to 3.5 mm^2 and their number gradually decreases with increased age (1, 6).

4. Histology of the Omentum:

The omentum is a unique organ with a translucent, rich vascular network with adipocytes embedded in a loose connective tissue surrounding human omental microvascular endothelial (HOME) and mesothelial (MESO) cells, fibroblasts, mononuclear and phagocytic cells. The HOME/MESO cells in the omentum lining the peritoneal cavity share a lot of phenotypic features. A comprehensive panel of cell markers should be employed to distinguish HOME/MESO cells from each other. Examination of von Willebrand factor, Ulex europaeus I lectin, and Dil-AC-LDL which are conventional cell markers may not be sufficient for the differentiation of those cells. Specific surface markers

[E-selectin, P-selectin, Le-y, integrin (VLA-6)] of non-HOME cells and/or non-MESO cells are used to distinguish between these two cell types (1,9).

The lesser omentum minus is immobile and lies between the liver and the lesser curvature of the stomach. The lesser omentum, stomach, and gastrocolic ligament together form the anterior border of the omental bursa (the lesser peritoneal sac) (5). The greater omentum, on the other hand, functions as a bridge between the systemic immune system and the intraabdominal immune defense (the greater peritoneal sac) (6). There are fenestrations both in the endothelium covering the omental vessels and in the mesothelium covering MS (1). In an average person, there are approximately 570±33 cells in MS, the smallest lymphoid unit. Of these cells, 47.5% are macrophages, 29.1% are B-lymphocytes, 11.7% are T-lymphocytes and 6.1% are mast cells (10). The lymphocytes found in MS can increase up to 40 times in number in the stimulation performed by introducing a foreign antigen into the peritoneal cavity (embryological period: the greater peritoneal sac). There is also increased microvascular permeability from MS connective tissue matrix to neutrophils, monocytes, and fibrin deposits and a concomitant increase in cellular migration from the mesothelial lining to the peritoneal cavity. This migration is facilitated by fenestrations in the submesothelial connective tissue without a basement membrane (1,11).

5. Anatomy of the Omentum:

In adults, the lesser omentum extends like a fan from the liver with the hepatogastric ligament to the lesser curvature of the stomach, and the proximal duodenum with the hepatoduodenal ligament to the liver. Due to its anatomy, it lines off the anterior border of the omental bursa (the lesser peritoneal sac) together with the stomach and gastrocolic ligament. It is fed by the branches of the truncus coeliacus (the branches of the left gastric artery) (5,6,12).

In a normal adult person, the area of the greater omentum varies from 300 cm2 to 500 cm2, weight from 300 g to 2000 g, width from 20 cm to 46 cm, and length from 14 cm to 36 cm (1,6,8). In a cadaver study, it is most commonly quadrangular (13). Due to its limited fixation and smooth mesothelial surface, the greater omentum can move passively and freely in the intraperitoneal cavity (the greater peritoneal sac) secondary to gravity, respiration, and peristaltic movements. The left gastro-omental artery of the greater omentum receives blood from the celiac trunk through the splenic artery, and its right gastro-omental artery through the gastroduodenal artery, which is a branch of the

common hepatic artery. It also receives blood from the superior mesenteric artery through the inferior pancreaticoduodenal branch. In short, the greater omentum has a rich vascular network consisting of the anastomotic arcuate between the superior mesenteric artery and the celiac trunk (6) **(Figure 1).**

The venous drainage of both the greater and the lesser omentums is achieved via the portal vein, and both sympathetic and parasympathetic autonomic nerve fibers such as the visceral peritoneum are involved in the inversion. Furthermore, there is no real lymph node network. The greater omentum (subpyloric lymph nodes on the right and splenic lymph nodes on the left) and the lesser omentum (lymph nodes in the omental bursa) are drained to regional lymph nodes through the endothelial sacs in milky spots or the endothelial duct network in the stroma (6,8,14).

6. Functions of the Omentum

6.1. Immunological Functions:

Milky spots are rich immunological cells interlarded in the adipose tissue of the omentum. These units, which contain phagocytic and mononuclear cells, proliferate rapidly with the stimulation of secondary stimulating factors [macrophage colony-stimulating factors: GM-CSF, M-CS/Granulocyte colony-stimulating factor: G-CSF] in the activated omentum (1,3,10). Moreover, in the case of intraperitoneal inflammation, the migration of neutrophils in the systemic circulation from the endothelial venules of the omentum to the intraperitoneal cavity is faster as compared to conventional postcapillary venules. The presence of fenestrations in the layer of the mesothelial cell and the absence of a basement membrane facilitates the migration of phagocytic and mononuclear cells (1,3,6,15). Therefore, in the literature, the omentum is considered a part of systemic immunology in the intraperitoneal area (6).

6.2. Formation of Neovascularization (Angiogenesis):

It has been long known that the omentum having a rich vascular network supports angiogenic activity (1). Peptides such as basic fibroblast growth factor (b-FGF), and vascular endothelial growth factor (VEGF) expressed from omental microvascular endothelial cells are potent stimulants of myofibroblast growth, adhesion, and angiogenesis. The activated omentum provides vascular support to the intraabdominal adjacent tissues in the neovascular process, allowing the healing of ischemic or inflammation tissues (3,16,17).

6.3. Formation of Adhesion:

Activated omentum tries to limit contaminated intraabdominal areas by adhering to them. The mobile contact point of the greater omentum rapidly produces fibrin to adhere to the contaminated area. In a few days, fibrin becomes organized with the influence of developing angiogenesis and increasing myofibroblasts. In the long term, the contaminated area is surrounded by collagen tissue, resulting in the formation of adhesions. Due to this specific characteristic, Rutherford Morrison called the omentum as the "abdominal policeman" (2,3,16) **(Figure 1).**

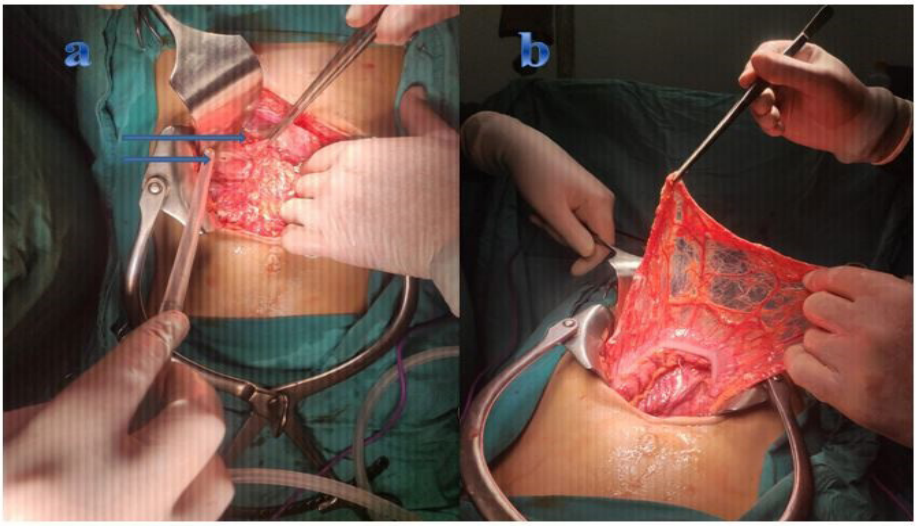


Figure 1: Acute Peptic Ulcus Perforation and the Greater Omentum Segment Trying to Line the Perforation Area (a: Peptic ulcer perforation and the segment of the omentum trying to limit it; b: Greater omentum and its vascular network)

6.4. Hemostatic Function:

Tissue factor (TF), which is a transmembrane glycoprotein, acts as a receptor in the initiation of the extrinsic pathway in blood coagulation (18). It is thought that the hemostatic properties of pedicled omentoplasty, which is used in the management of surgical hemorrhage, are due to the structure of the omentum with high concentration of tissue factor (19).

6.5. Incubator Function:

It was reported in the literature that embryonic kidney, spleen fragments, pancreatic islet cells, pancreas, and osteochondral tissues implanted in an omental sac rapidly developed and completed the natural process of maturation. This extraordinary outcome mainly results from the rich vascular network and optimal microenvironment that the omentum has. For this reason, the omentum is an excellent in-vivo incubator for the cultivation and preservation of embryonic organs or tissues (3).

6.6. Tissue Healing and a Source for Stem Cells:

Tissue engineering requires a source of autologous pluripotent stem cells for cell-based therapies. One resource for mesodermal tissue engineering is mesenchymal stromal cells (MSCs). For the first time, MSCs were detected in the bone marrow. At the same time, MSCs have the potential to differentiate into endoderm and ectoderm derived cells such as lung epithelial cells, cardiomyocytes, neurons, pancreatic islet cells, and hepatocytes (3). The properties of the specified cells are similar and these cells have been also isolated from adipose tissue of mesodermal origin (20). In a recent omental experimental model, two cell groups were identified to promote tissue repair: omnipotent stem cells resembling mesenchymal stem cells and immunomodulatory myeloid suppressor cells. These stem cells in the omentum rapidly regenerate the tissue by seeding the injured areas (21).

7. Emergency Disorders of the Omentum:

Despite the numerous functional advantages, the omentum provides in modern medicine, they may be omentum-related pathologies requiring emergency treatment (1). Such pathologies of the omentum that require urgent medical or surgical treatment can be classified as omental infarction and/or omental torsion, omental hemorrhage, omental acute mechanical intestinal obstruction, and rupture of omental benign and malignant masses (22-26).

7.1. Omental Infarction and Omental Torsion:

Omental infarction is considered to be one of the factors causing the condition called abdominopelvic acute abdomen. In the literature, omental infarction was reported by Bush in 1896 and omental torsion by Eitel in 1899

(22,27). The distribution of cases in the literature is 75%-85% adult patients in their twenties to fifties and 15-25% pediatric patients (28,29). These cases account for 0.1% of diagnostic laparotomy operations performed for the acute abdomen. The etiology of primary or spontaneous omental infarction has not been fully understood. Secondary omental infarction (vasculitis, polycythemia, thrombophilia, hypercoagulability) and/or omental torsion develops following omental torsion caused by underlying tumors, hernias, localized inflammations, adhesions, trauma, and congenital anomalies (28-30,31).

Omental torsion occurs after the partial or complete rotation of the omentum around a fixed proximal point (unipolar fixation or unipolar torsion) or a long axis between two fixed points (bipolar fixation or bipolar torsion). Vascular compression, stasis, and edema occur after rotation. As torsion severity increases, arterial occlusion causes necrosis and hemorrhagic infarction. In all omental torsion cases developing secondary to an underlying pathology, 62.5% are bipolar torsion cases, and therefore bipolar torsion can be said to be more common (27-34).

Pain is the most common symptom and 100% of patients show this symptom. Although the localization of pain varies depending on the affected area of the omentum, it is most commonly localized to the right lower quadrant. In the differential diagnosis, it is confused with cholecystitis, diverticulitis, gynecological pathologies, and acute appendicitis depending on the localization of pain (28,31).

Abdominal US and computed tomography(CT) are effective radiological imaging modalities to exclude omental infarction and/or omental torsion in the differential diagnosis. In the abdominal US image, it is viewed as a hyperechoic round non-compressive intraabdominal mass attached to the umbilicus or peri-umbilical area on the anterior abdominal wall corresponding to the greater omentum. On abdominal CT, linear, fibrotic lines and whirl signs are seen within the fat folds. The “whirl” sign is a radiological finding specific to omental infarction or omental torsion (30,31).

In the literature, two different treatment approaches are mentioned for omental infarction and primary omental torsion: medical therapy and surgery. In medical therapy, combinations of oral analgesics, anti-inflammatories, and prophylactic antibiotherapy are started for patients who have got a clear diagnosis by excluding other potential causes in differential diagnoses (35). However, in the management of delayed diagnosis or conservative medical therapy, the recommended treatment is open or laparoscopic surgical resection due to the

risk of several complications such as adhesion, abscess, and sepsis, (36). Due to the development of surgical technology, the increase in laparoscopic surgery experience, minimally invasive surgery becoming widespread, reduction in the length of postoperative, and the intraabdominal diagnostic advantage of the procedure, laparoscopic surgical resection comes to the fore as the preferred technique (37) **(Figure 2).**

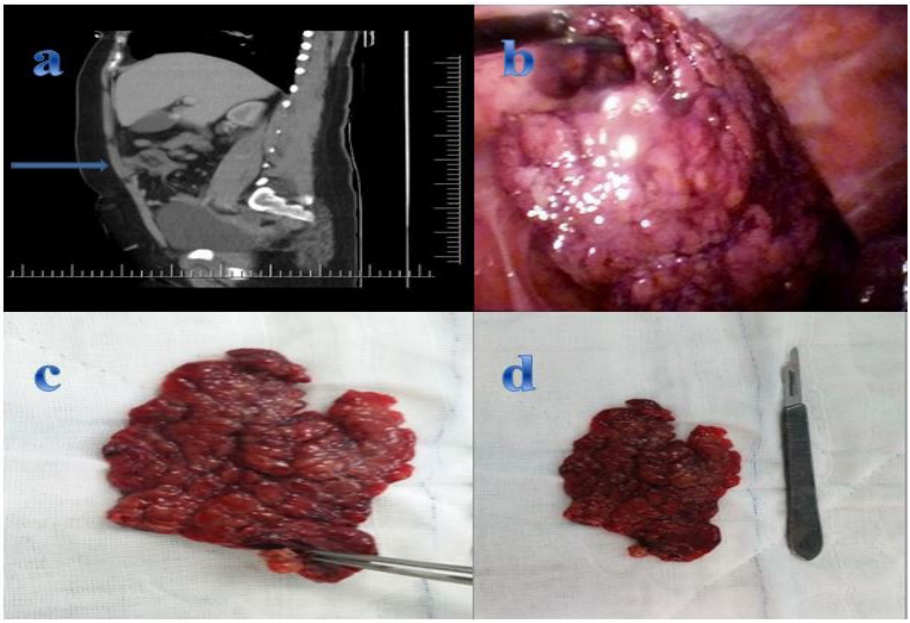


Figure 2: Torsion of the Omentum and Laparoscopic Resection (a: Abdominal computed tomographic image of segmental omental torsion; b: Laparoscopic image of segmental omental torsion; c and d: Resection image of segmental omental torsion)

7.2. Omental Hemorrhage

Despite the hemostatic function of the omentum, one of the pathologies that require abdominopelvic emergency surgical intervention is omental hemorrhages (18,19). In the literature, abdominal vascular trauma secondary to trauma has been reported in 2.7% to 33.8% of patients. In patients who underwent diagnostic laparotomy, the rate of vascular trauma is greater in patients with penetrating trauma than in patients with blunt trauma (38). Whereas the majority of omental hemorrhages (OH) develop following blunt and penetrating traumas,

spontaneous OH can be seen rarely in patients without a history of trauma. Thirty percent of spontaneous OH cases may end in death. Omental neoplasia, arteriovenous malformations, sildenafil citrate, hypertension, vasculitides, granulomatous diseases, collagen tissue diseases, and coagulation disorders due to anticoagulant and antiplatelet agents are considered responsible for its etiology (23,26,39).

In acute intra-abdominal OH, patients may present to emergency services with abdominal distension, abdominal pain, weakness, tachycardia, and hypotension. In delayed presentations or cases of severe acute intraabdominal OH, the signs and symptoms may deepen. These patients may have the symptoms and laboratory results showing abdominal compartment syndrome, hemorrhagic shock, confusion (Glasgow<14), decrease in body temperature (<35 °C), Acidosis (Arterial pH<7.2), Lactic acidosis (>5 mmol/L), Base deficit (>8 mmol/L), International Normalized Ratio (>1.5) (23,38).

Stabilizing the airway, breathing, and circulation is the first step in the management of spontaneous OH without trauma. After the analysis of the coagulopathy, the deficits in blood products and fluid are replaced and vitamin K is administered. When patients are hemodynamically stabilized, diagnostic tests for etiology such as US, CT, CT angiography (arterial and venous phase), and conventional angiography are performed. Radiologists can distinguish the features of blood in the ascitic fluid by looking at Hounsfield units (HU) [(Water:0 HU; Acute blood:30-45 HU; Coagulated blood 50-60 HU; Blood extravasation >85 HU)] (39). Although it has been reported in the literature that peritoneal lavage may be useful in distinguishing the characteristics of abdominal fluid, it is not one of the first-line diagnostic methods due to the risk of intestinal perforation (23).

Simultaneous minimally invasive trans-arterial embolization (TAE) can be performed in hemodynamically stable patients in whom the focus of bleeding has been identified with imaging methods. However, the success rate is 80% because of the rich vascular network and rich collaterals of the omentum (40). Regardless of the underlying etiology, surgery is the treatment option for OH in hemodynamically unstable patients with an unconfirmed diagnosis. Diagnostic laparotomy and laparoscopy are performed in these patients who are indicated to have surgery. Ligation, excision of the focus of bleeding, and partial or total omentectomy are performed within the scope of surgical treatment. These surgical interventions aiming to achieve hemodynamic stability are part of ongoing resuscitation (23,25,38).

7.3. Omental Acute Mechanical Intestinal Obstruction:

Acute mechanical intestinal obstruction (AMIO) is one of the abdominopelvic disorders that require emergency surgical intervention. Patients present to the emergency department with the symptoms of stomachache and intestinal obstruction. AMIO cases form 15% of the cases that present to the emergency services with an acute stomachache. The most common causes of AMIO respectively include adhesions (69%), neoplasms (20%), and hernia (10%) (41). An internal herniation is the protrusion of an abdominal organ through a defect in the peritoneum or mesentery due to congenital or acquired causes. AMIO develops as a result of herniated bowel loops getting stuck in such defects. Internal hernias are responsible for 0.2% to 0.9% of AMIO cases. Furthermore, transomental hernias compose 1% to 4% of all internal hernias. The majority of transomental hernias result from a defect in the right side of the greater omentum. On the other hand, cases of internal hernias resulting from a defect in the lesser omentum are quite rare (42,43). Additionally, there can be rare cases of AMIO secondary to congenital omental bands due to developmental anomalies between the greater and lesser omentums in etiology (24).

AMIO can be seen at any age (from 1 year to 80 years of age) and on all continents of the world. Patients apply to the emergency department with complaints of abdominal swelling, abdominal pain, vomiting, nausea, and constipation. In the physical examination, patients have cold and pale skin due to dehydration. In the rectal examination, the ampulla is empty. Symptoms of hypovolemic shock (tachycardia, hypotension, cold and pale skin), metabolic acidosis, leukocytosis, electrolyte imbalance, and prerenal azotemia may be seen secondary to impaired oral intake (41). The reason for emergency room presentation may be intermittent nonspecific symptoms or acute abdomen, depending on the herniated internal organs, the size of the defect, and the length of the herniated bowel loop. The causes of the abdominopelvic acute abdomen should be taken into consideration while making differential diagnosis (42,43). The first radiological approach is an upright abdomen X-ray performed to evaluate the air-fluid levels and bowel loop dilation. Additionally, barium X-rays provide useful information to assess the level and extend of intestinal obstruction (24). However, abdominal CT is more advantageous for the evaluation of conditions such as coexisting pathologies and bowel ischemia (air bubbles on the gastrointestinal wall) (41). In pregnant women, however, US and magnetic resonance imaging (MRI) are the first choices (44). Despite the use of such imaging methods, the diagnosis of omental AMIO is made perioperatively in most cases (42).

In the management of omental AMIO, the first step is fluid resuscitation with appropriate crystalloids to eliminate hypovolemia and electrolyte imbalance. Then, patients are prepared for emergency surgical intervention following the placement of a nasogastric tube for decompression. Preoperatively, a comprehensive examination (exploration) is performed to determine the intraabdominal organs that cause the obstruction, and then the herniated bowel segment is reduced. If present, the ischemic bowel segment is resected and an anastomosis or stoma is created. The omental defect is closed (42).

7.4. Rupture of Omental Benign and Malignant Masses

There may be rare cases of benign and malignant soft tissue tumors derived from the primary omentum (1). Primary omental tumors that have been reported in the literature include leiomyosarcoma, fibrosarcoma, rhabdomyosarcoma, myosarcoma, hemangiopericytoma (solitary fibrous tumor), leiomyoma, leiomyoblastoma, lipoma, fibroma, mesothelioma, cystic lymphangioma, endothelioma, and omental extra gastrointestinal stromal tumors. These tumors derive from the vessels forming the omentum, lymphatic adipose tissue, and the interstitial cells of Cajal. They may be rarely ruptured (26,45-48).

The complaints at the presentation include stomachache, distention, weight loss, and weakness. However, these signs and symptoms are non-specific as they can be generally observed in other gastrointestinal pathologies due to the mobile nature of the omentum (2,6,26,28,31,41,43,45-48). For this reason, in the cases of acute abdomen, radiological methods including US, CT, and MRI provide useful information prior to emergency surgery regarding the location, size, and characteristics (solid, cystic, semisolid) of the ruptured mass. However, exact information about the primary origin and immunohistological type can be obtained with a histopathological examination after surgical resection. Ruptured primary omental mass is treated with surgical resection in emergency open or laparoscopic surgery (26,47-49).

REFERENCES

1- Platell C, Cooper D, Papadimitriou JM et al. The omentum. World J Gastroenterol. 2000;6(2):169-176.

2-Atay A, Dilek ON. Is omentectomy necessary in the treatment of benign or malignant abdominal pathologies? A systematic review. World J Gastrointest Surg. 2021; 13(11):1497-1508.

3- Nicola VD. Omentum a powerful biological source in regenerative surgery. Regen Ther. 2019;11:182-191.

4- Kubai L, Auerbach $. A new source of embryonic lymphocytes in the mouse. Nature 1983;301(5896):154-6.

5- Elmohr MM, Blair KJ, Menias CO et al. The Lesser Sac and Foramen of Winslow: Anatomy, Embryology, and CT Appearance of Pathologic Processes. AJR Am J Roentgenol 2020;215(4):843-851.

6- Wang AW, Prieto JM, Cauvi DM et al. The Greater Omentum-A Vibrant and Enigmatic Immunologic Organ Involved in Injury and Infection Resolution. Shock 2020;53(4):384-390.

7- Suzuki D, Kim JH, Shibata S et al. Topographical anatomy of the greater omentum and transverse mesocolon: a study using human fetuses. Anat Cell Biol. 2019;52(4):443-454.

8- Liebermann-Meffert D. The greater omentum. Anatomy, embryology, and surgical applications. Surg Clin North Am. 2000;80(1):275-293.

9- Chung-Welch N, Patton WF, Shepro D et al. Human omental microvascular endothelial and mesothelial cells: characterization of two distinct mesodermally derived epithelial cells. Microvasc Res. 1997;54(2):108-20.

10- Shimotsuma M, Takahashi T, Kawata et al. Cellular subsets of the milky spots in the human greater omentum. Cell Tissue Res. 1991;264(3):599-601.

11- Cranshaw ML, Leak LV. Milky spots of the omentum: a source of peritoneal cells in the normal and stimulated animal. Arch Histol Cytol.

12-Nagano H, Goi T, Taguchi S et al. Capillary hemangioma arising from the lesser omentum in an adult: A case report. Medicine (Baltimore). 2020;99:e18693.

13- Zhetimkarimov DS, Ostrovskiĭ VK. [Significance of greater omentum anatomic structure]. Khirurgiia (Mosk). 1997;(6):41-43.

14-Cleypool CGJ, Schurink B, Horst DEM et al. Sympathetic nerve tissue in milky spots of the human greater omentum. J Ant. 2020;236(1):156-164.

15- Buscher K, Wang H, Zhang X, et al. Protection from septic peritonitis by rapid neutrophil recruitment through omental high endothelial venules. Nat Commun 2016;7:10828

16- Konturek Sj, Brzozowski T, Majka I et al. Omentum and basic fibroblast growth factor in healing of chronic gastric ulcerations in rats. Dig Dis Sci. 1994;39(5):1064-71. (doi: 10.1007/BF02087559.).

17- Bikfalvi A, Alterio J, Inyang AL et al. Basic fibroblast growth factor expression in human omental microvascular endothelial cells and the effect of phorbol ester. J Cell Physiol 1990;144(1):151-8.

18- Hisada Y, Mackman N. Tissue Factor and Extracellular Vesicles: Activation of Coagulation and Impact on Survival in Cancer. Cancers (Basel). 2021;13(15):3839.

19- Logmans A, Schoenmakers CH, Haensel SM et al. High tissue factor concentration in the omentum, a possible cause of its hemostatic properties. Eur J Clin Invest. 1996;26(1):82-83.

20- Zuk PA, Zhu M, Mizuno H et al. Multilineage cells from human adipose tissue: implications for cell-based therapies. Tissue Eng. 2001;7(2):211-28.

21- Shah S, Lowery E, Braun RK et al. Cellular basis of tissue regeneration by omentum. PLoS One. 2012;7(6):e38368.

22- Kamr WH, Taman SE, Tawfik AI. Multislice computed tomography evaluation of primary abdominal fat necrosis: a rare cause of acute abdominal pain. Pol J Radiol. 2019;84:e389-e396.

23-Lyu YX, Cheng YX, Li T. Spontaneous omental bleeding: a case report and literature review. BMC Surg. 2018;18(1):33.

24- Kassem MW, Patel M, Iwanaga J et al. Constriction of the Stomach by an Unusual Peritoneal Band. Cureus 2018;10(2):e2148.

25- Kataoka M, Saitoh T, Kawashima K et al. Primary Extragastrointestinal Stromal Tumor of Greater Omentum with Intraperitoneal Bleeding. Intern Med. 2021;60(21):3413-3419.

26- Murata T, Ishimori T, Naitou W et al. Laparoscopic resection for spontaneously ruptured primary extragastrointestinal stromal tumor of the greater omentum: A case report. Int Surg Case Rep. 2022;99:107567.

27- Eitel GG. Rare omental torsion. NY Med Rec. 1899; 55: 715–716

28- Montiel-Jarquin A, Lopez-Colombo A, Nava A et al. Clinical Characteristics of Torsion of the Omentum. Gastroenterology Res.2009;2(4):220-223.

29- Pinedo-Onofre JA, Guevara-Torres L. [Omental torsion. An acute abdomen etiology]. Gac Med Mex. 2007;143(1):17-20.

30- McCusker R, Gent R, Goh DW. Diagnosis and management of omental infarction in children: Our 10 year experience with ultrasound. J Pediatr Surg. 2018;53(7):1360-1364.

31- Subasinghe D, Jayasinghe R, Ranaweera G et al. Spontaneous omental infarction: A rare case of acute abdomen. SAGE Open Med Case Rep. 2022;10: 2050313X221135982.

32- Mihețiu A, Sandu A, Bratu D et al. Laparoscopic Management of Primary Omental Torsion. Case Rep Surg. 2021;2021:5536178.

33- Cremonini C, Bertolucci A, Tartaglia D et al. Acute abdomen caused by greater omentum torsion: A case report and review of the literature. Ulus Travma Acil Cerrahi Derg. 2016; 22(4): 391-4.

34- Corner EM, Grant L. A Case Of Torsıon Of The Great Omentum And Habıtual Partıal Reductıon En Masse. Br Med J. 1908;2(2497):1427-8.

35- Occhionorelli S, Zese M, Cappellari L et al. Acute Abdomen due to Primary Omental Torsion and Infarction. Case Rep Surg. 2014 ;208382: 4.

36- Tsironis A, Zikos N, Bali C et al. Acute Abdomen due to primary omental torsion : Case report. The Journal of Emergency Medicine 2013;44(1):45-48.

37- Ha JPY, Tang CN, Siu WT et al. Laparoscopic management of acute torsion of the omentum in adults.. JSLS. 2006; 10(3):351-4.

38- García A, Millán M, Burbano D et al. Damage control in abdominal vascular trauma. Colomb Med (Cali). 2021;52(2):e4064808.

39- Henry D, Satgunam S. Idiopathic omental bleeding. J Surg Case Rep. 2012;2012(9):2.

40- Maghrebi H, Zaiem A, Beji H et al. Spontaneous rupture of a left omental artery aneurysm treated by transcatheter arterial embolization: A case report. Ann Med Surg(Lond). 2022;82:104704.

41- Beg MY, Bains L, Lal P et al. Small bowel knots. Ann R Coll Surg Engl. 2020;102(8):571-576.

42- Rathnakar SK, Muniyappa S, Vishnu VH et al. Congenital Defect in Lesser Omentum Leading to Internal Hernia in Adult: A Rare Case Report. J Clin Diagn Res. 2016;10(8):PD08-9.

43- Ugianskis A. Lesser omental hernia without intestinal gangrene - Case report. Int J Surg Case Rep. 2022;96:107361.

44- Committee Opinion No. 723 Summary: Guidelines for Diagnostic Imaging During Pregnancy and Lactation. Obstet Gynecol. 2017;130(4):933-934.

45- Shin MK, Lee OJ, Ha CY et al. Malignant mesothelioma of the greater omentum mimicking omental infarction: a case report. World J Gastroenterol. 2009;15(38):4856-9.

46- Barel O, Qian C, Manolitsas T. Primary leiomyosarcoma of the omentum presenting as an ovarian carcinoma, case report and review of the literature. Gynecol Oncol Rep. 2016;17:75-78.

47-Yoshimura N, Ohara H, Miyabe K et al. A case of gastrointestinal stromal tumor with spontaneous rupture in the greater omentum. Int Semin Surg Oncol. 2008;5:19.

48- Takeda A, Ito H, Nakamura H. Large Omental Cystic Lymphangioma Masquerading as Mucinous Ovarian Neoplasia in an 8-Year-Old Premenarchal Girl: The Findings from Diagnostic Imaging and Laparoscopic-Assisted Excision. J Pediatr Adolesc Gynecol. 2017;30(6):659-662.

49-Tsopozidi M, Kepertis C, Godosis D et al. Laparoscopic-assisted excision of a huge polycystic omental lymphangioma in a 3 year old patient presenting with acute abdomen: case report and review. Pan Afr Med J. 2021;38:228.

CHAPTER XI

SURGICAL MANAGEMENT OF INFLAMMATORY BOWEL DISEASES

Emir Capkinoglu[1] & Cihan Atar[2]

(MD.), Acibadem University, Department of General Surgery
emircapkinoglu@gmail.com
ORCID: 0000-0002-4981-7623

(MD.), Osmaniye State Hospital, Department of General Surgery
cihanatar@hotmail.com
ORCID: 0000-0003-2359-5193

1. Ulcerative Colitis

Ulcerative colitis (UC) is an idiopathic, inflammatory, chronic disease affecting the mucosa of the colon and rectum with an increasing incidence for unknown reasons, affecting approximately 3.1 million people in the USA (1). It is more prevalent the ages of 15 and 30 and 55 and 65. The severity of the disease's symptoms changes throughout the course of a person's life, and remissions and relapses are part of its clinical presentation. Despite the continuous use of immunomodulatory drugs, 15-20% of patients undergo resection due to medically resistant disease and neoplasia(2). The primary determinant of disease severity and the key predictor of surgical intervention is the anatomical extent of mucosal inflammation.

1.1. Indications

1.1.1. Emergency Surgery Indications

Ulcerative colitis patients who experience multiple life-threatening complications may need urgent surgical intervention. These complications could include:

• Colon perforation - typically occurs due to toxic megacolon.

• Bleeding: Severe bleeding, typically associated with persistent, untreated anemia, is uncommon.

• Toxic megacolon, sometimes referred to as fulminant colitis, is characterized by complete or segmental hypotonic dilatation of the colon with a transverse diameter greater than 5.5 cm. Surgery should be performed if intensive intravenous steroid therapy is ineffective after 48–72 hours.

• Acute fulminant colitis resistant to medical treatment

1.1.2. Indications for Elective Surgery

Patients who are refractory to medical treatment are those who are resistant to therapies including steroids, immune modulators, and biologic medicines. Additionally, severe complications and adverse effects that arise from medical treatment are also reasons for elective surgery.

The need for elective surgery may also be indicated by dysplasia or cancer. In patients with ulcerative colitis, the cumulative risk rate for colorectal cancer is 2% in the first decade, 8% in second decade , and 18% in third decade (3).The malignancy diagnosis in patients with UC at an early stage are more difficult than patients with sporadic colorectal cancers. Regular colonoscopic examinations and several random biopsies should be carried out in long-term patients to rule out dysplasia.

1.2. Surgical Techniques

There are four surgical procedures used in ulcerative colitis surgery. All of these procedures involve complete resection of the colon, while reconstruction is performed in two of them, and an end ileostomy is performed in the other two. These operations can all be carried out via open, laparoscopic or robotic surgery.

In terms of short term outcomes like reduced surgical site infection, surgical trauma, analgesic use, fewer complication rate and shorter hospital stays, minimally invasive techniques outperform open procedures (4,5). Long-term results such as the recurrence rate and pouch functionality are identical(6). The patient's preferences and the surgeon's experience should be taken into consideration while determining a surgical strategy.

1.2.1. Total Proctocolectomy with Ileal Pouch Anal Anastomosis (IPAA): While entire colon and rectum are resected during this treatment, the anal

sphincter's functions are maintained. The pouch maintains a pelvic reservoir for intestinal contents. It is a surgical approach that provides positive outcomes for bowel functionality and fecal continence. IPAA can be performed in one, two or three stages after total proctocolectomy.

One stage IPAA- Anastomosis is completed in the same session with total proctolectomy.

Two-Stage IPAA- IPAA is performed with total proctocolectomy, although the diversion ileostomy is opened in the first session and closed in the second. This method is more popular today. There is insufficient evidence that diversion ileostomy prevents major complications such anastomotic leakage(7).

Three-Stage IPAA: In the first stage, resection of colon and end ileostomy are performed, in the second stage proctectomy-IPAA is performed and a diversion loop ileostomy is formed. In the third and final stage, the diversion loop ileostomy is closed. This method is routinely used in patients who have received anti-TNF therapy(8). Due to the elevated risk of septic complications and inadequate anastomosis healing, this approach is also preferable in patients who have undergone prolonged steroid treatment(9,10).

IPAA can be done using hand anastomosis or a stapler. The presence of dysplasia in the anal transitional zone must be taken into account. Hand anastomosis should be carried out following transanal mucosectomy if dysplasia is evident. A stapler can be used to perform anastomosis if there is no dysplasia. Patients with an intact anal transitional zone have greater continence outcomes(11).

1.2.2. Total Abdominal Colectomy with Ileorectal Anastomosis (TAC-IRA): In this procedure, the whole colon is resected and ileum is connected directly to the rectum. The results in terms of continence are better. This approach is not recommended as the patient has persistent symptoms and the risk of malignancy as a result of not resecting the affected rectum.

It can be applied if rectal involvement is minimal in young female patients who aim to preserve their fertility, in the patients with intermediate colitis where Crohn's disease cannot be ruled out, patients with advanced colon cancer accompanied by ulcerative colitis, in patients who are ineligible for IPAA but do not want a permanent ileostomy, and in patients for whom ileostomy is contraindicated (patients with ascites or portal hypertension).

1.2.3. Total Abdominal Colectomy(TAC) with End Ileostomy: In this procedure, the whole colon is resected, and the rectum is de-functionalized in

the form of a Hartmann's stump. It is a rapid procedure that is preferred in emergency surgeries.

1.2.4. Total Proctocolectomy with End Ileostomy: All of the colon and rectum are resected, and a permanent end ileostomy is created. It is a curative procedure for ulcerative colitis. This surgery is most suitable for patients who are eligible for a permanent stoma and cannot undergo IPAA.

1.3. Assessing Surgical Options

1.3.1. Emergency Surgery

The preferred procedures for UC patients undergoing emergency surgery are total colectomy and end ileostomy. Rather than being resected during this operation, the rectum is de-functionalized as a Hartmann's pouch. After TAC , a complementary proctectomy with an ultra-low Hartmann's pouch or suturing of the bleeding area via transanally is done to provide hemostasis in the event of persistent or refractory rectal bleeding. (12).

1.3.2. Elective Surgery

The most frequently performed procedure in patients undergoing elective surgery is the total proctocolectomy with IPAA procedure. Without the necessity for a permanent ileostomy, patients who undergo this procedure have a quality of life that is nearly normal.

Patients with inadequate anal sphincter function prior to surgery, complete proctocolectomy with end ileostomy or total colectomy with ileorectal anastomosis should be preferred since the entire proctocolectomy-IPAA method puts patients at risk for fecal incontinence.

Total colectomy with ileorectal anastomosis is the first surgical option for young female patients who are thinking about getting pregnant in order to prevent adhesion-related infertility. Total proctocolectomy-IPAA should be carried out when the patient's intention for conception ceases.

Appropriate surgical approach for elderly patients, individuals with severe comorbidities, and patients who also have concurrent rectal cancer is total proctocolectomy with end ileostomy. End ileostomy has benefits over total proctocolectomy with IPAA, including faster recovery times and fewer complications(13).

No distinction can be made between Crohn's disease and UC in 15-20% of patients with inflammatory bowel disease; this condition is known as

"intermediate colitis." Patients with fulminant colitis have it considerably harder to distinguish between the two. Patients with intermediate colitis frequently receive treatment for ulcerative colitis as their symptoms resemble UC more than Crohn's disease. However, these patients are more likely to experience post-operative pouch problems and perineal complications(14,15).

1.4. Perioperative Evaluation

For every patient who will have surgery for ulcerative colitis, the following measures should be routinely taken.

• Prior to surgery, the patient's conditions such as anemia, coagulopathy, nutritional disorder, acid-base imbalances, and electrolyte imbalances should be corrected to the greatest extent possible.

• If an ostomy is planned, its site should be marked before surgery.

• Mechanical bowel preparation should be done in patients who will undergo elective surgery.

• Prophylactic intravenous antibiotics should be administered. Oral antibiotics administered after mechanical bowel preparation substantially reduce surgical site infection(16).

• It is not recommended to discontinue anti-TNF agents and thiopurines before surgery(17).

• Venous thromboembolism prophylaxis should be applied as routine care for every patient who will have ulcerative colitis surgery(18).

1.5. Complications

In ulcerative colitis surgery, overall mortality is 1% and morbidity is 30% (19).

• **Strictures:** It is seen in 11% of patients(20). Transanal or endoscopic dilatation is beneficial for nonfibrotic strictures but reoperation is necessary for fibrotic strictures.

• **Pelvic Sepsis:** Its incidence has been reported as 9.5% (21). Due to pelvic fibrosis and reduced pouch compliance, it may lead to pouch failure (22).

• **Pouch Failure:** Depending on the follow-up intervals, this rate has been observed to range from 6.5-8.5% (23).

• **Fecal Incontinence:** Rates of mild and severe fecal incontinence were 17% and 3.7% during the day and 13.1% and 4.5% during the night, respectively(24).

- **Sexual Dysfunction:** There are very little evidence that IPAA causes sexual dysfunction. Patients who have undergone multiple pelvic surgeries are more likely to suffer from it.
- **Female Infertility:** After IPAA, women's fertility is drastically decreased (25).

2. Crohn's Disease

Crohn's Disease(CD) is an uncurable, chronic, idiopathic, inflammatory disease that affects more than 1 million people in the USA, and its incidence is growing constantly(26). The symptoms of the disease are variable, sometimes with acute exacerbations. Continuous immunosuppression is used to keep symptoms under control. As distinct from UC, it is not possible to resect all the organs at risk of Crohn's disease, hence there is no likelihood of curative surgery. Surgery is typically considered as a last resort for patients who do not respond to medical therapy and for the management of complications.

Between 50-70% of patients with CD require surgery at some point in their lives(27). After surgical resection, endoscopic recurrence is observed in 70–90% of patients, and 35% of them need surgical resection within 10 years(28,29). Multidisciplinary evaluation is crucial in patients with CD who need surgery due to the complicated clinical and long-term recurrence and reoperation requirements.

2.1. Preoperative Evaluation and Preparation

Many of the individuals with CD who require surgical therapy are young and may have a severe clinical presentation like sepsis or persistent complications like malnutrition. Before surgery, it is important to manage conditions including hypovolemia, electrolyte imbalance, anemia, and nutritional deficiencies.

Total parenteral nutrition's (TPN) effectiveness in improving nutritional status is controversial. Patients with long-term oral intolerance may benefit from TPN, although long-term complete parenteral nutrition prior to surgery should be avoided. In patients with fistulizing Crohn's disease, enteral feeding therapy has been demonstrated to lower postoperative septic complications (30).

While most Crohn's patients are under the influence of high-dose steroids, immunomodulators or biologic agents, surgical treatment may be required and these treatments may have an impact on the outcomes of the surgery performed. Prior to elective surgery, it is advised that patients using steroids

should progressively lower their dose to less than 20 mg, as excessive doses of these drugs increase the risk of postoperative infectious complications (31). Most immunomodulators (eg, azothiopurine, mercaptopurine) can be used until the time of surgery (9). The effects of preoperative use of biological agents on surgical outcomes are controversial.

2.2. Surgical Techniques

2.2.1. Endoscopic Dilation

In certain patients who are not suitable for surgery, dilation using an endoscopic hydrostatic balloon can be utilized to treat small intestinal strictures or post-surgical anastomotic strictures (32). Success of the balloon or the requirement for further surgery are unaffected by the active disease severity or medical therapy following dilation (33).

2.2.2. Small Bowel Resection or Ileocecal Resection

If a patient has short segment stenosis or fistulizing disease due to CD , the most effective approach to control the disease and improve quality of life is resection of small bowel (34). Small bowel resection in Crohn's disease is made in the presence of a diseased or perforated segment or in the presence of an adjacent organ-associated abscess or fistula. If the terminal ileum is affected, ileocecal resection should be performed. Given the likelihood that these individuals may need several operations during their lifespan, resection should be kept to a minimum.

During surgery, intestinal segments should be spared as much as possible since the disease frequently recurs. Surgical margins can be identified by inspection since microscopic disease at the resection margins doesn't raise the likelihood of recurrence. A frozen study during surgery is not necessary (35). Anastomosis following resection is totally at the decision of the surgeon, and no particular kind of anastomosis has been shown as the best technique for the management of CD (36).

In Crohn's disease, laparoscopic small bowel resection is becoming more common. Less small intestinal obstruction, a decreased risk of incisional hernias, lower morbidity, and shorter recovery times are benefits of laparoscopic surgery over open surgery (37). Laparoscopic surgery should therefore be performed at centers with adequate experience.

2.2.3. Strictureplasty

Strictureplasty is an option for treating small intestinal strictures caused by Crohn's disease, either by alone or in conjunction with resection of another intestinal segment. If a significant portion of the ileum was resected during prior procedures, strictureplasty is a viable substitute for small bowel resection.

Three types of strictureplasty are currently used (38).

• Heineke-Mikulicz is the most commonly used technique (85%). A lengthwise enterotomy is applied on the antimesenteric side of the strictured segment, and it is subsequently transversely closed. Heineke-Mikulicz strictureplasties can be carried out more than once in a single session. It may be used in strictures that are up to 10 cm long.

• The frequency of Finney strictureplasty is 5-10%. A lengthwise enterotomy is performed on the antimesenteric side of the diseased segment, the intestine is folded over itself and the enterotomy is closed antiperistaltically side by side. It is performed in strictures with 10-20 cm length.

• If there are multiple narrowed segments occurring in a long bowel part, we should performe side-by-side isoperistaltic strictureplasty (SSIS) . It accounts for 5-10% of all strictureplasties. The narrowed segment is divided in the middle to include the mesentery, and the distal and proximal segments are closed isoperistaltically side by side by enterotomy. It is applied in stenoses longer than 20 cm.

2.2.4. Large bowel and rectum resection

Segmental resection of colon, total colectomy with ileorectal anastomosis, total proctocolectomy with end iloestomy and proctectomy can be performed for Crohn's colitis and proctitis

• **Colectomy:** In colon limited cases, such as colonic strictures that preclude endoscopic surveillance, segmental colectomy is adequate. When two or more colon segments are affected, a total colectomy should be done. While recurrence occurs sooner following segmental colectomy, the effectiveness of both procedures are comparable(39). Patients without rectal involvement should have ileorectal anastomosis after total colectomy.

• **Proctectomy:** Proctectomy can be performed in patients with refractory proctitis without colonic involvement. Intersphinteric dissection should be

performed instead of abdominoperineal resection to minimize the risk of non-healing perineal wound and sexual dysfunction in Crohn's patients (40). Rectal involvement of Crohn's disease should not be mixed up with perianal CD, which includes symptoms and findings such as anal fissure, fistula and abscess. Perianal Crohn's disease should be treated with medical therapy and surgical procedures without resection.

• **Proctocolectomy:** Patients with precancerous or malignant lesions in the colon or rectum as well as those with long-term disease may benefit from total proctocolectomy. In eligible patients, total proctocolectomy is linked to lower morbidity, low recurrence risk, and a prolonged disease-free period (41).

2.3. Surgical Approaches and Indications

Refractory Disease: The therapy is deemed ineffective and a surgical approach is recommended if the symptoms persist despite aggressive treatment, deteriorate when the treatment dose is reduced, or develop complications as a result of the medical approach. In this scenario, anastomosis and resection of the affected segments should be carried out.

Perforation: Urgent surgery is required to control sepsis and peritonitis after intestinal perforations. Perforation is the indication in 1-16% of CD patients who underwent surgery (42). The perforated segment needs to be resected immediately. In cases such as hemodynamic instability, edematous bowels, intra-abdominal contamination or malnutrition, a diversion ostomy should be preferred over anastomosis after resection.

Abscess: In patients with intra-abdominal abscesses due to CD, treatment option is antibiotics and percutaneous or surgical drainage. The most favored method for intra-abdominal abscesses is percutaneous drainage. Depending on the location of the abscess, it can be applied transabdominal or transgluteal. It can also be repeated for residual and recurrent abscesses. Percutaneous drainage is used in 70% of Crohn-associated abscesses (43). If the abscess-related diseased segment is not resected after the abscess is treated, 30% of the abscesses will recur. In order to avoid short bowel syndrome and malnutrition, patients with long segment disease or with a history of previous resection, surgical resection may not be performed and abscesses are managed without surgery (44).

When percutaneous drainage is not possible or is unable to control peritoneal sepsis, surgical drainage is used. The decision of surgical drainage is made in accordance with patient's condition and intraoperative findings.

Fistula: It's believed that transmural inflammation can cause the development of sinus tracts. Sinus tracts reaching the serosa may cause fistulas. Enteric fistulas may develop in 15% of Crohn's patients and are most often associated with the bladder, skin, vagina, or other intestinal segments.

In almost half of individuals with fistulizing Crohn's, biological agents are effective (45). Resection of the affected intestinal segment and repair of the adjacent organ are necessary for refractory fistulas. Surgeons should prevent performing bypass surgery of intestines. Permanent illness in the bypassed section may result in adverse effects such as abscess, hemorrhage, bacterial overgrowth, or cancer.

Strictures: Strictures can be seen in 5-24% of Crohn's patients (46). The strictures may be inflammatory, fibrostenotic, or both. Inflammatory strictures are treated with medical treatment and fibrostenotic strictures are treated with endoscopic dilation or surgery, so it is crucial to identify the type of stenosis before treatment.

Treatment options for small bowel strictures include strictureplasty, resection, and endoscopic dilation. The treatment decision to be applied is determined according to the length of the stenosis, whether it is complex or not, and the intestinal reserve. If they can be accessed endoscopically, strictures less than 5 cm that are not accompanied by any inflammation or penetrating disease can be treated with dilation.

Surgery should be performed in strictures longer than 5 cm, multifocal, complex and in which endoscopic treatment fails (31).

In patients with common and recurrent strictures of the duodenum, jejunum, ileum, neoterminal ileum (after ileocecal resection) and especially in patients with short bowel syndrome , strictureplasty should be preferred. It is contraindicated in the presence of inflammatory mass, thick and inflexible bowel wall, malignancy, bleeding and malnutrition (31).

Colorectal stenosis occurs in 9-13% of Crohn's stenosis. They typically occur in a single segment, and 2-6% of them are associated with malignancy or dysplasia (47). Crohn-related colorectal strictures should be evaluated with endoscopic biopsy. Surgical resection should be performed in patients who cannot underwent endoscopic dilation successfully. Strictureplasty cannot be applied in colorectal stenosis (48).

Malignancy: Crohn's disease, due to long-term chronic inflammation, can lead to malignant transformation of the mucosa. Colon and rectum are much more likely to develop malignant lesions compare to small intestines. Routine

colonoscopic follow-up should be planned in patients with Crohn's disease no later than 8 years after the onset of symptoms (49).

Patients who have colonic malignancy due to CD should be managed as follows (31): Endoscopic resection can be applied to patients with dysplasia and then they can be followed up. If endoscopic resection cannot be performed or if dysplasia is multifocal, total colectomy or proctocolectomy should be performed. For patients with adenocarcinoma, total colectomy or proctocolectomy is performed.

Hemorrhage: If the patient is stable, endoscopic or angiographic management is typically used to treat gastrointestinal hemorrhages associated with CD. Surgery is indicated if the patient is unstable. Targeted surgery is carried out if the cause of the bleeding can be identified by preoperative imaging or during the procedure. Colonic hemorrhages with multiple foci or for which it is impossible to identify the bleeding source can be treated with total colectomy (50).

Inflammation: A medical treatment-responsive inflammatory phenotype is observed in 56–81% of CD patients (46). However, patients who are resistant to medical therapy, are incompatible with therapy, or experience complications require surgical treatment.

REFERENCES

1. Rubin DT, Ananthakrishnan AN, Siegel CA, et al. ACG Clinical Guideline: Ulcerative Colitis in Adults. Am J Gastroenterol. Mar 2019;114(3):384-413.

2. Holubar SD, Privitera A, Cima RR, et al. Minimally invasive total proctocolectomy with Brooke ileostomy for ulcerative colitis. Inflamm Bowel Dis. Sep 2009;15(9):1337-42.

3. Itzkowitz SH, Harpaz N. Diagnosis and management of dysplasia in patients with inflammatory bowel diseases. Gastroenterology. May 2004;126(6):1634-48.

4. Douard R. Systematic review and meta-analysis of laparoscopic versus open colectomy with end ileostomy for non-toxic colitis (Br J Surg 2013: 100: 726–733). British J of Surg 2013;100(6):733-734.

5. Gill TS, Karantana A, Rees J, et al. Laparoscopic proctocolectomy with restorative ileal-anal pouch. Colorectal Disease. 2004;6(6):458-461.

6. Larson DW, Dozois EJ, Piotrowicz K, et al. Laparoscopic-assisted vs. open ileal pouch-anal anastomosis: functional outcome in a case-matched series. Dis Colon Rectum. Oct 2005;48(10):1845-50.

7. Remzi FH, Fazio VW, Gorgun E, et al. The outcome after restorative proctocolectomy with or without defunctioning ileostomy. Dis Colon Rectum. Apr 2006;49(4):470-7.

8. Schluender SJ, Ippoliti A, Dubinsky M, et al. Does infliximab influence surgical morbidity of ileal pouch-anal anastomosis in patients with ulcerative colitis? Dis Colon Rectum. Nov 2007;50(11):1747-53.

9. Aberra FN, Lewis JD, Hass D, et al. Corticosteroids and immunomodulators: postoperative infectious complication risk in inflammatory bowel disease patients. Gastroenterology. Aug 2003;125(2):320-7.

10. Lake JP, Firoozmand E, Kang JC, et al. Effect of high-dose steroids on anastomotic complications after proctocolectomy with ileal pouch-anal anastomosis. J Gastrointest Surg. Jul-Aug 2004;8(5):547-51.

11. Fazio VW, O'Riordain MG, Lavery IC, et al. Long-term functional outcome and quality of life after stapled restorative proctocolectomy. Ann Surg. Oct 1999;230(4):575-84; discussion 584-6.

12. Yokoyama T, Masaki T, Ono M, et al. Per anal suturing of a bleeding ulcer to achieve successful hemostasis of massive hemorrhage associated with ulcerative colitis: report of two cases. Surg Today. 1998;28(11):1179-81.

13. da Luz Moreira A, Lavery IC. Ileorectal anastomosis and proctocolectomy with end ileostomy for ulcerative colitis. Clin Colon Rectal Surg. Dec 2010;23(4):269-73.

14. Yu CS, Pemberton JH, Larson D. Ileal pouch-anal anastomosis in patients with indeterminate colitis. Diseases of the Colon & Rectum. 2000/11/01 2000;43(11):1487-1496.

15. Delaney CP, Remzi FH, Gramlich T, et al. Equivalent function, quality of life and pouch survival rates after ileal pouch-anal anastomosis for indeterminate and ulcerative colitis. Ann Surg. Jul 2002;236(1):43-8.

16. Oshima T, Takesue Y, Ikeuchi H, et al. Preoperative oral antibiotics and intravenous antimicrobial prophylaxis reduce the incidence of surgical site infections in patients with ulcerative colitis undergoing IPAA. Dis Colon Rectum. Oct 2013;56(10):1149-55.

17. Lau C, Dubinsky M, Melmed G, et al. The impact of preoperative serum anti-TNFα therapy levels on early postoperative outcomes in inflammatory bowel disease surgery. Ann Surg. Mar 2015;261(3):487-96.

18. Irving PM, Pasi KJ, Rampton DS. Thrombosis and Inflammatory Bowel Disease. Clinical Gastroenterology and Hepatology. 2005;3(7):617-628.

19. Fazio VW, Kiran RP, Remzi FH, et al. Ileal pouch anal anastomosis: analysis of outcome and quality of life in 3707 patients. Ann Surg. Apr 2013;257(4):679-85.

20. Prudhomme M, Dozois RR, Godlewski G, et al. Anal canal strictures after ileal pouch-anal anastomosis. Dis Colon Rectum. Jan 2003;46(1):20-3.

21. Hueting WE, Buskens E, van der Tweel I, et al. Results and complications after ileal pouch anal anastomosis: a meta-analysis of 43 observational studies comprising 9,317 patients. Dig Surg. 2005;22(1-2):69-79.

22. Kiely JM, Fazio VW, Remzi FH, et al. Pelvic sepsis after IPAA adversely affects function of the pouch and quality of life. Dis Colon Rectum. Apr 2012;55(4):387-92.

23. Hahnloser D, Pemberton JH, Wolff BG, et al. Results at up to 20 years after ileal pouch-anal anastomosis for chronic ulcerative colitis. Br J Surg. Mar 2007;94(3):333-40.

24. Banasiewicz T, Marciniak R, Paszkowski J, et al. Pouchitis may increase the risk of dysplasia after restorative proctocolectomy in patients with ulcerative colitis. Colorectal Dis. Jan 2012;14(1):92-7.

25. Johnson P, Richard C, Ravid A, et al. Female infertility after ileal pouch-anal anastomosis for ulcerative colitis. Dis Colon Rectum. Jul 2004;47(7):1119-26.

26. Dahlhamer JM, Zammitti EP, Ward BW, et al. Prevalence of Inflammatory Bowel Disease Among Adults Aged ≥18 Years - United States, 2015. MMWR Morbidity and mortality weekly report. 2016;65(42):1166-1169.

27. Gardiner KR, Dasari BV. Operative management of small bowel Crohn's disease. Surg Clin North Am. Jun 2007;87(3):587-610.

28. Olaison G, Smedh K, Sjödahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualised ileal ulcers preceding symptoms. Gut. Mar 1992;33(3):331-5.

29. Frolkis AD, Lipton DS, Fiest KM, et al. Cumulative incidence of second intestinal resection in Crohn's disease: a systematic review and meta-analysis of population-based studies. Am J Gastroenterol. Nov 2014;109(11):1739-48.

30. Li G, Ren J, Wang G, et al. Preoperative exclusive enteral nutrition reduces the postoperative septic complications of fistulizing Crohn's disease. Eur J Clin Nutr. Apr 2014;68(4):441-6.

31. Lightner AL, Vogel JD, Carmichael JC, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Surgical

Management of Crohn's Disease. Dis Colon Rectum. Aug 2020;63(8):1028-1052.

32. Bhalme M, Sarkar S, Lal S, et al. Endoscopic balloon dilatation of Crohn's disease strictures: results from a large United kingdom series. Inflamm Bowel Dis. Feb 2014;20(2):265-70.

33. Van Assche G, Thienpont C, D'Hoore A, et al. Long-term outcome of endoscopic dilatation in patients with Crohn's disease is not affected by disease activity or medical therapy. Gut. 2010;59(3):320-324.

34. Delaney CP, Kiran RP, Senagore AJ, et al. Quality of life improves within 30 days of surgery for Crohn's disease. J Am Coll Surg. May 2003;196(5):714-21.

35. Fazio VW, Marchetti F, Church M, et al. Effect of resection margins on the recurrence of Crohn's disease in the small bowel. A randomized controlled trial. Ann Surg. Oct 1996;224(4):563-71; discussion 571-3.

36. Michelassi F. Crohn's recurrence after intestinal resection and anastomosis. Dig Dis Sci. Jul 2014;59(7):1352-3.

37. Lee Y, Fleming FJ, Deeb AP, et al. A laparoscopic approach reduces short-term complications and length of stay following ileocolic resection in Crohn's disease: an analysis of outcomes from the NSQIP database. Colorectal Dis. May 2012;14(5):572-7.

38. Duraes LC, Holubar SD. Bowel-Preserving Surgery for Diffuse Stricturing Crohn's Jejunoileitis. Dis Colon Rectum. Oct 1 2022;65(10):1167-1171.

39. Tekkis PP, Purkayastha S, Lanitis S, et al. A comparison of segmental vs subtotal/total colectomy for colonic Crohn's disease: a meta-analysis. Colorectal Dis. Feb 2006;8(2):82-90.

40. Bauer JJ, Gelernt IM, Salk BA, et al. Proctectomy for inflammatory bowel disease. Am J Surg. Jan 1986;151(1):157-62. doi:10.1016/0002-9610(86)90026-7

41. Fichera A, McCormack R, Rubin MA, et al. Long-term outcome of surgically treated Crohn's colitis: a prospective study. Dis Colon Rectum. May 2005;48(5):963-9.

42. Werbin N, Haddad R, Greenberg R, et al. Free perforation in Crohn's disease. Isr Med Assoc J. Mar 2003;5(3):175-7.

43. Xie Y, Zhu W, Li N, et al. The outcome of initial percutaneous drainage versus surgical drainage for intra-abdominal abscesses in Crohn's disease. Int J Colorectal Dis. Feb 2012;27(2):199-206.

44. Fleshman JW. Pyogenic complications of Crohn's disease, evaluation, and management. J Gastrointest Surg. Dec 2008;12(12):2160-3.

45. Taxonera C, Barreiro-de-Acosta M, Bastida G, et al. Outcomes of Medical and Surgical Therapy for Entero-urinary Fistulas in Crohn's Disease. J Crohns Colitis. Jun 2016;10(6):657-62.

46. Aniwan S, Park SH, Loftus EV, Jr. Epidemiology, Natural History, and Risk Stratification of Crohn's Disease. Gastroenterol Clin North Am. Sep 2017;46(3):463-480.

47. Sonnenberg A, Genta RM. Epithelial Dysplasia and Cancer in IBD Strictures. J Crohns Colitis. Sep 2015;9(9):769-75.

48. Broering DC, Eisenberger CF, Koch A, et al. Strictureplasty for large bowel stenosis in Crohn's disease: quality of life after surgical therapy. Int J Colorectal Dis. Apr 2001;16(2):81-7.

49. Kiran RP, Khoury W, Church JM, et al. Colorectal cancer complicating inflammatory bowel disease: similarities and differences between Crohn's and ulcerative colitis based on three decades of experience. Ann Surg. Aug 2010;252(2):330-5.

50. Raphaeli T, Menon R. Current treatment of lower gastrointestinal hemorrhage. Clin Colon Rectal Surg. Dec 2012;25(4):219-27.

CHAPTER XII

DIVERTICULAR DISEASE OF THE COLON AND EMERGENCY PRESENTATIONS

Caner Doğan

(General Surgeon.), Gaziantep 25 Aralık State Hospital,
Department of General Surgery
E-mail: dr_canerdogan@hotmail.com
ORCID: 0000-0002-5710-4420

1. Diverticulosis

1.1. General Information

Diverticulosis refers to the presence of diverticula in the absence of inflammation. While diverticula can involve almost all intestinal segments in the gastrointestinal system, their clinical picture is mostly characterized by sigmoidal colon involvement. Most cases are referred to as pseudo-diverticula due to mucosal and submucosal protrusions and are observed in weak areas where blood vessels infiltrate the intestinal walls secondary to increased intraluminal pressure.

Diverticular disease refers to cases in which the diverticula have become symptomatic, with such symptoms as diverticular bleeding, diverticulitis and associated segmental colitis (1). They are common in industrialized countries, with increased incidence in the Western world (2,3). The condition remains asymptomatic in most cases, and is identified incidentally during colon imaging in some patients, while almost 25% present with clinical signs (4).

On the other hand, diverticulitis refers to diverticula accompanied by infection and inflammation.

1.2. Etiology

While the exact cause of diverticulosis remains unknown, high segmental intraluminal pressure and impaired intestinal peristalsis have been implicated

in the etiology, and some lifestyle choices and environmental factors are also suggested to play a role (5,6). Several studies have reported an association between the development of diverticulosis and low-fiber and red meat-rich diets (7), while other studies have reported a greater risk of diverticulitis and bleeding in the obese (8), and an increased incidence of diverticular abscess and perforation in smokers (9).

1.3. Epidemiology

Diverticulosis is more commonly associated with Western lifestyles, and affects some 5–45% of the Western world population, with prevalence increasing by age (9). It most commonly localizes in the left colon, with almost 95% of patients developing diverticula in the sigmoidal colon (10,11). In contrast, the incidence of diverticulitis varies between 13% and 25% in Asian populations, and most commonly develops in the right colon (9).

1.4. Pathophysiology

Diverticulosis was for many years considered an age-dependent condition, however, several other contributing factors have been established more recently. Factors such as micro changes in the intestinal environment, genetics, environmental factors, mucosal inflammation, and enteric nervous system and neuroimmune changes have been suggested to play significant roles in the pathophysiology of the disease (4).

1.5. Patient Assessment

While the majority of patients with diverticulosis will experience an asymptomatic clinical course, those with diverticulitis generally present with pain in the left lower quadrant, accompanied sometimes by a palpable mass in the same region. Fever may also be encountered, as well as cramping pains accompanied by altered intestinal habits. Sepsis and extensive peritoneal findings are among the potential complications.

Biochemical examinations will reveal leukocytosis and elevated inflammatory markers (12).

A physical examination and biochemical analysis can be followed by ultrasonography (US), barium enema and colonoscopy. Due to the risk of perforation, barium-based investigations and colonoscopy are contraindicated in acute cases, and so a pelvic and abdominal computerized tomography (CT) with

oral and intravenous contrast approach is more commonly preferred due to its diagnostic sensitivity (13), allowing such complicated findings of diverticulitis as abscess, fistula formation and intraabdominal free air to be more easily detected (14).

1.6. Differential Diagnosis

Due to the localization of diverticulitis, a long list of differential diagnoses, varying from acute appendicitis to pelvic inflammatory disease, should be kept in mind. The condition is almost always asymptomatic, and sometimes the only sign can be rectal bleeding. The below diagnoses should thus be considered in differential diagnosis:

- Acute gastritis
- Acute cholecystitis
- Acute appendicitis
- Acute pancreatitis
- Acute pyelonephritis
- Acute cholangitis
- Mesenteric ischemia
- Irritable bowel disease
- Pelvic inflammatory disease (PID)
- Colon polyps
- Colon Cancer
- Hemorrhoids

1.7. Treatment Algorithm – Patient Management

When encountering a case of diverticulitis, it should first be established whether it is complicated, as the treatment algorithm will vary accordingly.

1.7.1. Emergency Cases

1.7.1.1. Bleeding: Some 5–15% of patients with diverticulosis develop bleeding, and one-third of cases will develop massive bleeding. Of all the diverticular bleedings, 50–60% originate from right colon diverticulitis. The closeness of the vasa recta to the bowel lumen increases the risk of bleeding in diverticulitis. Diverticular bleeding typically develops in the absence of diverticular inflammation or infection (diverticulitis) (9). Along with

angiodysplasia, diverticulosis is a significant cause of gastrointestinal system bleeding. It can often be difficult to identify the origin of bleeding, and bleeding stops spontaneously in almost 80% of cases (15). In some cases, colonoscopy or angiography can allow an intervention thorough identification of the bleeding diverticulitis. In rare cases where the bleeding continues or recurs, laparotomy and segmental colectomy may become necessary (15).

1.7.1.2. Diverticulitis: Diverticulitis refers to cases of diverticula accompanied by infection and inflammation. Microscopic or macroscopic perforations of diverticula can lead to peri-diverticular or peri-cholic infection, and can follow various clinical courses, varying from uncomplicated diverticulitis that can be managed on an outpatient basis, to acute abdominal presentations requiring emergency surgery. The life-long risk of people with diverticula who develop diverticulitis has been reported to be almost 20% (16), with diverticulitis development being correlated with increasing age. Smoking, obesity, low-fiber diets and alcohol use increases the risk of diverticulitis in patients with diverticulosis (17). Regular (2 to 3 times a week) NSAID use also increases the risk of complicated diverticulitis and perforation (17,18). Of those who develop diverticulitis, 12% can become complicated with a clinical picture characterized by perforation, abscess, obstruction and fistula (19). Diverticulitis episodes do not recur in 50–70% of cases (15), with a 5-year recurrence rate following the first episode of around 20% being reported (20). While post-episode resection was previously recommended, recent studies have reported that recurrent episodes increase neither the risk of complications nor surgery (15). In exceptional cases, colectomy after the first episode is still recommended in immunodeficient patients (15) and the rate of mortality and morbidity is elevated in these patients (21). Elective colonoscopy (recommended 6-8 weeks after) is recommended to all those who have a diverticulitis episode to exclude malignity.

1.7.2. Non-Complicated Diverticulitis: Non-complicated diverticulitis is generally characterized by left lower quadrant pain and tenderness. Most patients can be treated on an outpatient basis with wide-spectrum antibiotics, analgesics, 2–3 days of a low-sediment diet, and mostly fluid. Antibiotic therapy is given for 7 to 10 days, however, the efficacy on gram-negative and anaerobic bacteria must be considered when selecting a drug (22). The clinical picture of most patients improves within 48–72 hours of the start of antibiotic therapy.

A lack of improvement may indicate abscess development, which should be managed using such advanced techniques as CT.

Diverticulitis does not always require hospitalization, and can be successfully managed by such conservative approaches as antibiotics and an appropriate diet (23). In non-complicated diverticulitis, inflammation and potential micro-perforations are localized in the intestinal walls and mesenterium, and CT may reveal an increase in pericolic fat density in these patients (24).

1.7.3. Complicated diverticulitis

In cases of complicated diverticulitis, CT most commonly reveals abscesses (24), while fistula, strictures and free perforations may also be present. The incidence of complicated diverticulitis varies between 12% and 40%, and while 80% of cases can be successfully managed without the need for surgery (17,24,25), inpatient treatment may be needed in patients with immunosuppression, sepsis, old age or oral intake intolerance.

Patients with abscesses can be treated with antibiotherapy when they are smaller than 3–4 cm and localized along the colon, without considering surgery (26). In cases of abscesses larger than 4 cm, percutaneous drainage should be considered in addition to antibiotherapy (26).

Fistula formation is another complication of acute diverticulitis, reported in less than 5% of cases. While it can be observed in colovesical, colovaginal, coloenteric, colouterine and colocutaneous forms, the colovesical form is observed in 65% of cases (27). Fecalurea is the pathognomonic finding of a colovesical fistula.

Complete intestinal obstructions are rarer than partial intestinal obstructions in the presence of diverticulitis, and such obstructions are generally managed by a conservative approach.

When present, free perforation may be accompanied by extensive peritonitis and sepsis, and will require surgical treatment.

Recent studies have reported no association between the use of antibiotics and significant outcomes when compared to non-use in patients selected after the exclusion of peritonitis, perforation and hemodynamic instability (28).

Despite the availability of several grading systems for the classification of complicated diverticulitis, the CT-based modified Hinchey classification (table 1) is currently the most popular.

Table1. Modified Hinchey Classification

Stage	Description
Modified Hinchey classification	
0	Mild clinical diverticulitis
Ia	Confined pericolic inflammation or phlegmon
Ib	Confined pericolic abscess
II	Pelvic, distant intra-abdominal or retroperitoneal abscess
III	Generalized purulent peritonitis
IV	Generalized fecal peritonitis

1.7.4. Surgical Procedures

Hinchey 1a and 1b (table) diverticulitis can be successfully managed by medical treatment.

In the absence of perforated diverticulitis findings, Hinchey 2 (table 1) diverticulitis can be treated with percutaneous drainage, and such cases may be considered for elective sigmoid colectomy and primary anastomosis.

In the presence of findings of perforated diverticulitis (Hinchey 3-4) (table 1), sigmoid colectomy, Hartmann procedure and opening an edge-colostomy are advised, protecting the patient from the risk of anastomosis leak. Another suggested approach to the management of Hinchey 3-4 (table 1) diverticulitis involves resection followed by colorectal anastomosis and proximal deviator ileostomy, although there have to date been an insufficient number of studies comparing the two methods (29).

In patients undergoing resection, resecting the sigmoid colon up to the rectum will minimize the risk of diverticulitis recurrence.

1.8. Role of Elective Surgery

Deciding on the optimum time for elective surgery remains difficult. The number of elective sigmoid resections over the last 10 years has decreased as a result of the effective use of both medical treatments and interventional methods in cases of diverticulitis (24,30-32).

1.9. Patient Education

To protect the patient from diverticulitis recurrence, patients must be advised to follow a high-fiber diet, to drink plenty of water and to take regular

exercise, and to soften their diet in the event of constipation. It is of vital importance that they be aware of any changes in bowel movements.

References

1- Cuomo R, Cargiolli M, Cassarano S et al. Treatment of diverticular disease, targeting symptoms or underlying mechanisms. Curr Opin Pharmacol. 2018 Dec;43:124-131.

2- Cuomo R., Barbara G., Pace F et al. Italian consensus conference for colonic diverticulosis and diverticular disease. United Eur. Gastroenterol. J. 2014;2:413–442.

3- Etzioni D.A, Mack T.M, Beart R.W et al. Diverticulitis in the United States: 1998–2005: Changing patterns of disease and treatment. Ann. Surg. 2009;249:210–217.

4- Barbaro MR, Cremon C, Fuschi D. et al. Pathophysiology of Diverticular Disease: From Diverticula Formation to Symptom Generation, Int J Mol Sci. 2022 Jun; 23(12): 6698.

5- Almadi MA, Barkun AN. Patient Presentation, Risk Stratification, and Initial Management in Acute Lower Gastrointestinal Bleeding. Gastrointest Endosc Clin N Am. 2018 Jul;28(3):363-377.

6- Tursi A. A critical appraisal of advances in the diagnosis of diverticular disease. Expert Rev Gastroenterol Hepatol. 2018 Aug;12(8):791-796.

7- Manousos O, Day NE, Tzonou A et al. Diet and other factors in the aetiology of diverticulosis: an epidemiological study in Greece. Gut. 1985 Jun;26(6):544-9.

8- Brandl A, Kratzer T, Kafka-Ritsch R et al. Diverticulitis in immunosuppressed patients: A fatal outcome requiring a new approach? Can J Surg. 2016 Aug;59(4):254-61.

9- Naren S. Nallapeta; Umer Farooq. Diverticulosis, Statpearls Publishing, 2022 Sep

10- Yang F, Lin L, Jiang X, Lv H, Sun C. Increasing Diverticulosis in an Aging Population: A Colonoscopy-Based Study of 5-Year Trends in 26 463 Patients in Northern China. Med Sci Monit. 2018 May 06;24:2825-2831.

11- Freckelton J, Holt D, Borsaru A et al. The role of body composition in diverticular disease. Int J Colorectal Dis. 2018 Sep;33(9):1299-1302.

12- Young-Fadok TM. Diverticulitis. N Engl J Med. 2018 Oct 25;379(17):1635-1642.

13- Špičák J, Kučera M, Suchánková G. Diverticular disease: diagnosis and treatment. Vnitr Lek. 2018 Summer;64(6):621-634.

14- Kandagatla PG, Stefanou AJ. Current Status of the Radiologic Assessment of Diverticular Disease. Clin Colon Rectal Surg. 2018 Jul;31(4):217-220.

15- Brunicardi FC, Dana K.Andersen, Timothy R et al. Schwartz's Principles of Surgery, 10th ed, McGraw-Hill, 2016. 1309 – 1341.

16- Böhm S.K. Risk factors for diverticulosis, diverticulitis, diverticular perforation, and bleeding: a plea for more subtle history taking. Viszeralmedizin. 2015; 31: 84-94

17- Strate LL, Morris AM. Epidemiology, pathophysiology, and treatment of diverticulitis. Gastroenterology. 2019;156(5):1282–1298.e1.

18- Swanson SM, Strate LL. Acute colonic diverticulitis. Ann Intern Med. 2018;168(9):ITC65–ITC80.

19- Peery A.F., Shaukat A., Strate L.L. AGA Clinical Practice Update on Medical Management of Colonic Diverticulitis: Expert Review. Gastroenterology. 2021;160:906–911.e1.

20- Angenete E, Bock D, Rosenberg J et al. Laparoscopic lavage is superior to colon resection for perforated purulent diverticulitis-a meta-analysis. Int J Colorectal Dis. 2017 Feb;32(2):163-169.

21- Van Dijk ST, Daniels L, Nio CY, Somers I et al. Predictive factors on CT imaging for progression of uncomplicated into complicated acute diverticulitis. Int J Colorectal Dis. 2017 Dec;32(12):1693-1698.

22- Meara MP, Alexander CM. Emergency presentations of diverticulitis. Surg Clin North Am. 2018;98(5):1025–1046.

23- Cirocchi R, Randolph JJ, Binda GA et al. Is the outpatient management of acute diverticulitis safe and effective? A systematic review and meta-analysis. Tech Coloproctol. 2019;23(2):87–100.

24- Sartelli M, Weber DG, Kluger Y et al. 2020 update of the WSES guidelines for the management of acute colonic diverticulitis in the emergency setting. World J Emerg Surg. 2020;15(1):32.

25- Gregersen R, Andresen K, Burcharth J et al. Long-term mortality and recurrence in patients treated for colonic diverticulitis with abscess formation: a nationwide register-based cohort study. Int J Colorectal Dis. 2018;33(4):431–440.

26- Donovan E, Rizzolo D, Managing a patient with acute colonic diverticulitis. JAAPA. 2022 Jul 1;35(7):23-30.

27- Linzay CD, Pandit S. Acute Diverticulitis. In: StatPearls. StatPearls Publishing, Treasure Island (FL); 2022. PMID: 29083630.

28- Huston JM, Zuckerbraun BS, Moore LJ et al. Antibiotics versus No Antibiotics for the Treatment of Acute Uncomplicated Diverticulitis: Review of the Evidence and Future Directions. Surg Infect (Larchmt). 2018 Oct;19(7):648-654.

29- Shaban F, Carney K, McGarry K et al. Perforated diverticulitis: To anastomose or not to anastomose? A systematic review and meta-analysis. Int J Surg. 2018 Oct;58:11-21.

30- Francis NK, Sylla P, Abou-Khalil M et al. EAES and SAGES 2018 consensus conference on acute diverticulitis management: evidence-based recommendations for clinical practice. Surg Endosc. 2019;33(9):2726–2741.

31- Hall J, Hardiman K, Lee S et al. The American Society of Colon and Rectal Surgeons clinical practice guidelines for the treatment of left-sided colonic diverticulitis. Dis Colon Rectum. 2020;63(6):728–747.

32- Regenbogen SE, Hardiman KM, Hendren S et al. Surgery for diverticulitis in the 21st century: a systematic review. JAMA Surg. 2014;149(3):292–303.

CHAPTER XIII

INTRAUTERINE DEVICE AND ITS COMPLICATIONS

Ali Gursoy

(Asst. Prof.), Maltepe University Hospital,
Department of Obstetrics and Gynecology
E-mail: aligursoy44@hotmail.com
ORCID: 0000-0001-7275-3800

1. Introduction

The first known scientific article in terms of intrauterine contraception methods was published in 1909 in Germany by Richard Richter. The ring produced using silkworm material had 2 ends and these ends protruded from the cervical os. Thus, he could use the device both to control and to remove it. In the 1920s, Ernest Graefenberg designed another intrauterine contraceptive device (IUD) with a spiral metal ring made of an alloy of copper, nickel and zinc. This method, which was also frequently called as Graefenberg ring, lost its popularity in the following years when its negative effects in terms of not providing sufficient protection, susceptibility to infection and carcinogenic potential emerged (1).

Among the contraception methods, the application of IUD is one of the most popular and frequently preferred methods. IUDs have many advantages such as safety, ease of use, painless insertion without anesthesia, low cost, and long-term protection. Despite these advantages, it should be kept in mind that unfortunately it can cause some complications. It should be noted that the IUD may cause serious complications such as dislocation, displacement, inability to provide contraception, formation of intrauterine or extrauterine pregnancy, pain, menstrual irregularity, intermenstrual bleeding, bowel perforation, ileus, adjacent organ perforation, pelvic and abdominal inflammation disease (2,3).

2. Properties of Intrauterine Device Types

The copper-containing IUD produces a sterile inflammatory response at the endometrial level. This inflammation plays a role in reducing sperm motility and decreasing the efficiency of sperm. There are many factors that affect the contraceptive effectiveness that occurs with the dissolution of copper ions. The pH value of the intrauterine fluid, the phase of the menstrual cycle, the amount of intrauterine urea, the amount of intrauterine protein, the oxygen concentrations and the release of hemoglobin during menstruation are the main factors affecting the dissolution of copper ions. Studies have shown that the contraceptive efficacy of TCu380A type IUD is higher than MLCu250, TCu220 and TCu200. The higher active copper surface area on the IUD is associated with less pregnancy rate (4-6).

Apart from copper IUDs, another type of IUD that we use in our daily practice is those containing hormones. The hormone-containing IUD known as Mirena® is the most commonly used type. It contains 52 mg of levonorgestrel. This IUD is contained in a polyethylene frame with a central chamber from which the hormone is released. After it is placed in the uterus, approximately 20 μg/day levonorgestrel release begins as soon as it is administered. As time passes, this oscillation rate decreases. This hormone-containing IUD shows its contraceptive efficacy with its anti-proliferative effect on the endometrium and cervical mucus (4).

3. Insertion Technique of Intrauterine Device

IUD can be applied during the menstrual period or any time after confirming that the woman is not pregnant with a pregnancy test. Application during menstrual period is technically easier due to the opening of external cervical os. On the other hand it may be inserted apart from the menstrual period, for example in case of post-coital contraception. The hormone containing IUD be inserted in the first 7 days after the onset of menstruation and shows its effectiveness immediately. At any later stage of the cycle, the clinician should exclude unprotected sex since the last menstrual period. In this case, it is recommended to use additional contraception for the first 7 days and hormone containing IUD can be inserted. The use of intrauterine devices as an emergency contraception has been investigated for many years. A systematic review of 42 studies conducted between 1979 and 2011 involving eight different types of IUD and 7034 women showed that copper-containing IUDs are a highly effective method of emergency contraception after unprotected intercourse. The pregnancy rate was found to be approximately 0.09% (7).

In a study conducted in the Netherlands, the safety and complication rates of the IUD application in nulliparous women and women who had given birth were investigated. In the study, no significant difference was found in terms of complications between nulliparous and women who gave birth (8).

4. Contraindications

A known or suspected pregnancy is a contraindication for IUD insertion. In cases of doubt, the application should not be performed without excluding the possibility of pregnancy. In addition, in the presence of pelvic inflammatory disease, septic abortion, purulent cervicitis or puerperal sepsis, IUD insertion is contraindicated before the infection is completely treated. Another contraindication is the presence of unexplained vaginal bleeding. The etiology of these bleedings should be investigated before applying intrauterine contraception method. Likewise, administration is not recommended in women with a history of gestational trophoblastic disease before the beta-hCG value turns negative. Among the contraindications, one should not forget about cervical cancer and its suspicion. In people with cancer diagnosis, the application is not performed before the treatment process is completed. IUD application is not recommended in the presence of uterine anomalies that may prevent the correct placement of the IUD and in the presence of large leiomyomas located in the uterus. Other contraindications are the presence of ischemic heart disease, migraine with aura, breast cancer and severe liver disease (7).

5. Uterine perforation

Uterine perforation is one of the most serious complications of IUD insertion. The risk of developing uterine perforation during insertion ranges from 1/1000 to 9/1000 (9,10). The reason why these rates vary is that not every perforation case results clinical findings. While some practitioners perform IUD placement under ultrasound guidance, some practitioners do not perform IUD placement under ultrasound guidance. Minor perforations may not be diagnosed due to not being controlled by ultrasonography after the application. Another important factor in the difference in rates is the clinical experience of the practitioner.

Ultrasound during application is a very safe option to reduce possible uterine perforation cases. In addition, ultrasonography should be used to check whether the IUD is in the correct location after insertion. A perforation that may occur during the application can be easily managed with early diagnosis. Thus, future complications will be prevented as well as preventing the occurrence of

an unwanted pregnancy. In uterine perforation, the IUD can move freely into the abdominal cavity following the perforation. Perforation cases lead to chronic pelvic and abdominal pain over time. In cases that can be diagnosed with pain secondary to adhesion to surrounding tissues and infection, it is necessary to first determine the location of the IUD. The location of the IUD, its integrity and whether it is a single piece can be determined anatomically by ultrasonographic imaging and plain pelvic X-ray (3,9,11).

Examination findings, laboratory results and imaging of the patient should be evaluated together in the diagnosis or suspicion of a possible perforation. Pain in the pelvic region, abdominal pain, nausea, vomiting, absence of gas, inability to defecate and fever are possible signs of bowel injury in cases of uterine perforation. Since it is fast and non-invasive, the first preferred imaging method in such a situation is ultrasonography. If an IUD is not observed by ultrasonography, an x-ray of the entire abdomen can be taken to detect intra-abdominal localization. Oral and intravenous contrast computed tomography should be preferred if intestinal injury due to perforation is suspected. Magnetic resonance imaging is preferred if the IUD is thought to be associated with soft tissue.

It is thought that IUD, which acts by creating an inflammatory response, may cause some inflammatory responses and reactive cytological changes in endometrial and endocervical epithelial cells over time. Although it has been stated in the studies that nonspecific inflammatory cells of different structures, atypical glandular cells can occur and irregular endometrial cell shedding can be observed in the presence of IUD. There is no information with a high level of evidence on this subject in the literature (12).

6. Insertion failure

Two important risk factors have been identified for insertion failure. The first risk factor is the experience of the physician who will insert the IUD. Studies have shown that the success of IUD placement is significantly higher in experienced physicians. The failure rate of doctors with limited experience was twice that of experienced doctors, and three times that of inexperienced doctors. Another risk factor for insertion failure is that the person has no previous history of vaginal delivery. Unstretched cervical canal, cervical problems and bradycardia were observed at a higher rate in women who had not given birth before. Therefore, implantation failure was less common in those with a history of vaginal delivery. When we evaluate the complications related to IUD insertion, it is seen that the success rate is related to the anatomical and physiological factors as well as the experience of the doctor who inserts the IUD (13).

7. Migration

Transvesical migration following perforation of the IUD is a rare complication and it is difficult to diagnose. In a reported case in the literature, calcified intravesical intrauterine device leads to a false diagnosis of bladder stone was reported. The diagnosis was made by removing the calcified plaque consisting of copper containing IUD following cystoscopic imaging. This possibility should be reviewed in such episodic cases of bladder stones and recurrent urinary tract infections, especially in women presenting with recurrent unexplained stones (14).

8. Ectopic Pregnancy

Even if there is an opinion that there is an increased risk of ectopic pregnancy in women using IUDs, this is actually not true. In the presence of an IUD, the risk of ectopic pregnancy is 20 times less than in women who do not use contraception. The absolute ectopic risk is low, about 0.02 per 100 woman-years. If pregnancy occurs in the presence of an IUD, the probability of this being an ectopic pregnancy is 10%. Because of this increased risk of ectopic pregnancy compared to a person who does not use any birth control method, the possibility of ectopic pregnancy should definitely be excluded in women who become pregnant with an IUD. In addition, a previous history of ectopic pregnancy is not a definite contraindication for IUD (7,15).

9. Pelvic Inflammatory Disease

Studies have shown that IUD use in women is associated with the risk of pelvic inflammatory disease. The estimated risk is increased by 1.6 to 9.3 due to IUD. This risk factor varies with the person's age, partner, number of partners and frequency of sexual intercourse. Looking at the literature, non-gonococcal PID forms are more common among IUD users. It is recommended that patients be informed of the potential risk of pelvic inflammatory disease. Barrier protection methods can be recommended for patients at risk (16).

10. Conclusion

The intrauterine device is one of the safe methods of contraception that women often prefer. Although it causes failure and complications, these risks can be minimized by applying by experienced specialists. Women who are protected by IUD should not neglect their annual routine check-ups.

REFERENCES

1. Margulies L. History of intrauterine devices. Bull N Y Acad Med. 1975;51(5):662-667.

2. Wildemeersch D, Goldstuck ND, Hasskamp T. Current status of frameless anchored IUD for immediate intracesarean insertion. Dev Period Med. 2016;20(1):7-15.

3. Koo HR, Oh YT, Kim YT, Kim SW, Kang JH, Kim KW. Intrauterine device found in an ovarian carcinoma. J Comput Assist Tomogr. 2008;32(1):69-71. doi:10.1097/RCT.0b013e31805b7ed9

4. Wu JP, Pickle S. Extended use of the intrauterine device: a literature review and recommendations for clinical practice. Contraception. 2014;89(6):495-503. doi:10.1016/j.contraception.2014.02.011

5. O'Brien PA, Kulier R, Helmerhorst FM, Usher-Patel M, d'Arcangues C. Copper-containing, framed intrauterine devices for contraception: a systematic review of randomized controlled trials. Contraception. 2008;77(5):318-327. doi:10.1016/j.contraception.2007.12.011

6. Wildemeersch D. New frameless and framed intrauterine devices and systems - an overview. Contraception. 2007;75(6 Suppl):S82-S92. doi:10.1016/j.contraception.2006.12.023

7. Stephen Searle E. The intrauterine device and the intrauterine system. Best Pract Res Clin Obstet Gynaecol. 2014;28(6):807-824. doi:10.1016/j.bpobgyn.2014.05.004

8. Veldhuis HM, Vos AG, Lagro-Janssen AL. Complications of the intrauterine device in nulliparous and parous women. Eur J Gen Pract. 2004;10(3):82-87. doi:10.3109/13814780409044540

9. Sirikci A, Sarica K, Bayram M. Ureteral displacement due to a migrated intrauterine contraceptive device. Urol Int. 2000;65(3):179-180. doi:10.1159/000064869

10. Siddle N. Risks of intrauterine contraceptive devices. Br Med J (Clin Res Ed). 1984;288(6430):1554-1555. doi:10.1136/bmj.288.6430.1554

11. Mbarki C, Ben Abdelaziz A, Sahnoun R, et al. Actinomycose pelvienne : aspects diagnostiques et thérapeutiques [Pelvic actinomycosis: Diagnostic and therapeutic aspects]. Gynecol Obstet Fertil. 2016;44(3):168-174. doi:10.1016/j.gyobfe.2016.01.003

12. Pillay B, Gregory AR, Subbiah M. Cytopathologic changes associated with intrauterine contraceptive devices. A review of cervico-vaginal smears in 350 women. Med J Malaysia. 1994;49(1):74-77.

13. Farmer M, Webb A. Intrauterine device insertion-related complications: can they be predicted?. J Fam Plann Reprod Health Care. 2003;29(4):227-231. doi:10.1783/147118903101197854

14. Singh I. Intravesical Cu-T emigration: an atypical and infrequent cause of vesical calculus. Int Urol Nephrol. 2007;39(2):457-459. doi:10.1007/s11255-006-9021-9

15. A multinational case-control study of ectopic pregnancy. The World Health Organization's Special Programme of Research, Development and Research Training in Human Reproduction: Task Force on Intrauterine Devices for Fertility Regulation. Clin Reprod Fertil. 1985;3(2):131-143.

16. Burkman RT. Intrauterine device use and the risk of pelvic inflammatory disease. Am J Obstet Gynecol. 1980;138

CHAPTER XIV

APPROACH TO HEMATURIA IN THE EMERGENCY MEDICINE DEPARTMENT

Salih Karakoyun

(Ast. Prof. MD), Düzce University, School of Medicine, Department of Emergency Medicine, Düzce-Turkey, E-mail: salihkarakoyun@hotmail.com
ORCID: 0000-0002-6424-3015

1. Definition And Epidemiology

The presence of blood in the urine is defined as hematuria. Macroscopic (gross) hematuria is defined as the standard yellow color of the urine becoming visible in a spectrum ranging from light pink to dark brown. Microscopic hematuria is the presence of erythrocytes ≥ 3 RBC/HPF (Red blood cell/high-powered field), which we could not detect by inspection in a suitable urine sample. Microscopic hematuria can be found in the range of 1% to 18% in urine samples obtained from patients (1).

While benign causes such as renal colic (urological stone disease) may cause hematuria; bladder, prostate, and kidney malignancies may also cause hematuria, especially in individuals over the age of 35-40. Infections, menstruation, trauma, heavy exercise, surgical interventions, sexual objects or physical foreign bodies, familial diseases, cystic kidney diseases, and chemical or radiation exposure are other causes that can cause blood in the urine, that is, hematuria. Hematological causes, coagulation disorders, renal vascular pathologies, various drugs, and renal parenchymal diseases may also cause hematuria (1).

While hematuria may be the first complaint to family physicians or emergency services, it may also be detected incidentally in asymptomatic individuals. International health institutions do not recommend the use of urinalysis as a cancer screening test in healthy adults since the etiology of hematuria may be idiopathic and cause unnecessary workload and cost increase.

Since the underlying malignant disease is detected in 10% to 40% of patients with gross hematuria, further examination and urological evaluation

are required in these patients. Although the underlying cause of microscopic hematuria in asymptomatic individuals can be determined in 5% of the cases, the microscopic hematuria is usually urinary. It occurs due to benign reasons such as calculus, menstruation, exercise, infectious causes, trauma, interventional procedures, and benign prostate enlargement. Since the risk of cancer is high in males over 35 years of age with asymptomatic hematuria, in the general population over 40 years of age, in patients with ten packs/year of smoking and overexposure to chemical-carcinogenic substances, further investigation and malignancy are required. In the case of hematuria observed in patients using blood thinners, it is useful to investigate the etiology (1).

Risk factors for malignancy are; being older than 50 years of age, male gender, smoking, chronic infections such as schistosoma haematobium, arsenic, aromatic amines, long-term foley catheter use, phenacetin, and macroscopic hematuria. Colic abdominal pain with gross hematuria suggests urological stone disease, whereas the underlying malignancy mainly causes gross hematuria without pain. Attributing hematuria to a single benign cause poses a risk for overlooked emergency pathologies that cause gross hematuria (1). Some authors recommend that all patients with gross hematuria have an emergency urology consultation since the presence of gross hematuria has high mortality and morbidity, such as underlying malignancy, and a high potential for clues for emergency pathologies (1).

Causes of renal hematuria are; infectious causes and neoplasms such as trauma, glomerulonephritis, familial diseases, autoimmune diseases, vasculitis, and pyelonephritis. Causes of postrenal hematuria are; trauma, obstructive causes, infectious causes, neoplasms, hematological (coagulation disorder, sickle cell anemia), and vascular pathologies (2).

2. Pseudohematuria

A visibly red-colored urine sample may not actually be true hematuria. After the urethra is cleaned, the first part of the urine is expelled, and the midstream urine sample is examined first with a dipstick and then under the microscope for the presence of red blood cells in the urine. The foods we eat and the drugs we take can dye the urine color similar to blood in the external view. In this case, the dipstick test will be negative.

The dipstick test is negative in some diseases, such as porphyria, hypercalciuria, and bilirubinuria, but its urine morphology is similar to hematuria.

In diseases that cause hemoglobinuria and myoglobinuria (such as burns), dipstick-positive pseudohematuria is present. In some drugs, dipstick-positive pseudohematuria can be observed.

Exceptionally, true hematuria may result in false negative dipstick results in patients using vitamin C (2).

In psychiatric conditions such as Munchausen syndrome, there may be a case of deliberately smearing blood in the urine sample; although this is rare, this should be kept in the back of our minds.

3. Clinical Approach

In patients presenting with or found to have hematuria, it should be examined whether there is an underlying emergency diagnosis that may lead to morbidity and mortality. After evaluating vital parameters and physical examination, symptoms, and signs at admission, presence of fever, chills, medications used, chronic diseases (such as bleeding diathesis), smoking consumption, occupational exposures, exercise, consumed food and beverages, family history, time of onset of symptoms and signs should be questioned.

Accompanying hematuria; anemia, persistent hematuria despite bladder irrigation, acute kidney dysfunction, glob vesicale, inconsistent findings such as hypotension and tachycardia, coagulation disorders, pain and vomiting resistant to medical treatment, vascular pathologies, traumatic injuries, infection accompanied by acute renal failure and nephrolithiasis may indicate the presence of an urgent clinical picture that requires rapid intervention (2). In these cases, urology and nephrology consultation within the indication may be requested to speed up the diagnosis and treatment.

Although nephrolithiasis is a common clinical diagnosis in microscopic or macroscopic hematuria accompanied by acute onset colic abdominal, flank, groin, or back pain, it should not be forgotten that conditions such as vascular thrombosis and dissection may be the underlying cause (2). Pyelonephritis, urethritis, cystitis, prostatitis, and other urinary system infections should be evaluated in the differential diagnosis in the presence of the symptoms mentioned above and the signs.

Rectal examination should be performed in male patients to evaluate benign prostatic hypertrophy. Detection of globe vesical in the physical examination may be due to benign prostatic hyperplasia as well as to obstruction due to malignant events, mass effect, or bleeding (blood clots).

In female patients, normal menstrual bleeding can be mistakenly interpreted as hematuria originating from the urinary system and hematuria in the menstrual cycle due to endometriosis in the urinary system, so menstrual dates should also be questioned. Since painless hematuria carries the risk of malignancy, other malignancy risk factors should be examined, and malignancy research and follow-up should be performed with further examinations (2).

Glomerulonephropathy is considered in the picture of hematuria accompanied by peripheral edema with hypertension, and nephrological evaluation is recommended.

In hypotensive and tachycardic patients presenting with back pain or flank pain, it should not be overlooked that there may be an underlying aortic aneurysm or aortic dissection in the presence of hematuria.

Nutcracker syndrome (NCS), which can lead to renal vein thrombosis, is accompanied by hematuria, proteinuria, and abdominal pain, and there is compression on the left renal vein between the superior mesenteric artery and the aorta radiologically (3).

4. Diagnostic Examination and Imaging

The basic approaches and diagnostic tests are detailed anamnesis, physical examination, dipstick, microscopic urine sample evaluation, blood hemoglobin level, urea, creatinine values, and urinary system ultrasonography.

Urethrocystoscopy, urine cytology, computed tomography, and magnetic resonance imaging methods are advanced tests used to investigate the etiology of microscopic hematuria in patients with malignancy risk (4).

Further examinations should be performed to diagnose the increased risk of malignancy and potentially dangerous diseases, especially in individuals over 40 with gross hematuria, and patients should be followed up by urology (4). Especially in patients with increased risk for cancer, urethrocystoscopy may help us to diagnose earlier since only radiological evaluation may give erroneous results (5).

In the national guidelines of many countries, asymptomatic cytology in patients with hematuria and urine Markers (e.g., NMP22, BTA-stat, UroVysion FISH) may result in false positive results, so unnecessary biopsy examinations are required, and emotional distress in humans. It is not recommended as it may cause stress (6).

In microscopic evaluation, dysmorphic red blood cells are detected in hematuria of glomerular origin. Alport syndrome, Mesangial proliferative

glomerulonephritis, Ig A nephropathy, and Loin pain syndrome are some of the causes of glomerular hematuria. In the presence of glomerular hematuria, a kidney biopsy should be performed by evaluating the risk-benefit ratio. Especially in the presence of proteinuria, renal dysfunction, and autoimmune disease, patients should be evaluated together with a kidney biopsy. This patient group should be referred to nephrology and followed up at 6-month intervals (4).

In individuals with a family history of kidney tumors, in the presence of unexplained resistant hematuria, further investigation and examination should be performed if asymptomatic microscopic hematuria is found in these patients since there may be diseases such as hereditary von-Hippel-Lindau, hereditary papillary renal cancer, leiomyomatosis, tuberous sclerosis (5, 7).

While hematuria may arise from any focus on the urinary system in adult patients, it should be remembered that glomerular diseases can often be involved in the etiology of children and adolescents (8).

Schistosomiasis, which is a parasitic infection, can be seen in animals from east-central and African natives, whose sociocultural level is not good, bad living conditions, and dirty water. Schistosoma haematobium can cause dysuria, hematuria, calcification in the bladder lumen and bladder cancer. They are treated with oral praziquantel and should be followed up with cystoscopy (9).

It may give sonographic/radiological findings mimicking tuberculosis, endometriosis, diverticulum, cystic formations, cystitis, lymphoma bladder cancer. Bladder cancer, which is the most common cancer of the urinary system with hematuria, can be diagnosed early and accurately by cystoscopy, which provides direct imaging (10).

5. Treatment and Follow-up

First of all, the general condition of the patients, vital parameters, unstable findings such as hypotension, tachycardia, and whether there is a life-threatening condition are evaluated. Fluid replacement and blood resuscitation are done within the indication. Bladder irrigation is performed with a three-way catheter in patients with macroscopic hematuria. Tranexamic acid can be administered intravesically. The process is continued until the urine color is clear. As we mentioned in the diagnostic examination and imaging section in gross hematuria, urology consultation is requested for further examination and treatment after the basic examinations for hematuria are evaluated. If patients with gross hematuria are planned to be discharged after treatment, it is

recommended that they apply to the urology outpatient clinic within 2 weeks. Suprapubic catheterization or cystoscopic intervention may be required if the foley catheter cannot be successfully applied in patients with urinary retention. Pain due to urinary retention, tachycardia, and hypertension may be observed in these patients. Treatment of urinary retention, analgesic and palliative support is required (11, 12).

The American Urological Association guideline recommends that patients over 35 years of age with hematuria without an obvious benign cause should be referred for urology evaluation and that patients without malignancy risk factors should be re-evaluated 1 month later. It is recommended that patients aged 18 years and older with microscopic hematuria should be checked for repeated urinalysis and, if necessary, evaluation with computed tomography (11).

Patients with persistent vomiting and pain resistant to treatment, poor oral intake and poor oral drug compliance, co-morbidities, obstruction at the level to stop urine outflow in the bladder, and poor hemodynamic status should be consulted by urology, nephrology if necessary, and hospitalized. In patients who use anticoagulants, antiplatelets or have hematological disorders, coagulation parameters should be checked and hospitalization may be required (11, 12).

References

1. Peterson LM, Reed HS. Hematuria. Prim Care. 2019 Jun;46(2):265-273.

2. Willis GC, Tewelde SZ. The Approach to the Patient with Hematuria. Emerg Med Clin North Am. 2019 Nov;37(4):755-769.

3. Ichihara Y, Azuma T, Saito S, Niinami H. Nutcracker syndrome due to chronic aortic dissection. J Card Surg. 2021 Mar;36(3):1138-1139.

4. Bolenz C, Schröppel B, Eisenhardt A, Schmitz-Dräger BJ, Grimm MO. The Investigation of Hematuria. Dtsch Arztebl Int. 2018 Nov 30;115(48):801-807.

5. Barocas DA, Boorjian SA, Alvarez RD, et al. Microhematuria: AUA/SUFU Guideline. J Urol. 2020 Oct;204(4):778-786.

6. Linder BJ, Bass EJ, Mostafid H, Boorjian SA. Guideline of guidelines: asymptomatic microscopic haematuria. BJU Int. 2018 Feb;121(2):176-183.

7. Vlasschaert C, Lanktree MB. Microscopic hematuria. CMAJ. 2020 Apr 6;192(14):E370.

8. Kashtan CE. Genetic testing and glomerular hematuria-A nephrologist's perspective. Am J Med Genet C Semin Med Genet. 2022 Sep;190(3):399-403.

9. Duan M, Popat S, Coburn M, Woc-Colburn LE. A 26-Year-old Woman With Dysuria and Hematuria. Urology. 2021 Feb;148:e25-e26.

10. Wentland AL, Desser TS, Troxell ML, Kamaya A. Bladder cancer and its mimics: a sonographic pictorial review with CT/MR and histologic correlation. Abdom Radiol (NY). 2019 Dec;44(12):3827-3842.

11. Kim L. Askew, Urinary Tract Infections and Hematuria. In Tintinalli JE, John Ma OJ, Yealy DM, Meckler GD, Stapczynski JS, Cline DM, Thomas S, editors. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 9th Edition. McGraw-Hill Education; 2020. p:585.

12. Manthey DE, Story DJ. Acute Urinary Retention. In Tintinalli JE, John Ma OJ, Yealy DM, Meckler GD, Stapczynski JS, Cline DM, Thomas S, editors. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 9th Edition. McGraw-Hill Education; 2020. p:589.

CHAPTER XV

ANORECTAL ABSCESS

Emre Ozoran

(MD., General Surgeon), Koc University School of Medicine,
Department of General Surgery
eozoran@ku.edu.tr
ORCID: 0000-0002-9371-6811

1. Introduction

Anal (perirectal, perianal) abscesses are mainly caused by the obstruction in the crypt glands in the anal region. The obstruction lead to the accumulation of pus in the neighboring areas. These areas are the subcutaneous tissue, intersphincteric space that could lead to accumulation in supralevator and/or ischiorectal planes. As the surgical rule of thumb "Every abscess should be drained", adequate surgical drainage is the main line of treatment. Although, anal abscesses could be regarded as a local form of infection, infection to the adjacent organs/spaces and systemic infection could ensue.

Anal abscesses could be the first symptom of a patient with an anal fistula. After initial drainage 30-35% of patients present with an anal fistula (1-3). Cryptoglandular origin is responsible for 90% of anal abscesses. Obstetric injuries; anal fissure; anal fistula; infectious diseases like tuberculosis, HIV; Crohn's disease are among the other conditions that could lead to abscess.

2. Epidemiology

The anal abscess incidence is 8.6-20 in 100,000 in the United States. The presentation age is 40 years, and the male to female ratio ranges from 2.4 to 1; to 3 to 1. (4)

3. Anatomy and Pathogenesis

As stated above, the anal crypt glands' infection are responsible for 90% of the anorectal abscesses. These glands are located within the anal canal, in the

dentate line. Eight to 10 glands are seen in a person. The ducts of the glands run through the internal anal sphincter draining into the intersphincteric area. The occlusion of the anal crypt gland gives way to the overgrowth of bacteria, and eventually formation of an abscess. The flow and the dispersal of the abscess forms the final presentation of the disease. Perianal abscess occurs when the abscesses flow distally in the intersphincteric groove into the perianal skin. Perianal abscess's signs and symptoms are a tender, fluctuant mass, which could be seen during the anal examination. The other types of abscesses form by "following the path of least resistance" to different locations (intersphincteric, ischiorectal, supralevator).

4. Classification

The classification is made based on the anatomical location of the abscess. Perianal abscesses are located in the anorectal region. However, perirectal abscesses are rather complex and complicated, both clinically and during the management. The classification of perirectal abscesses is based on their anatomic locations.

4.1. Ischiorectal abscess (Ischioanal abscess)

These abscesses infiltrate the external anal sphincter leading to accumulation of pus in the ischiorectal space. Clinical signs and symptoms include tenderness, induration, and fluctuation within the buttocks.

4.2. Intersphincteric abscess

These abscesses are seen in the intersphincteric groove located between the internal and external sphincters, accounting for only 2-5%. Skin changes in the perianal region are not apparent; they are diagnosed via digital rectal examination. The clinician feels a mass with a protrusion the lumen and fluctuation.

4.3. Supralevator abscess

These abscesses could have two separate origins. The first origin is the infection in the cryptoglandular region could spread superiorly through the intersphincteric plane to the supralevator space. The second origin could occur secondary to inflammation in Crohn's disease, colonic perforation in diverticulitis or cancer. Patient history could be of paramount importance to understand the origin of the infection. These patients have pain in the perianal

region that is severe and fever. Urinary retention could sometimes be observed. However, during the inspection no external sign could be evident. During digital rectal examination, fluctuation or induration could be palpated superior to the anorectal ring. Imaging modalities (magnetic resonance imaging or computed tomography) could help in diagnosing this condition.

4.4. Horseshoe abscess

It is a perirectal abscess which is complicated, occurring posterior to the anal canal. The origin of the abscess, a potential space, is covered in the superior aspect by the pelvic floor, inferiorly by the anal canal, the coccyx and the anococcygeal ligament. The components of this space are tight together, thus, the abscess in this region is directed to advance to the ischiorectal space in a bilateral or unilateral fashion; forming a horseshoe appearance.

5. Signs & Symptoms

These patients share pain, fever, and feeling of mass symptoms. The pain does not alleviate unless the abscess drains spontaneously, in this case the patient could have a drainage.

"Rubor, calor, dolor, tumor" Redness, fever, pain and mass are the classical findings in any abscess. In patients with more superficial abscess, these could be evident during inspection, however in patients with deeper abscess some of these could be obscene. Digital rectal examination could be the first source of diagnosis in deeper abscesses and imaging could be needed.

6. Diagnosis & Imaging Studies

External inspection and digital rectal examination are the two main components leading to a diagnosis. However, imaging modalities (computed tomography, magnetic resonance imaging and endorectal ultrasound) could be utilized for deeper abscesses (5). Routine use of diagnostic imaging for superficial abscesses is not recommended.

7. Differential Diagnosis

7.1. Anal fissure

It is a tear in the anoderm which could easily be diagnosed during anal inspection. The two conditions share the pain, however the pain in the anal fissure mainly occurs during defecation; while the pain in the abscess is constant.

7.2. Anal fistula

It is a track connecting the abscess with skin or the neighboring organs. Anorectal abscesses can present with a concomitant anal fistula. In chronic fistulas, there are chronic purulent drainage and a pustule-like lesion in the perianal or buttock area (external orifice). The pain characteristic in these patients are intermittent, and the drainage is more characteristic.

7.3. Thrombosed external hemorrhoid

It has perianal pain and a perianal "mass", which is similar to the symptoms in perianal abscess. The thrombosed external hemorrhoid can be differentiated from the perianal abscess by the findings during anal inspection.

7.4. Prolapsed internal hemorrhoid

Internal hemorrhoids could be felt as fluctuant masses in the digital rectal examination. These are easily observed to be vascular structures and the distinction could be made during the physical examination.

7.5. Pilonidal disease –

Pilonidal disease can lead to acute abscess, although these abscesses usually are located in the intergluteal area superior/dorsal to the anus. The sacral region should be inspected in every patient.

7.6. Skin abscess

These could occur in any area of the skin, however they are more superficial, with less pain and usually there are no systemic symptoms.

7.7. Bartholin abscess

It is located in the vulvar area, which is the main factor in distinguishing it from perianal abscesses.

7.8. Hidradenitis suppurativa

It is a chronic disease with occlusion of the follicles located in the skin of the axillary, groin, perianal, perineal, and inframammary regions. Purulent discharge could be observed. This condition has characteristic skin lesions (sinus tracts, inflammatory nodules, comedones, and scarring). These are not seen in perianal abscesses.

8. Management

The primary treatment of anorectal abscess, like any other abscess, is surgical drainage. Perianal and ischiorectal abscesses should be drained through the skin overlying the area with fluctuation. Care should be utilized to drain the entire abscess and unroofing so that no future abscess forms once the skin starts to heal. It should be kept in mind that, if not drained or when not properly drained the abscess could infiltrate the neighboring structures with a risk to transform into systemic infection. When the abscess cavity is large, it should be drained with an incision as close to the anal canal as possible. Since there is a chance for future fistula formation, placing the drainage incision further from the anal canal could potentially turn the fistula into a longer one.

The drainage of intersphincteric and supralevator abscesses are more complicated. The drainage should be effective and potential iatrogenic injury to the sphincters should be avoided. The route for draining an intersphincteric abscess is internally at the dentate-line by a sphincterecmoty when no fluctuation is present externally. Supralevator abscesses should be drained according to their origins. When the origin is from the abdomen, the abscess should be drained transabdominally by interventional radiology or transrectally. When the origin is from an extending ischiorectal abscess, it should be drained transcutaneously.

A horseshoe abscess should be drained via bilateral transcutaneous ischiorectal drainage in combination with posterior drainage (Hanley procedure).

8.1. Surgical principles

8.1.1. Incision

All skin incisions should be made as close to the anal verge as possible to minimize the length of a potential fistula while still providing adequate drainage of the abscess.

8.1.2. Wound Packing

After drainage, wound packing is not recommended. (6-8)

8.1.3. Drains

Catheters could be put in the abscess cavity to ensue that drainage continues and to keep the skin incision open avoiding early closure.

8.1.4. Concomitant Fistulotomy

An anal fistula may be present in 30-70% of the anorectal abscess cases. However, performing fistulotomy during the drainage for the abscess is controversial. First of all the tract at this phase is not mature and it will turn into a real fistula in 30-35% of the patients. (1-3). A false route could be created when trying to find the fistula tract in the presence of the acute inflammation. If the surgeon could identify a tract than primary fistulotomy could be performed in addition to the drainage for the abscess. A seton could be placed in the fistula tract. The risk of incontinence, creation of a false route, unnecessary fistulotomy remain the main disadvantages of this procedure

8.2. Antibiotics

Antibiotics have been recommended for extensive cellulitis, sepsis or in immunocompromised patients. (9) The antibiotic should be a broad-spectrum antibiotic with coverage for gram negative, anaerobic and gram-positive skin associated bacteria. Although the guidelines do not recommend their routine use, several studies has shown that fistula formation decreased with their utilization (10-12).

Sample regimens could be amoxicillin-clavulanate or a combination of ciprofloxacin and metronidazole for four-five days after drainage (13).

8.3. Wound culture

Routine wound culture is not recommended. It could be useful in patients receiving antibiotics, in patients who will receive antibiotics, in immunocompromised patients, in patients with risk of methicillin-resistant Staphylococcus aureus infection. For most patients who undergo drainage of an anorectal abscess, routine wound culture is not necessary.

9. Recurrence

The rates of recurrence are as high as 44% after the initial drainage within the first year (14,15). The risk factors for recurrence are the presence of loculations or a horseshoe-type abscess, and when a primary fistulotomy cannot be performed (15-17).

REFERENCES

1- Ramanujam PS, Prasad ML, Abcarian H, Tan AB. Perianal abscesses and fistulas. A study of 1023 patients. Dis Colon Rectum. 1984;27(9):593–7.

2- Cox SW, Senagore AJ, Luchtefeld MA, Mazier WP. Outcome after incision and drainage with fistulotomy for ischiorectal abscess. Am Surg. 1997;63(8):686–9.

3-Vasilevsky CA, Gordon PH. The incidence of recurrent abscesses or fistula-in-ano following anorectal suppuration. Dis Colon Rectum. 1984;27(2):126–30.

4-Ommer A, Herold A, Berg E, et al. German S3 guidelines:anal abscess and fistula (second revised version). Langenbecks Arch Surg. 2017;402(2):191–201.

5- Expert Panel on Gastrointestinal Imaging, Levy AD, Liu PS, et al. ACR Appropriateness Criteria® Anorectal Disease. J Am Coll Radiol 2021; 18:S268.

6- O'Malley GF, Dominici P, Giraldo P, et al. Routine packing of simple cutaneous abscesses is painful and probably unnecessary. Acad Emerg Med. 2009;16(5):470–3.

7-Perera AP, Howell AM, Sodergren MH, et al. A pilot randomized controlled trial evaluating postoperative packing of the perianal abscess. Langenbecks Arch Surg. 2015;400(2):267–71.

8-Tonkin DM, Murphy E, Brooke-Smith M, et al. Perianal abscess: a pilot study comparing packing with nonpacking of the abscess cavity. Dis Colon Rectum. 2004;47(9):1510–4.

9-Vogel J, Johnson E, Morris A, et al. Clinical practice guideline for the management of anorectal abscess, fistula-in-ano, and rectovaginal fistula. Dis Colon Rectum. 2016;59(12):1117–33.

10-Lohsiriwat V, Yodying H, Lohsiriwat D. Incidence and factors influencing the development of fistula-in-ano after incision and drainage of perianal abscesses. J Med Assoc Thail Chotmaihet Thangphaet. 2010;93(1):61–5.

11-Ghahramani L, Minaie MR, Arasteh P, et al. Antibiotic therapy for prevention of fistula in-ano after incision and drainage of simple perianal abscess: a randomized single blind clinical trial. Surgery. 2017;162(5):1017–25.

12-Mocanu V, Dang JT, Ladak F, et al. Antibiotic use in prevention of anal fistulas following incision and drainage of anorectal abscesses: a systematic review and meta-analysis. Am J Surg. 2019;217(5):910–7.

13-Sawyer RG, Claridge JA, Nathens AB, et al. Trial of short-course antimicrobial therapy for intraabdominal infection. N Engl J Med 2015; 372:1996.

14-Hanley PH, Ray JE, Pennington EE, Grablowsky OM. Fistula-in-ano: a ten-year follow-up study of horseshoe-abscess fistula-in-ano. Dis Colon Rectum 1976; 19:507.

15-Hämäläinen KP, Sainio AP. Incidence of fistulas after drainage of acute anorectal abscesses. Dis Colon Rectum 1998; 41:1357.

16-Hanley PH. Conservative surgical correction of horseshoe abscess and fistula. Dis Colon Rectum 1965; 8:364.

17- Browder LK, Sweet S, Kaiser AM. Modified Hanley procedure for management of complex horseshoe fistulae. Tech Coloproctol 2009; 13:301.

CHAPTER XVI

ACUTE GASTROINTESTINAL BLEEDING

Fuat Kulaksız & Halil Emre Koyuncuoğlu & Batu Başaran

[1](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,
Department of Emergency Medicine
e-mail: fuatkulaksiz@hotmail.com,
ORCID: 0000-0002-8132-6787

[2](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,
Department of Emergency Medicine
e-mail: hekgazi57@gmail.com
ORCID: 0000-0002-3634-6850

[3](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,
Department of Emergency Medicine
e-mail: batu_basaran@hotmail.com,
ORCID: 0000-0002-8732-4133

1. INTRODUCTION

Acute gastrointestinal bleeding (AGB) is among the most common surgical reasons of emergency department admissions. Owing to enhancements in treatment approaches and increase in preventive measures such as Helicobacter Pylori eradication, widespread use of endoscopy and progress in drug therapies; morbidity and mortality have remarkably reduced in the last two decades (1). Nevertheless, AGB still maintaining its importance in clinical practice. Prevalence of most common causes of upper and lower gastrointestinal bleeding are given in Table-1.(2)

Table1. Most Common Causes of Acute UGIB and LGIB

Cause of Bleeding	Prevalence (%)
Upper GI tract	
Peptic ulcer	53.1
Varices	11.5
Acute erosion	10.4
Mallory-Weiss tear	3.0
Esophagitis	4.3
Hypertensive gastropathy	2.4
Tumor	5.2
Angioectasia or Dieulafoy lesion	2.8
Raze or undetermined	7.4
Lower GI tract	
Diverticulosis	30-65
Ischemic colitis	5-20
Hemorrhoids	5-20
Colorectal neoplasms	2-15
Angioectasia	5-10
Polypectomy	2-7
Inflammatory bowel disease	3-5
Infectious colitis	2-5
Stercoral ulceration	0-5
Colorectal varices	0-3
Radiation proctopathy	0-2
NSAIDS induced colopathy	0-2
Dieulafoy lesion	Raze

2. ACUTE UPPER GASTROINTESTINAL BLEEDING

The term acute upper gastrointestinal bleeding refers to gastrointestinal hemorrhage that is originating proximal of the ligament of Trietz. They are generally classified into two; non-portal and portal (variceal). Non-portal etiologies constitute 80-90% of cases. Traditionally, negative patient outcomes include re-bleeding and mortality, commonly associated with decompensation of pre-existing co-morbid medical conditions precipitated by the acute bleeding event. (3).

2.1. Non- Portal Upper Gastrointestinal Bleeding

2.1.1. Peptic Ulcer Disease

Among the causes of upper GI bleeding, peptic ulcer disease is the most frequent one representing over 40% of all cases (4). Although the decreased number of reported cases which commonly attributed to the more rational use of NSAID, better PPI therapy and effective Helicobacter pylori eradication; its prevalence is still estimated to be about 5-10% and incidence is 0.1–0.3% per year (5).

Peptic ulcers can occur either in duodenum or in stomach which are called gastric ulcers. Bleeding occurs as a result of peptic ulcer is a consequence of erosion resulted from the acid-peptic erosion on the inner mucosal surface of gastrointestinal tract. Presentation of peptic ulcer bleeding usually includes the following symptoms: Abdominal pain, vomiting, nausea, hematemesis and melena. The pain associated with duodenal ulcers usually improves after meals, whereas the pain associated with gastric ulcers generally intensifies after meals (6). If the perforation of the GI tract occurs the intensity of the pain is usually higher, however especially in elderly patients it is quite often that the severity of the pain does not corresponds to the amount of bleeding. Additionally, almost half of the patients with bleeding do not have such warning symptoms (7).

Diagnosis of the peptic ulcer bleeding includes the endoscopy within 24 hours. A patient with the possibility of peptic ulcer bleeding should receive PPI immediately while waiting for endoscopy in order to prevent further destructive effect of acid peptic. Acid suppression also has an important role regarding prevention of rebleeding (8). The Forest Classification classifies the types of peptic ulcer bleedings and it is a useful tool calculating the rebleeding risk (Table-2)

Table2. The Forrest Classification

Forrest score	Endoscopic appearance	Risk of rebleeding[a]
Ia	Ulcer with active pulsating bleeding	
Ib	Ulcer with active non-pulsating bleeding	%55
IIa	Ulcer with a visible non-bleeding vessel	%43
IIb	Ulcer with an adherent clot	%22
IIc	Ulcer with hematin on ulcer base	%10
III	Ulcer with a clean base without signs of recent bleeding	%5

[a] *Bleeding risk if endoscopic therapy is not performed.*

Treatment after endoscopy is performed according to the type of bleeding. Prediction and estimation of rebleeding defines the treatment strategies and extension of prophylactic measures. The cases with active bleeding (Forest Ia, Ib) and visible vessel (IIa) are treated with endoscopy. Patients with an adherent clot (IIb) are commonly treated with endoscopic removal of the cloth and an evaluation of cloth should be done. Ulcers with a black spot (IIc) or clean non-bleeding ulcers have low risk of bleeding and can be treated pharmacologically (8). Despite the achievements in endoscopic therapy approximately 10% of patients require surgical treatment (9). The most important parameters that affect the decision of surgical treatment is presence of low hemoglobin and signs of hemodynamic instability in admission. Clinical judgement and expertise are critical in this decision (10).

2.1.2. Mallory-Weiss Syndrome

Mallory-Weiss syndrome is one of the most common causes of upper GI bleeding with an estimation to represent 5-10% of non-variceal bleeding, characterized as superficial longitudinal lacerations (Mallory-Weiss tears) in esophagus. They frequently occur at the gastroesophageal junction and in some cases extend distally to involve proximal stomach. Alcohol consumption with heavy amounts is the most common history among the patients with this syndrome. A large number of patients who presented with this syndrome has hematemesis as symptom. As in other etiologies, severe bleeding can also manifest with melena. Endoscopic evaluation is the gold standard in patients with mild to moderate bleeding. If the bleeding site is inaccessible or origin of bleeding could not be assessed with endoscopy, angiography is indicated. Although rarely necessary, surgery is indicated if other procedures fail to control the bleeding (11).

2.1.3. Stress Gastritis

In the presence of severe illness, the gastric mucosal barrier is commonly irritated and becomes disrupted by the inflammatory processes. Such inflammations sometimes resulted with the lesions which are often superficial and clinically silent, however in some cases they can present with significant GI bleeding (12). There are two clinically common conditions that give rise to such lesions that are prone to bleeding: Cushing ulcers, which occur as a result of the acute traumatic brain lesions and Curling ulcers, which form after severe burns. Gastric body and fundus are common sites of these lesions and less frequently they can occur in antrum and duodenum (13). It is often that the anti-acid therapy

is sufficient for the patients with stress gastritis related bleeding. When that fails vasopressin, octreotide, endoscopy and angiography could be applied.

2.1.4. Esophagitis

Although it is among the most frequent causes of upper GI bleeding; compared to the other causes, esophagitis is a source of prognostically more benign bleedings. Underlying cause of the esophageal inflammation is most commonly gastroesophageal reflux which can lead to erosive esophagitis. Other possible etiologies are infections, radiation, medications and eosinophilic esophagitis (14). The common denominator of these etiologies are they all cause irritation and consequently inflammation to esophageal mucosa which result with mucosal ulceration in some cases. Treatment of such lesions include commonly proton pomp inhibitor (PPI) therapy. Bleeding occurs as a result of esophagitis is usually a good candidate for endoscopic treatment if needed.

2.1.5. Dieulafoy Lesion

These lesions are large tortuous arteries that runs along the muscularis mucosa of the GI wall for variable distances. They can erupt at the surface as small mucosal lesions (15). These mucosal finding is often very small as 2 to 5 mm and it is challenging to identify it endoscopically (16). Since the underlying lesion could be much larger, the bleeding from these lesions could be massive. Endoscopic management is applied successfully in most cases.

2.1.6. Gastric Antral Vascular Ectasia

Gastric Antral Vascular Ectasia (GAVE) refers to the antral dilation of submucosal capillaries which radiate to the pylorus (17). The appearance often resembles the stripes on a watermelon which is the reason these lesions also called as “Watermelon stomach”. GAVE is often seen in patients with chronic liver diseases, autoimmune conditions and connective tissue related diseases such as liver cirrhosis, hepatocellular carcinoma, hypothyroidism, systemic lupus erythematous and sclerosis. Severe bleeding is rare and endoscopic treatment is successful in the majority of patients. Antrectomy is the possible last resort treatment in the patients that have persistent bleeding despite endoscopic intervention.

2.1.7. Hemobilia

Hemobilia is defined as bleeding that involves the biliary tree. It is uncommon and concluding the diagnosis is often hard. When the diagnosis cannot be made, consequence could be lethal. Etiology of hemobilia involves liver malignancies that include biliary tree and iatrogenic or other trauma. The fact that patients with hemobilia usually do not present with symptoms like right upper quadrant pain, jaundice and overt GI bleeding makes the diagnosis perplexing (18). After the diagnosis is made via endoscopic representation of blood in biliary tree, angiographic embolization is the preferred treatment of choice.

2.1.8. Iatrogenic Bleeding

Endoscopy of the gastrointestinal system hasbecome more popular among clinicians in different specialties in the last fifty years. This increased usage of endoscopic tools tied with some complications such as iatrogenic hemorrhage. Although the rate of complications during upper gastrointestinal endoscopy is controversial, a study conducted by the American Society of Gastrointestinal Endoscopy estimated the overall complication rate as %0.13. (19) Major complications are regarded as rare occurrences after gastroduodenoscopy and possible pathologies that may lead to bleeding include cardiopulmonary injuries, Mallory-Weiss tears, perforations (20).

2.1.9. Hemosuccus Pancreaticus

Hemosuccus pancreaticus (HP) is defined as the bleeding in the pancreatic duct (usually from ampulla of Vater). Source of the bleeding could be pancreas, pancreatic duct, or structures adjacent to the pancreas, such as the splenic artery and gastric artery (21). It is a very rare occurrence and resulting clinical unfamiliarity makes its diagnosis a challenge. HP should be considered in patients with chronic pancreatitis that presents with acute GI bleeding (22). Common clinical symptoms of HP are colic pain, melena and hematemesis. Symptoms are usually intermittent rather than continuous. Diagnosis of HP depends on the clinical suspicion and imaging modalities such as abdominal CT can be used. For patients with hemodynamic stability, endovascular treatments could be used in treatment; however surgical intervention is necessary if the patient is unstable.

2.1.10. Aortoenteric Fistula

Aortoenteric fistula (AEF) is a rare yet a challenging clinical entity because of its lethality. Infections are the common underlying etiology in development

of primary AEF, and it is observed commonly in males with advanced age. Other pathophysiological factors that are thought to precipitate the formation of AEF are mechanical factors like weakened aorta (abdominal aortic aneurism, pseudoaneurysm), immunodeficiency, nutritional deficiency and factors related with the prior abdominal aortic graft such as immunologic reaction to graft material or fracture of the graft. Surgical procedures of aorta are responsible for the secondary AEF in most cases (23). Clinical presentation could range from symptoms of infection and anemia to massive GI bleeding. Treatment includes removal and replacement of graft material as well as antibiotic therapy.

2.1.11. Malignancy

Approximately 5% of upper GI bleedings resulted from the malignancies. 70% of these malignancies are gastric cancer (24) and 90% of these are gastric adenocarcinoma (25). Other than gastric adenocarcinoma; lymphomas, leiomyomas and gastrointestinal stromal tumors can be underlying etiology in such bleedings. Clinical symptoms vary greatly from subtle to extensive. It is common that malignancy related upper GI bleedings frequently presented with the symptoms of anemia (for example, paleness, fatigue, palpitations) rather than more overt presentations of bleeding (such as hematemesis and melena). Acute treatment can be achieved with endoscopy in almost all cases however, rebleeding occurred in all cases as well (26). There is no agreed gold-standard approach in treatment. When other therapies failed, (especially when hemodynamic stability of the patient is at steak) as in general bleeding control guidelines suggests, laparotomy is indicated.

2.1.12. Cameron Lesion

Cameron lesion is one of the rarest causes of upper GI bleeding however, its oversight in endoscopy result with high mortality and morbidity. It is found as linear gastric ulcerations near the diaphragma in patients with large hiatal hernia. Presence of the constant mechanical irritation of the mucosal folds at the level of diaphragma is thought to be the most probable culprit (27). Their presence is not being in correlation with the NSAID use (28). Clinical presentation correlates with the usual symptomatology of the anemia and hiatal hernia which are abdominal pain, fatigue, pallor, melena, palpitations, dyspnea on exertion (29) and Gastroesophageal reflux disease (GERD) like symptoms (30). Diagnosis is usually made with endoscopy and laboratory evaluation which include hemogram and anemia related tests (31). Since endoscopy often misses these lesions, it is usual

they require multiple procedures (32). Treatment is commonly medical and involves prescription of PPIs or in severe cases fundoplication (33).

2.2. Portal Variceal Bleeding

Portal variceal bleedings (PVB) accounts for the 20% of upper GI bleedings and often presented as a consequence of cirrhotic liver disease. Approximately half of patients with cirrhotic liver disease have such bleeding during their lifetime and rebleeding frequency is high. Considering the high mortality rate, their diagnosis and treatment requires precision and meticulousness.

Liver receives 25% of cardiac output and in the presence of fibrotic changes such as in cirrhosis intrahepatic resistance increases. These increase in intrahepatic resistance followed by the increased pressure in the portosystemic anastomose points and new vessel formation occurs concurrently (34). An increase in pressure first observed in the microvascular vessels however this phase is mostly clinically silent (35). As portal blood venous pressure increases vasodilation occurs in the arteries in portosystemic anastomose areas which consequently increases the blood pressure in these areas even more. Eventually, these pressures increase leads to variceal bleeding and ascites.

Symptoms of variceal bleeding are hematemesis, melena and if present the signs of hemodynamic instability (for example, dizziness, hypotension and tachycardia). Given the high mortality and morbidity, it is essential to act proactive in patients with possible PVB. Screening endoscopies are highly recommended in such patients with risk factors (36). Acute treatment options of PVB are endoscopic ligation, balloon tamponade, transjugular intrahepatic portosystemic shunt and surgical therapy.

3. ACUTE LOWER GASTROINTESTINAL BLEEDING

Gastrointestinal bleedings that arise from the distal part of the ileocecal valve are considered as lower gastrointestinal bleeding (LGIB). Hematochezia is the most frequent presentation of these bleedings. Among the underlying etiologies, diverticular bleedings are the most common and accounts for over 20% of cases (37). Hemorrhoidal bleedings are the second most frequent cause and without anticoagulant use they are self-limited and benign. Other frequent causes of LGIB are colitis with various types, vascular malformations, and colorectal cancer.

3.1. Diverticular Bleedings

Diverticula are herniations of the colon which can originate from mucosal and submucosal layers. This process of herniation is mainly age dependent and most of the cases are asymptomatic. Diverticula require clinical attention very rarely when these so called "pouches" became inflamed then it is called diverticular disease. As the diverticulum herniates, vasa recta and other superficial arteries are exposed from the diverticulated pouches. Bleeding commonly occurs due to these mechanical injury to vasa recta and other superficial arteries.

In minority of diverticular disease, formation of abscesses, fistulas, obstruction and perforation occurs which can lead to LGIB as well. Diverticular bleedings present usually with hematochezia without significant abdominal pain however sometimes cramps with mild to moderate intensity occur (38). When the patient is hemodynamically stable and bleeding is not massive in amount, endoscopic treatment is recommended. Endoscopic treatment modalities include thermal coagulation, endoscopic band ligation, ligation using an endoscopic detachable snare and local administration of epinephrine (39).

3.2. Hemorrhoidal Bleedings

Hemorrhoid tissues are vascular accumulations in the anal canal which are found in healthy individuals and work as cushions that help continence (40). However, the term "hemorrhoid" refers to the pathologic events occurring in these tissues. They can be either external or internal. Internal hemorrhoids are the dilations of internal venous plexus of anal canal and they are found above the pectinate line. External hemorrhoids are also vascular cushions that are covered by skin and found below the pectinate line. Acute hemorrhoidal bleedings are usually present with anal pain. In order to exclude other causes of LGIB a detailed physical examination must be done. Use of anoscopy is referred as the most accurate option regarding the detection and evaluation of hemorrhoids by most authors (41). A more detailed LGI endoscopy could be useful when clinical suspicion exists about the origin of bleeding.

3.3. Colitis

Colitis is the inflammation process of the colon and caused by variety of diseases such as Crohn's disease (CD), ulcerative colitis (UC), infections, radiation therapy or ischemic vascular diseases. Regarding bleeding among inflammatory bowel disease patients, ulcerative colitis related bleedings are

much more common. Only 1% of CD patients experience massive hemorrhage whereas 15% of UC (42). Both CD and UC can present with abdominal pain, tenesmus and hematochezia when they are complicated with hemorrhage. Since these patients frequently experience symptoms of possible GI bleeding, their symptoms must be evaluated meticulously each presentation. Gastrointestinal infections are another frequent yet rather unproblematic causes of LGIB in the perspective of bleeding regarded aspects. They are usually in bacterial etiology and common microorganisms are: E. Coli, Salmonella, Campylobacter, Shigella and C. Difficle. Antibiotherapy is ordered when the confirmation of bacterial etiology is confirmed except in C. Difficle which most commonly occurs due to antibiotic use. Radiation therapy is commonly ordered to treat GI and other abdominopelvic malignancies (especially rectal, prostatic and gynecological cancers). Patients usually presents also with abdominal pain, tenesmus and hematochezia.

3.4. Vascular malformations (Angiodysplasia)

Angiodysplasias (AD) that cause bleeding in the lower GI are found most commonly at the caecum and colon (43). Pathophysiology of these vascular malformations are yet to be understood completely. One widely accepted explanation is proposed by Boley et al., (44) It is suggested that development of these lesions is a consequence of age-related intermittent obstruction of intestinal submucosal veins which occur due to the contraction in the muscularis propria layer. Decreased blood flow leads to formation of new vessels which eventually followed by bleeding in some of the cases.

Aortic stenosis, Von Willebrand disease and chronic renal failure are some conditions that are linked with the formation of AD. Treatment of AD is dependent on the possibility of bleeding. Most of the AD remains clinically silent and only requires follow up. For the minority of cases that require treatment there are several treatment modalities like endoscopic argon plasma coagulation, electrocoagulation, photocoagulation, endoscopic clips, endoscopic ligation, endoscopic resection and transcatheter angiographic intervention. Although there are numerous non-operative measures, surgical resection of the affected part of GI tract is sometimes used in cases of severe bleeding or bleedings that cannot be controlled with other various modalities.

3.5. Neoplasia

Colorectal carcinoma, especially adenocarcinoma is one of the frequent causes of LGIB in daily practice. Although frequent incidence, it rarely causes severe hemorrhage. Neoplasia related LGIB usually presents with hematochezia. Occult lower GI hemorrhage that lasts for a long time may present with symptoms of anemia and low blood volume as well (45). Other than colorectal carcinoma, polyps and gastrointestinal stromal tumors may cause LGIB in some cases. Management of neoplasia related bleedings usually include endoscopic intervention. In minority of cases surgery is the definitive treatment of choice.

References

1. El-Tawil AM. Trends on gastrointestinal bleeding and mortality: where are we standing? World J Gastroenterol 2012; 18:1154–1158.

2. Michael L. Wells, Stephanie L. Hansel, David H. Bruining, Joel G. Fletcher, Adam T. Froemming, John M. Barlow, Jeff L. Fidler, CT for Evaluation of Acute Gastrointestinal Bleeding, Journal Article, 2018, RadioGraphics, 1089-1107, 38, 4

3. I.M. Gralnek, A.M. Barkun, Bardou, N Engl J Med, 359 (2008), pp. 928-937

4. Rockey DC: Gastrointestinal bleeding. Gastroenterol Clin North Am 34:581–588, 2005

5. Lanas A, Chan FKL. Peptic ulcer disease. Lancet. 2017 Aug 5;390(10094):613-624. doi: 10.1016/S0140-6736(16)32404-7. Epub 2017 Feb 25. PMID: 28242110.

6. Singh G, Triadafilopoulos G. Epidemiology of NSAID induced gastrointestinal complications. J Rheumatol Suppl 1999; 56: 18−24.

7. Lau JY, Barkun A, Fan DM, Kuipers EJ, Yang YS, Chan FK. Challenges in the management of acute peptic ulcer bleeding. Lancet 2013; 381: 2033−43.

8. Holster, I.L. &Kuipers, Ernst. (2011). Update on the Endoscopic Management of Peptic Ulcer Bleeding. Current gastroenterology reports. 13. 525-31. 10.1007/s11894-011-0223-7.

9. Wang YR, Richter JE, Dempsey DT: Trends and outcomes of hospitalizations for peptic ulcer disease in the United States, 1993 to 2006. Ann Surg 251:51–58, 2010.

10. Townsend, J. C. M., Beauchamp, R. D., Evers, B. M., & Mattox, K. L. (2016). Sabiston textbook of surgery (20th ed.). Elsevier - Health Sciences Division.

11. Rawla P, Devasahayam J. Mallory Weiss Syndrome. [Updated 2022 Oct 9]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538190/

12. Siddiqui AH, Farooq U, Siddiqui F. Curling Ulcer. [Updated 2022 May 1]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482347/

13. Krag M, Perner A, Wetterslev J, Wise MP, Borthwick M, Bendel S, McArthur C, Cook D, Nielsen N, Pelosi P, Keus F, Guttormsen AB, Moller AD, Møller MH., SUP-ICU co-authors. Prevalence and outcome of gastrointestinal bleeding and use of acid suppressants in acutely ill adult intensive care patients. Intensive Care Med. 2015 May;41(5):833-45.

14. Antunes C, Sharma A. Esophagitis. [Updated 2022 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK442012/

15. Romãozinho JM, Pontes JM, Lérias C, Ferreira M, Freitas D. Dieulafoy's lesion: management and long-term outcome. Endoscopy. 2004 May;36(5):416-20. doi: 10.1055/s-2004-814322. PMID: 15100950.

16. Nguyen DC, Jackson CS: e Dieulafoy's lesion: An update on evaluation, diagnosis, and management. *J Clin Gastroen- terol*49:541–549, 2015.

17. Rider JA, Klotz AP and Kirsner JB. Gastritis with veno-capillary ectasia as a source of massive gastric hemorrhage. Gastroenterology 1953; 24: 118–123.

18. Zhornitskiy, A, Berry, R, Han, JY, Tabibian, JH. Hemobilia: Historical overview, clinical update, and current practices. *Liver Int*. 2019; 39: 1378– 1388.

19. Silvis SE, Nebel O, Rogers G, et al. Endoscopic complications. Results of the 1974 American Society for Gastrointestinal Endoscopy Survey. JAMA 1976;235(9):928–30.

20. Eisen GM, Baron TH, Dominitz JA, et al. Complications of upper GI endoscopy. GastrointestEndosc 2002;55(7):784–93.

21. Yu P, Gong J. Hemosuccuspancreaticus: A mini-review. Ann Med Surg (Lond). 2018 Mar 9;28:45-48. doi: 10.1016/j.amsu.2018.03.002. PMID: 29744052; PMCID: PMC5938526.

22. Shetty S, Shenoy S, Costello R, Adeel MY, Arora A. HemosuccusPancreaticus. J Ayub Med Coll Abbottabad. 2019 Oct-Dec;31(4):622-626. PMID: 31933323.

23. J.R. Duncan, A.A. Renwick, I. Mackenzie, D.G. Gilmour, Primary Aortoenteric Fistula: Pitfalls in the Diagnosis of a Rare Condition,Annals of Vascular Surgery, Volume 16, Issue 2, 2002, Pages 242-245,

24. Adler DG, Leighton JA, Davila REet al. ASGE guideline: The role of endoscopy in acute non-variceal upper-GI hemorrhage.Gastrointest. Endosc.2004;60: 497–504.

25. Schatz, R.A., Rockey, D.C. Gastrointestinal Bleeding Due to Gastrointestinal Tract Malignancy: Natural History, Management, and Outcomes. *Dig Dis Sci* **62**, 491–501 (2017). https://doi.org/10.1007/s10620-016-4368-y

26. Kim YI, Choi IJ. Endoscopic management of tumor bleeding from inoperable gastric cancer. Clin Endosc. 2015;48:121–127.

27. Brar HS, Aloysius MM, Shah NJ. Cameron Lesions. [Updated 2022 Mar 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK567776/

28. Weston AP. Hiatal hernia with cameron ulcers and erosions. GastrointestEndosc Clin N Am. 1996 Oct;6(4):671-9.

29. Camus M, Jensen DM, Ohning GV, Kovacs TO, Ghassemi KA, Jutabha R, Machicado GA, Dulai GS, Hines OJ. Severe upper gastrointestinal hemorrhage from linear gastric ulcers in large hiatal hernias: a large prospective case series of Cameron ulcers. Endoscopy. 2013;45(5):397-400.

30. Windsor CW, Collis JL. Anaemia and hiatus hernia: experience in 450 patients. Thorax. 1967 Jan;22(1):73-8.

31. Holt JM, Mayet FG, Warner GT, Callender ST, Gunning AJ. Iron absorption and blood loss in patients with hiatus hernia. Br Med J. 1968 Jul 06;3(5609):22-5.

32. Zaman A, Katon RM. Push enteroscopy for obscure gastrointestinal bleeding yields a high incidence of proximal lesions within reach of a standard endoscope. GastrointestEndosc. 1998 May;47(5):372-6.

33. Pauwelyn KA, Verhamme M. Large hiatal hernia and iron deficiency anaemia: clinico-endoscopical findings. Acta Clin Belg. 2005 Sep-Oct;60(4):166-72.

34. Sumanovski LT, Battegay E, Stumm M, et al. Increased angiogenesis in portal hypertensive rats: role of nitric oxide. *Hepatology.* 1999;29:1044–9.

35. Abraldes JG, Iwakiri Y, Loureiro-Silva M, et al. Mild increases in portal pressure upregulate vascular endothelial growth factor and endothelial nitric oxide synthase in the intestinal microcirculatory bed, leading to a hyperdynamic state. *Am J PhysiolGastrointest Liver Physiol.* 2006;290:G980–7.

36. The North Italian Endoscopic Club for the Study and Treatment of Esophageal Varices. Prediction of the first variceal hemorrhage in patients with cirrhosis of the liver and esophageal varices: a prospective multicenter study. N Engl J Med 1988;319:983-9.

37. Oakland K, Guy R, Uberoi R et al. Acute lower GI bleeding in the UK: patient characteristics, interventions and outcomes in the first nationwide audit. Gut 2018; 67: 654–662

38. Lisa L. Strate, Arden M. Morris, Epidemiology, Pathophysiology, and Treatment of Diverticulitis, Gastroenterology, Volume 156, Issue 5, 2019, Pages 1282-1298.e1.

39. Kaise M, Nagata N, Ishii N, Omori J, Goto O, Iwakiri K. Epidemiology of colonic diverticula and recent advances in the management of colonic diverticular bleeding. Dig Endosc. 2020 Jan;32(2):240-250. doi: 10.1111/den.13547. Epub 2019 Nov 5. PMID: 31578767.

40. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol. 2012 May 7;18(17):2009-17. doi: 10.3748/wjg.v18.i17.2009. PMID: 22563187; PMCID: PMC3342598.

41. Rivadeneira DE, Steele SR, Ternent C, Chalasani S, Buie WD, Rafferty JL. Practice parameters for the management of hemorrhoids (revised 2010). Dis Colon Rectum. 2011;54:1059–64.

42. Pardi DS, Loftus EV, Jr, Tremaine WJ, et al: Acute major gastrointestinal hemorrhage in in ammatory bowel disease. *GastrointestEndosc*49:153–157, 1999.

43. Foutch PG, Rex DK, Lieberman DA.Prevalence and natural history ofcolonic angiodysplasia among healthyasymptomaticpeople.Am JGastroenterol1995;90: 564–7.

44. Boley SJ, Sammartano R, Adams A,DiBiase A, Kleinhaus S, SprayregenS.On the nature and etiology of vascularectasias of the colon. Degenerativelesions of aging.Gastroenterology1977;72(4 Pt 1): 650–60.

45. Aun Raza Shah, Vikram Jala, Hammad Arshad, Mohammad Bilal, Evaluation and management of lower gastrointestinal bleeding, Disease-a-Month, Volume 64, Issue 7, 2018, Pages 321-332

CHAPTER XVII

ABDOMINAL TRAUMA

Fuat Kulaksız & Halil Emre Koyuncuoğlu
Batu Başaran & İrem Taçyıldız

[1](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,

Department of Emergency Medicine
e-mail: fuatkulaksiz@hotmail.com,
ORCID: 0000-0002-8132-6787

[2](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,

Department of Emergency Medicine
e-mail: hekgazi57@gmail.com
ORCID: 0000-0002-3634-6850

[3](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,

Department of Emergency Medicine
e-mail: batu_basaran@hotmail.com,
ORCID: 0000-0002-8732-4133

[4](MD.), Ankara Sincan Dr. Nafiz Körez State Hospital,

Department of Emergency Medicine
e-mail: iremtacyildiz98@gmail.com,
ORCID: 0000-0002-8303-4403

1. INTRODUCTION

In the emergency department, patients frequently present with abdominal trauma that are either blunt or penetrating in mechanism. Abdomen is the third most commonly injured site in trauma patients and the second most common cause of death with 15-20% after head trauma. Death as a result of abdominal trauma has the tendency to occur within the first 6 hours after admission to the hospital (1).

Patients with abdominal trauma, whether occur from direct impact, sudden deceleration, explosion or puncture wound, may result with significant intra-abdominal hemorrhage without any conspicuous sign or cues of peritoneal irritation. Therefore, consideration of the possibility of abdominal, vascular, or pelvic injury is important until they can be ruled out (2). When a patient has significant hemorrhage due to abdominal trauma, injury may result with death shortly after the occurrence of event. Even after the initial phases of injury, risk of infection may cause significant morbidity or mortality since it can lead to sepsis (1).

2. PATHOPHYSIOLOGY

Injuries that result from trauma are traditionally classified either as blunt or penetrating injuries. In Europe, blunt abdominal trauma is much more common than penetrating abdominal trauma (3).

2.1. Blunt Abdominal Trauma

Direct trauma to the abdomen can occur from a physical blow, which can cause damage to the skin and blood vessels on the surface or the deeper tissues. The deepness of the affected tissues is directly proportional to the physical energy transferred to the tissue. On the other hand, acceleration/deceleration injuries occur when an individual who is in motion suddenly stops. This type of injury can cause complete disruption of the deep organs and may not have many visible superficial signs (4). The abdomen contains organs that can be either mobile or fixed. Injuries tend to occur at the points where mobile and fixed organs meet with each other. One such site is the level of ligament of Treitz where the parts of the small intestine meets. Blow to this location frequently results with not only intestinal but also mesenteric injury.

The most common cause of blunt abdominal trauma is a motor vehicle collision, followed by falls, direct impacts to the abdomen and industrial accidents. The liver is the most frequently injured organ in cases of blunt abdominal trauma. The spleen, intestine and retroperitoneal organs are other organs that are also commonly affected (5).

2.2. Penetrating Abdominal Trauma

Penetrating wounds to the front wall of the abdomen can cause a variety of injuries, ranging from minor irritation to serious, life-threatening hemorrhage

and tissue damage (6). There are two frequent causes of this type of trauma in daily emergency medicine practice: stab wounds and gunshot wounds. Stab wounds are more common, but less deadly than gunshot wounds. Gunshot wounds, on the other hand, tend to be more serious due to the high energy transfer and missile trajectory, which can result with multiple bullet fragments that increase morbidity and mortality (7,8,9).

Stab wounds often affect nearby abdominal structures, with the liver being the most commonly injured organ (40%). The small intestine (30%), diaphragm (20%), and colon (15%) are also frequently affected by stab wounds. Gunshot wounds can cause additional damage within the abdomen based on the path of the bullet, the cavitation effect, and the possibility of bullet fragmentation. The small intestine (50%), colon (40%), liver (30%), and abdominal vascular structures (25%) are the most commonly injured by gunshot wounds (2).

3. CLINICAL FEATURES

Severe bleeding is the main cause of death in trauma cases, and it can often be prevented, especially when the injury is located in the abdomen (10). The primary survey is a systematic and step-by-step process used to address immediate threats to life in all trauma patients. This process is especially important for managing abdominal trauma, as the key to efficient treatment is determining whether there is life-threatening hemorrhage. This can be done through a combination effort that include; investigation of the mechanism of injury, physical examination, and bedside imaging. For patients who have experienced blunt or penetrating abdominal trauma and are have abnormal vital signs, immediate surgical exploration and aggressive resuscitation is necessary. A delay in surgical management of more than 10 minutes for patients with gunshot wounds and low blood pressure has been linked to a threefold increase in mortality (6,11).

3.1. First Assessment

It is crucial for all trauma patients to be managed according to the Advanced Trauma Life Support (ATLS) algorithm in order to ensure that they receive the appropriate care and treatment.

Table 1. Advanced Trauma Life Support (ATLS) (2)

A	**Airway**	Evaluate the airway while keeping the neck and spine immobilized to prevent further injury. Provide the patient with high levels of oxygen and consider intubation if necessary.
B	**Breathing**	Assess breathing by listening for breath sounds. If breath sounds are diminished or absent, it may be a sign of a possible pneumothorax. Then, check for uneven movement of the chest wall, open wounds, or flail segments.
C	**Circulation**	Evaluate the pulses, capillary refilling time, and blood pressure. If there is significant external hemorrhage, control it by applying direct pressure. Begin fluid resuscitation. It is important to perform a FAST examination, especially in patients who are experiencing unstable vital signs, as a positive result would indicate the need for emergency laparotomy.
D	**Disability**	Assess the size and reactivity of the pupils and determine the patient's Glasgow Coma Scale score. It is ideal to assess the patient's level of disability before administering any pain medication, sedatives, or paralytics.
E	**Exposure**	Expose the patient completely and try to locate and document all wounds.

3.2. Physical Examination

During the examination of the abdomen, look for external signs of trauma such as abrasions, lacerations, contusions, or seatbelt marks. It is important to note that the absence of these signs does not rule out the possibility of serious internal abdominal injuries. During the initial examination, it is possible that abdominal tenderness, rigidity, distention, or tympany may not be present and may take hours or days to manifest.

If a physical exam is relied upon an excessively high degree, particularly in cases of injury with a concerning mechanism, there may be a high rate of misdiagnosis. Research has shown that up to 45% of patients with blunt trauma who were initially believed to have a benign abdomen based on a physical exam were later discovered to have a significant intra-abdominal injury (8,12).

Table 2. Clinical Features of Possible Injuries (4, 8, 13, 14, 15)

Injury Type	Clinical Features
Abdominal Wall Injuries	Abdominal muscle contusions may result from a direct blow or muscle contraction and cause pain with trunk flexion and rotation, as well as tenderness to percussion. Rectus abdominis hematomas, which can mimic intra-abdominal injuries, may occur from epigastric trauma or abdominal wall vessel injury. These hematomas may cause pain and a palpable mass below the umbilicus.
Solid Organ Injuries	Solid organ injuries may result in various symptoms due to blood loss, such as an increase in pulse pressure and heart and respiratory rates. Hypotension may not occur until there is a significant decrease in circulating volume, leading to decreased urinary output and possible confusion and anxiety. Delayed rupture of the spleen and kidney may occur in some injuries with mild pain and minor bleeding.
Hollow Viscous and Mesenteric Injuries	Blunt abdominal trauma may result in bowel and mesenteric injuries in 1-12% of patients, with an incidence of about 5%. These injuries can cause symptoms due to blood loss and peritoneal contamination by gastrointestinal contents. Mesenteric injuries may cause minimal bleeding that is not detectable on physical exam, and chemical irritation or bacterial contamination of the abdominal cavity may cause delayed symptoms.
Retroperitoneal Injuries	Such injuries may include pancreas and duodenum as well as urinary organs. Pancreatic injuries, which occur in about 4% of patients with abdominal trauma, have high morbidity and mortality rates. There are no specific symptoms, but the mechanism of injury can be indicative of pancreatic trauma, which often results from rapid deceleration. At-risk individuals include unrestrained drivers who hit the steering wheel and bicyclists who fall against the handlebars. Duodenal injuries can also vary from no symptoms to gastric outlet obstruction symptoms such as abdominal pain, distention and vomiting. Fever and leukocytosis may indicate delayed presentation and a potential abscess or sepsis.
Diaphragmatic Injuries	The diaphragm may spasm as a result of a direct blow to the epigastrium, causing difficulty breathing as the diaphragm is unable to relax and allow the lungs to expand. Diaphragmatic rupture may be caused by a penetrating injury or blunt force and is uncommon, occurring in 0.8% to 5% of patients with thoracoabdominal injuries. It is almost always a left-sided injury and may lead to the delayed herniation or strangulation of abdominal contents through the tear when left undiagnosed and untreated.

4. DIAGNOSIS

To diagnose abdominal trauma includes a combination of a thorough physical examination, an evaluation of the circumstances and mechanisms of the injury and appropriate diagnostic studies. While not all patients with this type of trauma will require further testing beyond the initial physical exam, certain situations may warrant additional laboratory analysis, imaging studies, or repeat of exams.

There are several methods that can be used to supplement the diagnosis of abdominal trauma when serial physical examinations are not reliable, including:

1) diagnostic peritoneal tap/lavage,
2) bed-side ultrasound examination
3) contrast-enhanced computerized tomography (CT) of the abdomen and pelvis
4) diagnostic laparoscopy. (16)

Table 3. Abdominal Injuries That Need Expanded Evaluation (8)

Abdominal Injuries That Need Expanded Evaluation
Presence of abdominal pain, tenderness, distention, or external signs of trauma
Mechanism of injury with a high likelihood of causing an abdominal injury
Suspicious lower chest, back, or pelvic injury
Inability to tolerate a delayed diagnosis (e.g., patients who are elderly, on anticoagulants, or have liver cirrhosis/portal hypertension)
Presence of distracting injuries
Altered consciousness/sensorium (e.g., CNS injury, intoxicating substances)

4.1. Diagnostic Peritoneal Tap/Lavage (DPL)

During a DPL a tube is inserted through the patient's abdomen and into the peritoneal cavity. A small amount of fluid is then introduced into the cavity and immediately withdrawn. The fluid is then checked for red blood cells (RBC), which can be a sign of abdominal injury (8,9).

DPL is a fast and highly effective method for diagnosing abdominal trauma. It was initially used in the evaluation of patients who had sustained blunt trauma and were experiencing hypotension, uncertain abdominal symptoms, changes in mental status, or spinal cord injury. DPL quickly gained widespread acceptance due to its speed and accuracy, although it is invasive and may not be suitable for all patients. In some instances, DPL was overly sensitive and resulted with

an excessive number of unnecessary laparotomies. Additionally, it was unable to identify specific organ injuries and was not effective at detecting injuries to the diaphragm (12).

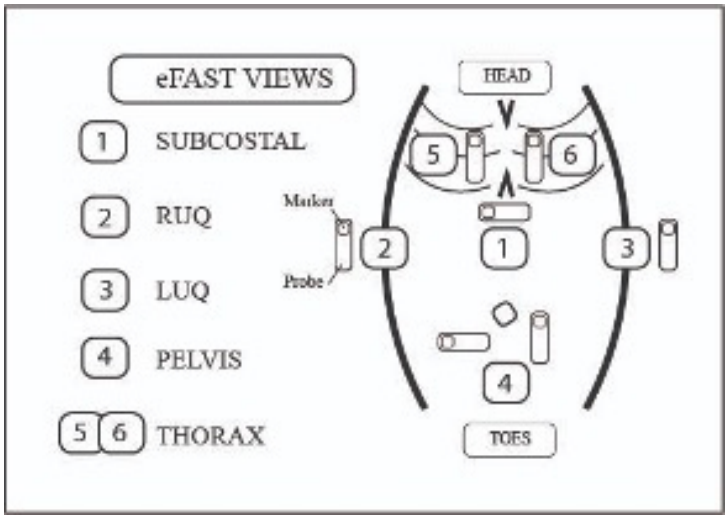
Criteria for positive diagnostic peritoneal lavage are more than 10 mL free flowing blood immediately on aspiration or >15,000 RBC/mm3 in abdominal wounds or >25,000 RBC/mm3 in lower chest wounds (8).

4.2. Bedside Ultrasound Examination

Ultrasound is a diagnostic tool that has several unique characteristics which make it particularly appealing to trauma surgeons, including being portable, non-invasive, fast, and easily repeatable. Another advantage is that the surgeon can serve as the sonographer and use the tool as an extension of the physical examination, receiving immediate feedback because of the real-time imaging (2,8,12).

A fast and specific way to assess trauma patients with ultrasound is Focused Assessment for the Sonographic Examination of the Trauma patient (FAST), a term first used by Dr. Steven R. Shackford who was incorporated it into the American College of Surgeons' Advanced Trauma Life Support Course curriculum. While some recognized that the FAST or the extended version eFAST test was not perfect, proponents of the test emphasized that it was intended to serve as a screening tool for detecting hemoperitoneum and hemopericardium, rather than a replacement for DPL or CT (2,12). The presence of free fluid in Morrison's pouch is concerning because it may indicate the presence of hemoperitoneum, which may require emergency surgery (7,10,17).

Figure 1. eFAST's ultrasound probes positions (7)



4.3. Contrast-Enhanced CT of the Abdomen and Pelvis

As technology improved and CT scans became faster and more detailed, it became a promising diagnostic tool for evaluating injured patients. In cases of severe abdominal trauma, a contrast enhanced CT scan can quickly identify bleeding lesions and provide a comprehensive overview of all bleeding sources and injuries, enabling a more timely and effective treatment plan to be put in place (10,12). For a hemodynamically stable patient, a CT-scan of the abdomen should be conducted to confirm or rule out an abdominal injury, regardless of the results of an ultrasound or clinical examination (18).

4.4. Diagnostic Laparoscopy

There has been a steady increase in the number of situations in which laparoscopic procedures are deemed appropriate in recent years (19). However, this method had some limitations in a trauma setting. These included the need for additional time to set up the equipment, which could lead to delays in surgery if necessary; difficulties in examining the intestine; and difficulties in exposing the retroperitoneum. Despite these challenges, laparoscopy was still useful in determining peritoneal penetration. Laparoscopy has been found to be reliable for detecting hemoperitoneum, solid organ injuries, diaphragmatic lacerations, and retroperitoneal hematomas. Laparoscopy has a very high specificity, but moderately low sensitivity for detecting gastrointestinal injuries (12,20).

5. MANAGEMENT

For patients with a known abdominal injury, it is important to ensure that they are up-to-date on their tetanus vaccination. Blood transfusions may be necessary, following the principles of permissive hypotension. This involves avoiding the use of large amounts of crystalloids to normalize blood pressure and instead using blood products to maintain a mean arterial pressure of 65. Excessive use of crystalloids can lead to coagulopathy, acidosis, and hypothermia, which can significantly increase the risk of complications and death. Patients with injuries to hollow organs may also benefit from antibiotic therapy (7,21).

5.1. Laparotomy

Laparotomy is considered as the definitive treatment for significant intra-abdominal injuries. In addition to the indications mentioned below in Table 4, laparotomy should be performed immediately in cases of circulatory

insufficiency and significant intraperitoneal fluid accumulation, according to guidelines from Europe and the United States (8,10).

Table 4. Indications for Laparotomy (8)

	Blunt Abdominal Trauma	**Penetrating Abdominal Trauma**
Absolute Indications	• Anterior abdominal injury with hypotension • Abdominal wall disruption • Peritonitis • Free air under diaphragm on chest radiograph • Positive FAST or DPL in hemodynamically unstable patient • CT-diagnosed injury requiring surgery	• Injury to abdomen, back, and flank with hypotension • Abdominal tenderness • GI evisceration • High suspicion for transabdominal trajectory after gunshot wound • CT-diagnosed injury requiring surgery
Relative Indications	• Positive FAST or DPL in hemodynamically stable patient • Solid visceral injury in stable patient • Hemoperitoneum on CT without clear source	• Positive local wound exploration after stab wound

5.2. Non-Operative Management

Abdominal injury management has undergone a shift in paradigm in recent years, moving away from the previous approach of mandatory exploration and towards a more selective approach of non-operative management (NOM). For hemodynamically stable patients with abdominal stab wounds that do not exhibit signs of peritonitis or widespread abdominal tenderness, a laparotomy is not routinely recommended (22). Currently, NOM is the preferred treatment for hemodynamically stable abdominal trauma patients, with a success rate of around 80%-90% (23). NOM modalities are summarized below in Table 5.

Table 5. Summary of recommendations for NOM in abdominal solid organ injuries (23)

Question	Liver	Spleen	Kidney	Pancreas
Which AAST-OIS grade feasibility?	Any	Any	Any, but operative intervention suggested in devascularized kidney.	I-II
Is CT with contrast required?	Yes	Yes	Yes, including excretory phase	Yes, but not sensitive for PDI
Who needs intensive monitoring?	Blunt medium/high-grade	Blunt grade III-V	Perhaps	Probably not
Who needs OR availability?	Blunt medium/high-grade, penetrating injury	Blunt grade III-V, penetrating injury	Perhaps	Perhaps
Is angiography useful?	Yes, hybrid suite for unstable, and for stable with PA/CE.	Yes, in grade IV/V and any grade with CE.	Yes, in any grade with PA/CE/AVF, but in traumatic RAT/RAD, it has high rate of renal loss.	No
Is ERCP useful?	Yes, in biliary complications	No	No	Yes, in PDI.
Who needs to repeat imaging?	Not routinely	Grade III-V within 48–72 h	Grade IV-V within 48 h or the patient with clinical signs of complications.	If inconclusive initial CT scan, MRI/ERCP for suspect PDI.
Who needs prophylaxis antibiotics?	Not routinely	Not routinely	May need in the patient with risk of infectious complication.	May need in clinically severe pancreatitis or concomitant bowel injury.

Note: AAST: the American Association for the Surgery of Trauma; OIS: the organ injury scales; PDI: pancreatic duct injury; OR: operating room; PA: pseudoaneurysm; CE: contrast extravasation; AVF: arteriovenous fistula; RAT: renal artery thrombosis; RAD: renal artery dissection; ERCP: endoscopic retrograde cholangio-pancreatography

Patients with suspected abdominal trauma who are in critical condition may benefit from resuscitative endovascular balloon occlusion of the aorta (REBOA) to quickly control suspected internal bleeding. Researches have shown that REBOA may improve survival rates, especially in patients who are experiencing low blood pressure but have not yet gone into cardiac arrest. This treatment can be effective in controlling bleeding from abdominal trauma, as long as there are no other injuries such as aortic dissection or cardiac tamponade in the chest area (7,8,24).

6. CONCLUSION

Abdominal trauma is commonly encountered in emergency departments and concerns many different medical branches. Diagnosis of abdominal trauma requires a meticulous investigation which includes repeated evaluation of the patient, laboratory tests and imaging studies. Regarding categorization and classification of injuries, there are a variety of guidelines which are highly useful in daily medical practice. Management of the injuries are made according to the possibility of the morbidity and mortality. When high clinical suspicion exists emergent laparotomy is the definitive choice of treatment.

REFERENCES

1. Demetriades D, Murray J, Charalambides K, et al. Trauma fatalities: time and location of hospital deaths. J Am Coll Surg. 2004;198(1):20-26.

2. ATLS, Advanced Trauma Life Support for Doctors(Student Course Manual). Chicago, IL: American College of Surgeons; 2018

3. Sido B, Grenacher L, Friess H, Büchler MW. Das Abdominaltrauma [Abdominal trauma]. Orthopade. 2005;34(9):880-888.

4. Intravia JM, DeBerardino TM. Evaluation of blunt abdominal trauma. Clin Sports Med. 2013;32(2):211-218. doi:10.1016/j.csm.2012.12.001

5. Mushtaq Ahmed RB. Frequency and pattern of intra-abdominal injuries in patients with blunt abdominal trauma. Journal of Trauma & Treatment. 2014;03(03).

6. Brenner M, Hicks C. Major abdominal trauma. Emergency Medicine Clinics of North America. 2018;36(1):149-160.

7. Nadir N-A. Abdominal Trauma. Clerkship Directors for Emergency Medicine. https://www.saem.org/about-saem/academies-interest-groups-affiliates2/cdem/for-students/online-education/m4-curriculum/group-m4-trauma/abdominal-trama. Published November 2018. Accessed January 5, 2023.

8. French L, Gordy S, Ma O. Abdominal Trauma. In: Tintinalli JE, Stapczynski J, Ma O, Yealy DM, Meckler GD, Cline DM. eds. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 8e. McGraw Hill; 2016.

9. Melville SC, Melville DE. Chapter 25. Abdominal Trauma. In: Stone C, Humphries RL. eds. CURRENT Diagnosis & Treatment Emergency Medicine, 7e. McGraw Hill; 2011.

10. Bouzat, P., Valdenaire, G., Gauss, et al. Early management of severe abdominal trauma. Anaesthesia Critical Care & Pain Medicine. 2020;39(2), 269–277.

11. Meizoso JP, Ray JJ, Karcutskie CA, et al. Effect of time to operation on mortality for hypotensive patients with gunshot wounds to the torso. Journal of Trauma and Acute Care Surgery. 2016;81(4):685-691.

12. Rozycki GS, Root HD. The diagnosis of intraabdominal visceral injury. J Trauma. 2010;68(5):1019-1023.

13. Malinoski DJ, Patel MS, Yakar DO, et al. A diagnostic delay of 5 hours increases the risk of death after blunt hollow viscus injury. J Trauma. 2010;69(1):84-87.

14. Lahiri R, Bhattacharya S. Pancreatic trauma. Ann R Coll Surg Engl. 2013;95(4):241-245.

15. Muroni M, Provenza G, Conte S, et al. Diaphragmatic rupture with right colon and small intestine herniation after blunt trauma: a case report. J Med Case Rep. 2010;4:289. Published 2010 Aug 24.

16. Feliciano DV. Abdominal Trauma Revisited. Am Surg. 2017;83(11):1193-1202.

17. Yates JG, Baylous D. Air Medical Ultrasound: Looking Back to See What We Have Learned for the Future. Air Med J. 2022;41(6):536-541.

18. Lindner T, Bail HJ, Manegold S, Stöckle U, Haas NP. Schockraumdiagnostik: Initiale Diagnostik beim stumpfen Abdominaltrauma. Eine Literaturübersicht [Shock trauma room diagnosis: initial diagnosis after blunt abdominal trauma. A review of the literature]. Unfallchirurg. 2004;107(10):892-902.

19. Beltzer C, Bachmann R, Strohäker J, et al. Wertigkeit der Laparoskopie beim penetrierenden und stumpfen Abdominaltrauma – ein systematisches Review [Value of laparoscopy in blunt and penetrating abdominal trauma-a systematic review]. Chirurg. 2020;91(7):567-575.

20. O'Malley E, Boyle E, O'Callaghan A, Coffey JC, Walsh SR. Role of laparoscopy in penetrating abdominal trauma: a systematic review. World J Surg. 2013;37(1):113-122.

21. Holcomb JB, Jenkins D, Rhee P, et al. Damage control resuscitation: directly addressing the early coagulopathy of trauma. J Trauma. 2007;62(2):307-310.

22. Como JJ, Bokhari F, Chiu WC, et al. Practice management guidelines for selective nonoperative management of penetrating abdominal trauma. J Trauma. 2010;68(3):721-733.

23. Kanlerd A, Auksornchart K, Boonyasatid P. Non-operative management for abdominal solidorgan injuries: A literature review. Chin J Traumatol. 2022;25(5):249-256

24. Scott DJ, Eliason JL, Villamaria C, et al. A novel fluoroscopy-free, resuscitative endovascular aortic balloon occlusion system in a model of hemorrhagic shock. J Trauma Acute Care Surg. 2013;75(1):122-128. doi:10.1097/ta.0b013e3182946746

CHAPTER XVIII

IMAGING FINDINGS OF PELVIC EMERGENCY DISEASES IN FEMALE PATIENTS

Ahmet Turan Kaya

(Asst. Prof,), Department of Radiology, Amasya University, Sabuncuoğlu Şerefeddin Research and Education Hospital, Amasya, Turkey
E-mail: hmttrnky.62@gmail.com
ORCID: 0000-0001-9803-453X

Gynecological emergencies are various in female patients, and imaging techniques are important for early diagnosis. Rapid diagnosis reduces the risk of mortality and morbidity. In many emergency pathologies, diagnosis is difficult because the symptoms and physical examination are nonspecific. Ultrasonography (US) and Color Doppler US (CDUS) is the first choice for the evaluation of vascularity since it does not contain radiation, and at the bedside if necessary. Computed tomography (CT) and magnetic resonance imaging (MRI), which are cross-sectional imaging methods, can be used in the definitive and differential diagnosis of the disease. It is important to increase awareness of imaging findings of gynecological emergencies, especially depending on the experience of the radiologist performing US and CDUS. CT is the first cross-sectional imaging method used after the US in patients presenting with acute abdomen in the emergency departments. The advantages of CT are that the acquisition is fast, it is generally not affected by motion artifacts, and metallic material outside the imaging area is not a contraindication. The disadvantage is radiation exposure, which is important in female patients of reproductive age. CT can be used as the first choice cross-sectional imaging for the differential diagnosis of gynecological and non-gynecological emergencies. However, conventional CT cannot provide lesion characterization as MRI. Thanks to the latest technological developments, dual-energy CT (DECT) that provides X-rays from a double tube can characterize some different materials (1). Due to its ability to recognize iodine, DECT can distinguish hemorrhage

from increased density due to contrast enhancement. Also, it can distinguish hemorrhagic material in ovarian cysts with its iron content, and subtracts iodine in contrast imaging, allowing virtual non-contrast images to be obtained. This results in less radiation exposure.[1]Although CT can reach faster cross-sectional imaging, tissue discrimination resolution like MRI is not sufficient. Because of the signal changes in different sequences, the hemorrhage distinction can be made more clearly and the stage of the hemorrhage can be determined. In addition, diffusion weighted imaging (DWI), a sequence of MRI, is very important in cases where blood circulation is impaired such as adnexial torsion, and in the diagnosis of dense collections such as a turbo-ovarian abscess. While it does not contain radiation, has high tissue resolution, and can be applied in pregnant women, MRI is an important advantage compared to CT, while the long duration of the scans and its sensitivity to motion artifacts are important disadvantages.

Acute gynecological diseases can be divided into three categories as anatomical and inflammatory pathologies.

1 ACUTE GYNECOLOGICAL EMERGENCIES IN ADNEXIAL areas

1.1 Acute hemorrhagic adnexial lesions

Intraperitoneal hemorrhages may occur due to both ectopic pregnancy and rupture of ovarian cysts. Especially in patients of reproductive age, the first imaging modality to be performed is the US and beta-human chorionic gonadotrophin (βhCG) as a laboratory test. The imaging findings of hemorrhagic adnexial lesions include significant reduction in size of ovarian cysts present in previous imaging, increased ipsilateral dense fluid, or newly developed adnexial cystic lesion suspicious for ectopic pregnancy, and a positive pregnancy test. For differential diagnosis in patients diagnosed with ectopic pregnancy, it is sufficient to perform CT instead of MRI, which takes a long time. The presence of fluid with contour irregularity and high density adjacent to it on CT is significant in terms of a hemorrhagic cyst rupture. However, MRI scan after the US will be more useful for the location of the gestational sac in a suspected ectopic pregnancy (Table 1). Measurement of βhCG levels is important in the differential diagnosis of a hemorrhagic cyst and ectopic pregnancy (2,3).

Table 1 Imaging Findings of Emergency Cystic Lesions in Adnexal Regions			
	US - CDUS	**CT**	**MRI**
Hemorrhagic ovarian cyst	First imaging technique	Not indicated unless cyst rupture with pain	When US fails to identify the cyst The appearance depends on the stage of the hemorrhage
	While it is isoechoic compared to the ovary parenchyma in the acute period, it is hypoechoic in the late period.	Hyperdense mass within the adnexal with a high attenuation area (>40 HU).	Typically, high T1 material is seen within the cyst.
	Posterior acoustic enhancement.	Smooth enhancing cyst wall.	Hyperintensity on both T1- and T2-weighted images **OR**
	It has a thin, reticular "cobweb" or lace-like pattern.	In some cases, contrast agent extravasation	Hyperintensity on T1-weighted images and hypointensity on T2-weighted images
	Sometimes, avascular clot material may be present in the cyst, adjacent to the wall.	*Hemoperitoneum:* High attenuation peritoneal free fluid (>30 HU).	*Hemoperitoneum:* As a result of cyst rupture, hypo-hyperintense T1W and T2W dense fluid can be detected in the pelvis.
	If the cyst ruptures, hypoechoic heterogeneous free pelvic fluid is seen.		Typical lace-like reticular pattern
Ectopic pregnancy (beta HCG < 2000 IU)	First imaging technique	Not indicated	Not indicated
	Adnexal cystic mass AND	Adnexal cystic mass AND	Adnexal cystic mass AND
	Empty uterine cavity	Peripheral enhancement at contrast-enhanced CT	Peripheral enhancement at contrast-enhanced MRI
	Thick echogenic endometrium		Hematosalpinx
	Complex extra-adnexal cyst/mass		Hemorrhagic or heterogeneous mass
			Hemoperitoneum
			Tubal dilatation
			Tubal wall enhancement
T1W = T1-weighted image, T2W = T2-weighted image.			

1.1.1 Hemorrhagic ovarian cyst

The increase in ovarian vascularity, especially in the luteal phase, may cause rupture (4). Cyst rupture is usually seen on the right side because the left ovary is protected by the sigmoid colon. Although cyst rupture can sometimes cause massive hemoperitoneum, surgical treatment is not applied unless patients are unstable (5). Dermoid cysts and endometriotic cysts may also cause acute pelvic pain by causing hemoperitoneum after rupture (Figure 1-2).

1.1.2 Ectopic pregnancy

It occurs when the gestational sac and fetus are located outside the endometrial cavity. It most often occurs in the ampulla of the fallopian tube. Typical imaging finding of tubal ectopic pregnancy is adnexal cystic sac-like structure and ipsilateral normal ovary (6). On contrast-enhanced CT and MRI, peripheral enhanced adnexal cystic mass and hemoperitoneum may be seen if ruptured.

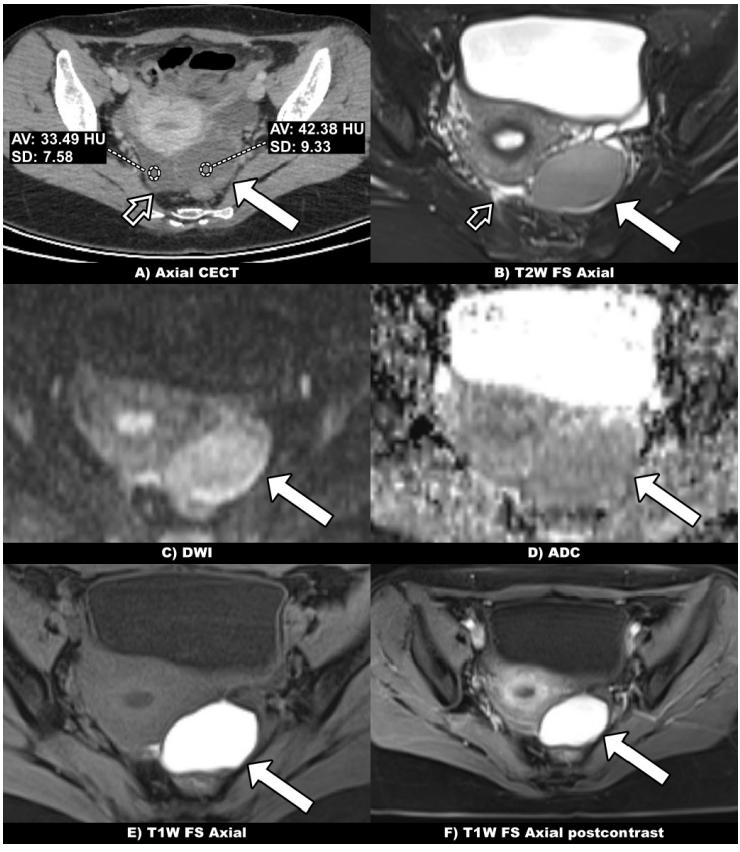


Figure 1 MRI images of a hemorrhagic cyst.

A 35-year-old female patient presented with the complaint of pelvic pain for 4 days. A cyst was seen in the left ovary (LO). A) In contrast-enhanced CT, there was a 42.38 HU density hemorrhagic cyst in LO (white arrow) and a 33.49 HU density peritoneal free fluid (A-B) at Douglas pouch (open arrow). In T2W FS (B), there was iso-hypointense T1W FS (E) hyperintense, postcontrast T1W (F) non-enhancing hemorrhagic cyst with mild diffusion restriction (C-D) consistent with early subacute hemorrhage (white arrow).

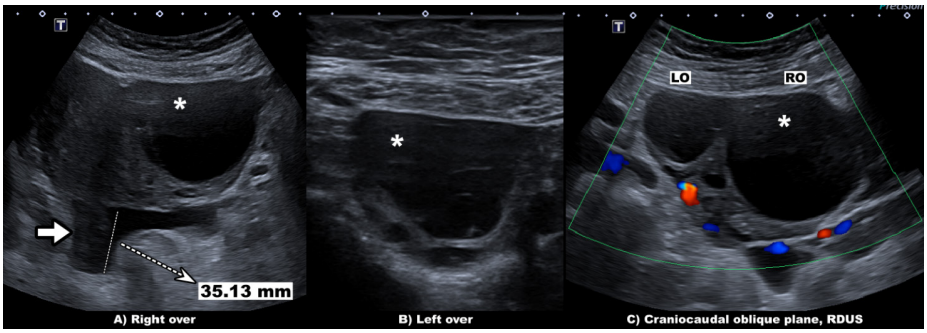


Figure 2 US images of a hemorrhagic cyst rupture.

A 38-year-old female patient had increased abdominal pain for about 3 days. Cysts were observed in both ovaries in the transabdominal US (LO: Left ovary; RO: Right ovary). There was an avascular, iso-hypoechoic clot (asterisk) adjacent to the walls of the cysts. A) Due to the rupture of the hemorrhagic cyst in the RO, there was free fluid at the Douglas distance measuring 35.13 mm due to hemorrhagic leveling (white arrow). B) Hyperechoic bands with a "thin, reticular cobweb or lace-like pattern" are seen in LO. C) In craniocaudal oblique plane CDUS imaging, vascularity is not observed in every cyst.

1.2 Acute disorders associated with adnexal masses

1.2.1 Adnexal torsion

Adnexal torsion causes only the ovary or fallopian tube, or both, to rotate around itself, resulting in impaired blood circulation (7-9). The term adnexal torsion is preferred, mostly because both are torsioned together (10). It occurs most frequently in reproductive age (15-30 years) and postmenopausal women and shows a double peak (7). In premenopausal terms, the most common non-tumoral cause is a follicle or corpus-luteum cyst, and the most common tumoral cause is masses larger than 5 cm, such as mature cystic teratoma (7,8,11). In postmenopausal women, torsion is more commonly associated with a malignant

mass (12). Torsion in the right ovary (2/3) is most commonly seen due to excessive mobility of the ileocecal region. Therefore, it can mimic acute appendicitis. Since the sigmoid colon restricts the movement of the left adnexal structures, torsion develops here less frequently (7,8,13). Malignancies, inflammatory disease, and endometriosis cause adhesions and reduce ovarian movement, thus reducing the likelihood of torsion (8,14,15). In a premenopausal woman, the normal ovary is on both sides of the uterus and can measure up to 20 cm^3 in volume (17). The ovaries and fallopian tubes receive a dual blood supply from the ovarian and uterine arteries.[18]When adnexal torsion develops, first venous and then arterial and lymphatic flow disappears. In partial torsion, venous and lymphatic flow is disrupted without affecting the arterial flow and edema occurs (7,11,19).

Imaging findings: Ovarian volume has increased (in the premenopausal period >20 cm^3, in the postmenopausal period>10 cm^3) (17). First choice is CDUS. CT or MRI is recommended in the subacute or chronic phase (**Figure 3**). Diagnosis of hemorrhagic infarct on CT and MRI is important for prognosis. Pre- and post-contrast fat-suppressed (FS) T1W sequence on MRI is important to demonstrate vascularity(13). A solid, complex, or cystic mass may be present in the adnexal localization. If there is a cystic mass, there may be a uniform thickening of its wall (more than 10 mm). The tuba uterina is edematous and thickened (more than 10 mm) (13). In most cases, if there is free dense fluid in the pelvis, it is necessary to pay attention to cyst rupture and hemorrhage (Table 2).

Table 2 Imaging Findings of Adnexal Torsion			
	US - CDUS	**CT**	**MRI**
Adnexal torsion	First imaging technique	CT or MRI is recommended in the subacute or chronic period. Diagnosis of hemorrhagic infarct on CT and MRI is important for prognosis.	
	The size of the ovary increases, its stroma becomes edematous, and the follicle cysts shift sweat to the periphery.		
	In the late period, infarcted secondary cystic or hemorrhagic degeneration may occur.		
	The ovary may be displaced in the midline or superior to the uterus.		
	The uterus deviates to the torsioned ovarian side. It may be a solid, complex, or cystic mass in the adnexal localization.		
	Twisted vascular pedicle		
	If there is pelvic-free fluid, the cyst may rupture and hemorrhage.		
	There is ipsilateral pain on compression with the transducer.	Hemorrhagic necrosis, ovarian density>50 HU on non-contrast CT.	In MRI, signal changes may show in T1W and T2W images according to the stage of blood in hemorrhagic necrosis.
	In the early period, a resistant arterial flow pattern is observed.		DWI images have diffusion restriction.
	In the late period, arterial flow is absent, or reversed diastolic flow is observed. This is a sign of poor prognosis.	On post-contrast images, there is the decrease in contrast enhancement.	
T1W = T1-weighted image, T2W = T2-weighted image.			

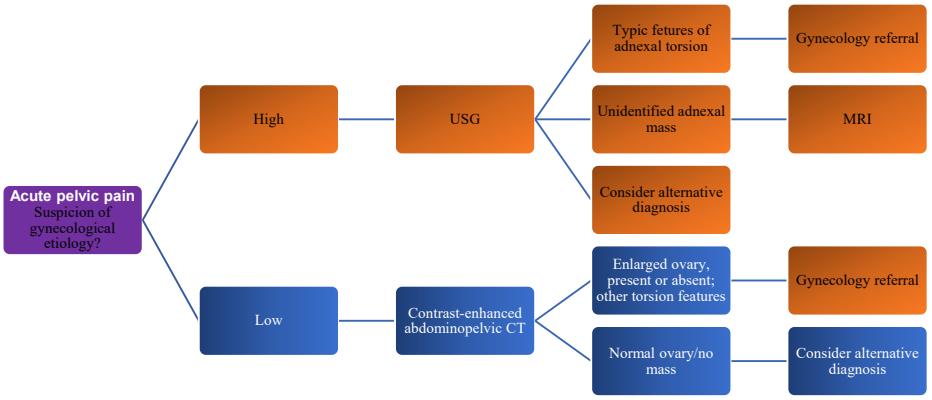


Figure 3 Algorithm of adnexal torsion

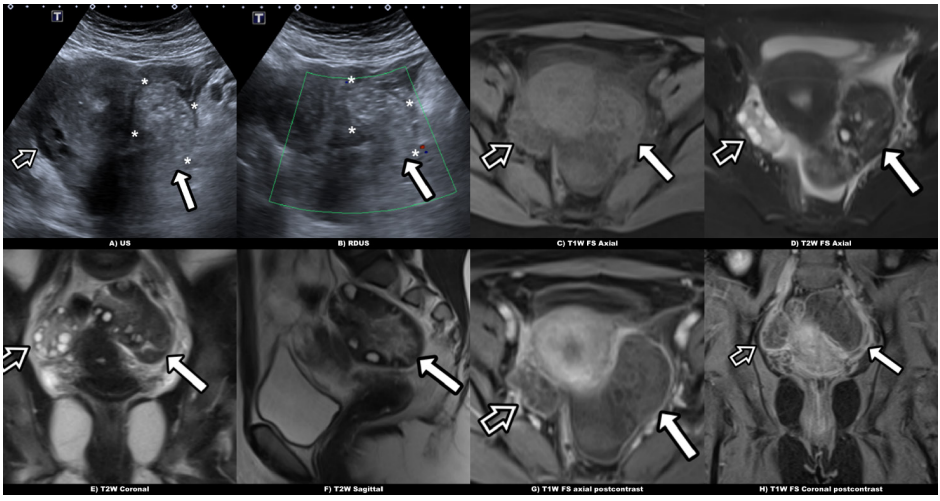


Figure 4 US and MRI images of adnexal torsion.

Transabdominal US was performed to a 25-year-old female patient due to pelvic pain for about 2 days. [Open arrow: Right ovary (RO); White arrow: Left ovary (LO)]. A-B) In the US and CDUS images, while the RO is of normal size and echogenicity, the LO (asterisk marks and white arrow) with increased dimensions and increased echogenicity in the central and no vascularity is observed. C-F) Signal changes due to edema in the central LO are observed as hypointense on T1W FS axial images and hyperintense on axial, coronal and sagittal T2W images. G-H) In post-contrast axial and coronal T1W FS images, contrast enhancement is observed in RO but not in LO.

Ultrasonography (US) and Color Doppler Ultrasonography (CDUS): It is the first imaging method in the premenopausal period as it does not contain radiation (Figure 4) (20). However, it is operator dependent. The whirlpool finding is pathognomonic (7,11). There is tenderness in the localization of the torsioned ovary in compression with the transducer. Since the ovaries are fed by the ovarian and uterine arteries in CDUS, the detection of arterial circulation does not exclude torsion. A resistive blood flow is observed. In the late period of torsion, no flow is detected, or reversed diastolic wave is observed. This is a pathognomonic sign of poor prognosis (7,11,13). The CDUS may help in determining the preoperative viability of the ovary. Fleischer et al. found that ovarian viability can be predicted if there is a central venous flow (21).

Cross-sectional imaging (CT and MRI) common features: They are helpful in excluding torsion in ovaries evaluated as normal in the US or differential diagnosis in suspicious cases (Figure 4) (7). Thanks to coronal and sagittal reformat images, it allows the evaluation of the adnexal area in different planes and its relationship with the surrounding deep tissue if there is a mass (7,11,13). If hemorrhagic necrosis develops, ovarian density increases (more than 50 HU on non-contrast CT). As a new approach, subtracted non-contrast images are obtained thanks to virtual non-contrast images of DECT. In this way, especially young patients are exposed to less radiation. In addition, it can be used as an aid in the diagnosis of patients with contraindications for MRI.[7]such as tubo-ovarian abscesses. Unusual adnexal torsion, such as massive ovarian edema, isolated fallopian tube torsion, and paraovarian cyst torsion, has also been described. Uterine disorders in gynecologic emergencies may be classified into two categories: (aContrast administration in these examinations, the radiation exposure in CT and the long duration of MRI are disadvantages compared to US.

1.3 Adnexal acute infectious disorders

1.3.1 Pelvic inflammatory disease (PID)

It is an infection of the upper genital organs (endometrium, fallopian tubes and ovaries) located in the pelvic fossa. Subgroups of PID: endometritis, salpingitis and tubo-ovarian abscesses. Typical symptoms are fever, pelvic pain, vaginal discharge and dyspareunia. It is more common in women of reproductive age, and complications such as infertility and ectopic pregnancy may develop as a result of late diagnosis. In the early stage of infection, imaging is usually normal. The common findings of PID subgroups on CT and MRI are streaking

and increased enhancement due to inflammation, especially in the mesosalpinx. In the late stages, uterine enlargement and thickening of the endometrium are seen in the US. If it progresses to salpingitis, it turns into pyosalpinx. Dilated tubes filled with dense contents are seen in the US (Table 3).

Table 3 Imaging Findings of Pelvic Inflammatory Diseases

	US - CDUS	CT	MRI
Pelvic inflammatory disease	Indicated	Not usually indicated	If US is indeterminate
	In the early period, imaging may be normal.		
	In the late period, uterine enlargement, thickened endometrium or pyosalpinx may be seen.		
	Dilated tubes filled with dense contents are seen in US.	In CT and MRI, there is an increase in streaking and contrast enhancement due to inflammation, especially in the mesosalpinx.	
Tubo-ovarian abscess	There is a single or multifocal collection with dense content, septa in it, thick walls and contamination in the adjacent mesosalpinx.		
	The blood supply in the adjacent mesosalpinx is increased and the fatty tissue has a dirty appearance.	Bilateral thick-walled contrast-enhancing masses	
		Increased peritoneal thickness surrounding the tuba and stranding due to inflammation	
		There is heterogeneous enhancement of the TOA wall and adjacent tissues.	
			T1W hypointense, T2W hyperintense heterogeneous, DWI has hyperintensity due to diffusion restriction.
			Signal increases in the mesosalpinx are more pronounced in fat-suppressed T2W sequences.
			Pyosalpinx: Wall thickening and dilated folded structures filled with dense content in T2W images.

CE = contrast-enhanced, T1W = T1-weighted image, T2W = T2-weighted image.

1.3.2 Tubo-ovarian abscess (TOA)

TOA is a serious complication of PID. TOA is seen in one-third of inpatients for PID, due to a lack of early diagnosis or appropriate treatment (22). At this stage, the treatment is more aggressive and there is a risk of sepsis and mortality as a result of perforation of the abscess. In the imaging, there is a single or multifocal collection with dense content, septa in it, thick-walled, and streaking in the adjacent mesosalpinx. In the US, blood flow is increased in the adjacent mesosalpinx and the fatty tissue has a dirty appearance. Contrast-enhanced CT (CECT) and MRI show heterogeneous enhancement of the TOA wall and adjacent tissues. In addition, in the MRI, there is heterogeneous hypointensity in T1Wimage, hyperintensity in T2W image, and hyperintensity due to diffusion restriction in DWI sequence (22). Signal increases are more prominent in fat-suppressed (FS) T2W image as a result of streaking secondary to inflammation in the mesosalpinx. In addition, in fat-suppressed contrast-enhanced T1W images, increased contrast enhancement is observed in the mesosalpinx, and adjacent organs. As a result of similar findings in the tuba, wall thickening and dilated folded structures filled with dense content are observed on T2W images and are called pyosalpinx (23,24).

2 ACUTE GYNECOLOGICAL EMERGENCIES OF UTERUS

2.1 Acute leiomyoma (fibroid) complications

Uterine leiomyoma is 20-40% over 30 years of age, and the two most important emergency pathologies in complicated patients are “Red Degeneration” and “Torsion of a Subserosal Leiomyoma”. Red degeneration develops in the periphery of the intramural leiomyoma due to hemorrhagic infarction secondary to venous thrombosis (25). It is seen as a rapid increase in size on US and a decrease or absence of blood flow on CDUS. Decreased enhancement due to degeneration and hypodense heterogeneous cystic areas are seen on CT. In the T1W image, diffuse or heterogeneous high-intensity within the leiomyoma, and in the T2W image hypointense rim can be observed on MRI. Diffuse or heterogeneous high-intensity can be seen in the center of the leiomyoma in the T1W image, and a hypointense rim in the periphery of the leiomyoma in the T2W image(Figure 5) (Table 4).

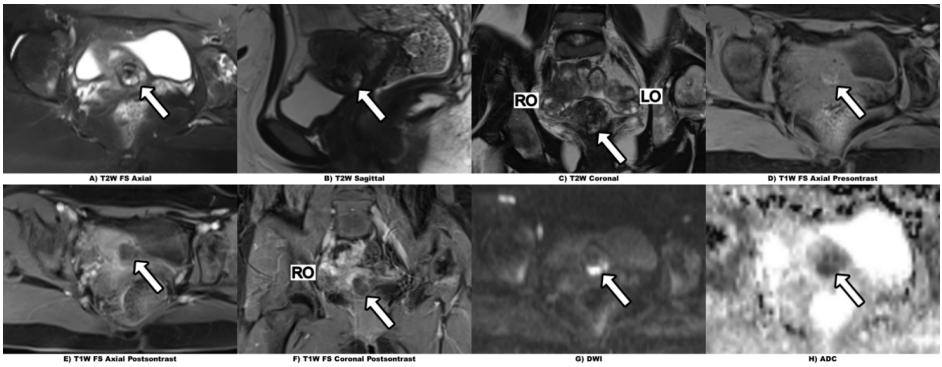


Figure 5 MRI images of hemorrhagic degeneration of intramural leiomyoma. MRI was performed to a 42-year-old female patient with the complaint of irregular menstrual bleeding. Both ovaries appeared normal [Right ovary (RO); Left ovary (LO)]. A-D) Triplanar T2W images showed intramural leiomyoma of the uterine corpus (white arrow) with a hyperintense heterogeneous central region and a hypointense ring at the periphery. T1W images showed hyperintense areas central and peripheral to the leiomyoma (white arrow), consistent with hemorrhagic degeneration. E-F) Contrast enhancement wasn't seen in leiomyoma (white arrow) in post-contrast images. G-H) DWI and ADC images showed diffusion restriction consistent with acute-subacute hemorrhage (white arrow).

Subserosal leiomyoma torsion, similar to adnexal torsion, occurs as a result of the leiomyoma rotating around itself and impairing its circulation (26). While the ovaries are normal on imaging, an unenhanced mass is observed on CT and MRI, and an avascular mass is observed on CDUS.

2.2 Acute uterine bleeding

The common cause of uterine bleeding in the late postpartum period is retained products of conception (RPOC) (27). In addition, although rare, uterine arteriovenous malformation (AVM) may cause bleeding in the late postpartum period (27). Both CT and MRI are important in the diagnosis of postpartum hemorrhage.

RPOC: It is defined as the remaining placental tissue in the uterus after delivery or abortion (28). RPOC is seen as a mass with vascularity in CDUS extending into the myometrium in the endometrial cavity. On the contrast-enhanced dynamic MR imaging, T1W and T2W images show an endometrial

mass with heterogeneous intensity and variable postcontrast enhancement. The signal intensity of RPOC may vary depending on the stage of bleeding and the presence of necrosis (27).

Uterine AVM: Hypervascular lesions that do not regress despite a negative pregnancy test in the postpartum period may be AVMs (29). On CT and MRI with dynamic contrast, it can be seen as a tortuous and tubular vascular tangle in the endometrium and myometrium in arterial and venous phases (27). Digital Subtraction Angiography is effective both in defining the anatomy and in the treatment with embolization.

Table 4 Imaging Findings of Uterine Emergencies			
	US - CDUS	**CT**	**MRI**
Red degeneration of myoma	Indicated	If patient has acute pain	May be used to differentiate the diagnosis
	Cystic-necrotic change areas in the central of the leiomyoma	Hypodense heterogeneous appearance of cystic-necrotic change areas in the center of the leiomyoma	Hyperintense heterogeneous appearance in T2W images of cystic-necrotic change areas in the center of the leiomyoma
	It is seen as a rapid increase in size in the US and decreases or absence of vascularity in CDUS.		
			T2W hypointense peripherally and T1W hyperintense centrally
Torsion of a subserosal leiomyoma	Decreased vascularity	The ovaries are normal on imaging, but a mass that is connected to the uterus and has no enhancement on CT and MRI.	
Acute uterine bleeding (RPOC and Uterine AVM)	Endometrial mass with vascularity (RPOC or AVM)	Endometrial mass with contrast enhancement (RPOC)	Endometrial mass with heterogeneous signal intensity, on T1WI andT2WI Variable enhancement on postcontrast images (RPOC)
		A vascular lesion with myometrial involvement (AVM)	
			Flow void within the mass(AVM)
AVM = arteriovenous malformation, CE = contrast-enhanced, RPOC = retained products of conception, T1W = T1-weighted image, T2W = T2-weighted image.			

References

1. Marin D, Boll DT, Mileto A, Nelson RC. State of the art: dual-energy CT of the abdomen. Radiology. 2014 May;271(2):327-42.

2. Kaakaji Y, Nghiem HV, Nodell C, Winter TC. Sonography of obstetric and gynecologic emergencies: Part I, Obstetric emergencies. AJR Am J Roentgenol. 2000 Mar;174(3):641-9.

3. Kaakaji Y, Nghiem HV, Nodell C, Winter TC. Sonography of obstetric and gynecologic emergencies: Part II, Gynecologic emergencies. AJR Am J Roentgenol. 2000 Mar;174(3):651-6.

4. Bennett GL, Slywotzky CM, Giovanniello G. Gynecologic causes of acute pelvic pain: spectrum of CT findings. Radiographics. 2002 Jul-Aug;22(4):785-801.

5. Kim JH, Lee SM, Lee JH, et al. Successful Conservative Management of Ruptured Ovarian Cysts with Hemoperitoneum in Healthy Women. PLoS One. 2014;9(3):e91171.

6. Kao LY, Scheinfeld MH, Chernyak V, Rozenblit AM, Oh S, Dym RJ. Beyond ultrasound: CT and MRI of ectopic pregnancy. AJR Am J Roentgenol. 2014 Apr;202(4):904-11.

7. Iraha Y, Okada M, Iraha R, et al. CT and MR imaging of gynecologic emergencies. Radiographics. 2017;37(5):1569-1586.

8. Chang HC, Bhatt S, Dogra VS. Pearls and pitfalls in diagnosis of ovarian torsion. Radiographics. 2008;28(5):1355–68.

9. Taufiq Dawood M, Naik M, Bharwani N, Sudderuddin SA, Rockall AG, Stewart VR. Adnexal torsion: Review of radiologic appearances. Radiographics. 2021;41(2):609-624.

10. Warner MA, Fleischer AC, Edell SL, et al. Uterine adnexal torsion: sonographic findings. Radiology. 1985;154(3):773-775.

11. Duigenan S, Oliva E, Lee SI. Ovarian torsion: Diagnostic features on CT and MRI with pathologic correlation. Am J Roentgenol. 2012;198(2):122-131.

12. Cohen A, Solomon N, Almog B, et al. Adnexal torsion in postmenopausal women: clinical presentation and risk of ovarian malignancy. J Minim Invasive Gynecol. 2017;24(1):94-97.

13. Rha SE, Byun JY, Jung SE, et al. CT and MR imaging features of adnexal torsion. Radiographics. 2002;22(2):283-294.

14. Huang C, Hong M-K, Ding D-C. A review of ovary torsion. Tzu-chi Med J. 2017;29(3):143.

15. Sommerville M, Grimes DA, Koonings PP, Campbell K. Ovarian neoplasms and the risk of adnexal torsion. Am J Obstet Gynecol. 1991;164(2):577-578.

16. Haskins T, Shull BL. Adnexal torsion: A mind-twisting diagnosis. South Med J. 1986;79(5):576-577. doi:10.1097/00007611-198605000-00013

17. Pavlik EJ, DePriest PD, Gallion HH, et al. Ovarian volume related to age. Gynecol Oncol. 2000;77(3):410-412.

18. Adeyemi-Fowode O, McCracken KA, Todd NJ. Adnexal torsion. J PediatrAdolesc Gynecol. 2018;31(4):333-338.

19. Ssi-Yan-Kai G, Rivain AL, Trichot C, et al. What every radiologist should know about adnexal torsion. EmergRadiol. 2018;25(1):51-59.

20. Lourenco AP, Swenson D, Tubbs RJ, Lazarus E. Ovarian and tubal torsion: imaging findings on US, CT, and MRI. EmergRadiol. 2014;21(2):179-187.

21. Fleischer AC, Stein SM, Cullinan JA, Warner MA. Color Doppler sonography of adnexal torsion. J ultrasound Med. 1995;14(7):523-528.

22. Kim SH, Kim SH, Yang DM, Kim KA. Unusual causes of tubo-ovarian abscess: CT and MR imaging findings. Radiographics. 2004 Nov-Dec;24(6):1575-89.

23. Sam JW, Jacobs JE, Birnbaum BA. Spectrum of CT findings in acute pyogenic pelvic inflammatory disease. Radiographics. 2002 Nov-Dec;22(6):1327-34.

24. Koh DM, Collins DJ. Diffusion-weighted MRI in the body: applications and challenges in oncology. AJR Am J Roentgenol. 2007 Jun;188(6):1622-35.

25. Ueda H, Togashi K, Konishi I, Kataoka ML, Koyama T, Fujiwara T, Kobayashi H, Fujii S, Konishi J. Unusual appearances of uterine leiomyomas: MR imaging findings and their histopathologic backgrounds. Radiographics. 1999 Oct;19 Spec No:S131-45.

26. Roy C, Bierry G, El Ghali S, Buy X, Rossini A. Acute torsion of uterine leiomyoma: CT features. Abdom Imaging. 2005;30(1):120-123.

27. Iraha Y, Okada M, Iraha R, et al. CT and MR imaging of gynecologic emergencies. Radiographics. 2017;37(5):1569-1586.

28. Sellmyer MA, Desser TS, Maturen KE, Jeffrey RB, Kamaya A. Physiologic, histologic, and imaging features of retained products of conception. Radiographics. 2013;33(3):781-796.

29. Huang MW, Muradali D, Thurston WA, Burns PN, Wilson SR. Uterine arteriovenous malformations: Gray-scale and Doppler US features with MR imaging correlation. Radiology. 1998;206(1):115-123.

CHAPTER XIX

ORCHESTRATING THE DIAGNOSIS & TREATMENT OF RECTAL CANCERS VIA MRI

Mujdat Yazıcı

(MD.), Institution: Hopa State Hospital,
Department of Radiology, Artvin, Turkey
E-mail: radiologymujdat@hotmail.com
ORCID: 0000 – 0003 – 2922 – 8976

1. Introduction

Colorectal cancer is one of the most common malignant diseases in the United States and Europe. It ranks third after lung and breast cancer in terms of incidence. According to the data of the Ministry of Health, colorectal cancer is the fourth most common cancer in Turkey and the second most common cancer in women *(1)*. Rectal cancer accounts for nearly half of colorectal cancers in both genders. When we analyze the causes of death from cancer, it ranks second in most countries. Genetic, experimental and epidemiological studies show that colorectal cancers occur as a result of a combination of hereditary and environmental factors. With the widespread use of screening programs, it is possible to detect rectal cancers at an early stage and to reduce mortality and morbidity *(2)*.

While rectal cancer was mostly surgically staged in the past, pre-operative imaging is increasingly used to assess local spread, choose the type of operation to be performed, and decide on pre-operative chemo-radiotherapy. Total mesorectal excision *(TME)* surgery and preoperative neoadjuvant chemo-radiotherapy, which are two important advances in treatment options, have begun to provide substantial effects in reducing the frequency of local recurrence and prolonging the survival of patients *(3)*. These advances in treatment have

increased the importance of preoperative staging, which provides information on tumor localization, size, configuration, and local infiltration depth *(3, 4)*.

Ultrasonography *(USG)*, endorectal ultrasonography *(ERUS)*, computerized tomography *(CT)*, virtual colonoscopy, phased array endorectal MRI, high resolution pelvic MRI *(HRMR)*, and recently positron emission tomography *(PET)* and PET-CT, which can be used especially in cases with recurrence With hybrid imaging methods such as intraluminal evaluation, not only can intralumen evaluation be performed, but also very valuable information can be obtained in terms of spread to neighboring tissues and systemic spread *(5, 6)*.

2. Imaging Techniques for Rectal Cancers

Barium radiographs and colonoscopy are important in diagnosis, but have a limited role in pre-operative staging. Today, the three basic imaging methods used in staging of rectal cancer are computerized tomography *(CT),* endorectal ultrasonography *(ERUS),* and magnetic resonance imaging *(MRI)*. The main limitation of CT is that it cannot distinguish the rectal wall layers due to its low spatial and contrast resolution and shows them as a single layer, therefore it is not successful in superficial staging *(6)*.

Although ERUS is a very accurate and reliable method for staging superficial rectal cancer, it is not suitable for the evaluation of meso-rectal excision plan. Staging of rectal cancer with high resolution MRI has become an increasingly accepted practice *(7)*. The advantages of this method over endoluminal techniques *(ERUS, MR imaging with an endorectal coil)* are that it can be applied in all tumor types that cause obstruction, large volume or high localization, can show the entire meso-rectum, meso-rectal fascia *(MRF)*, and reveal the relationship of the tumor with neighboring organs. The prognosis in rectal cancer is closely related to the extension of the tumor into the mesorectum and the complete clearance of the surgical resection margin from the tumor *(8)*.

2.1. Computerized Tomography (CT)

The depth of the lesion, its relationship with neighboring organs in the pelvis, and the search for systemic metastases are essential. Colorectal cancers can be seen on CT as a polypoid mass growing into the lumen or as an irregular wall thickening. If the cancer is only within the rectal wall, the outer surface borders are regular, the peri-rectal fatty area is homogeneous, and the surrounding structures and the plan can be distinguished.

In malignant lesions, although the appearance varies according to the stage of the tumor, it is irregular in the outer surface borders, heterogeneity in the surrounding fatty tissues, and effacement in the fatty planes. Because the contrast resolution of CT is low, the layers of the rectal wall cannot be distinguished and microscopic tumor spread in the surrounding fat planes cannot be demonstrated. Therefore, CT is insufficient to determine the depth of the cancer within the wall *(T staging)*, especially in early stage tumors *(9)*.

The inner structure of the lymph node and smaller metastases in the lymph node may not be visualized on CT. Accuracy rates for T staging in rectal cancer with CT range from 46 – 95%, and accuracy rates for N staging range from 52 – 79%. With the increasing number of cross-sections and high resolution, three-dimensional reformat images in CT technology, the accuracy rates in T staging with CT have reached 90%, and accuracy rates in N staging have reached 80% *(9, 10)*.

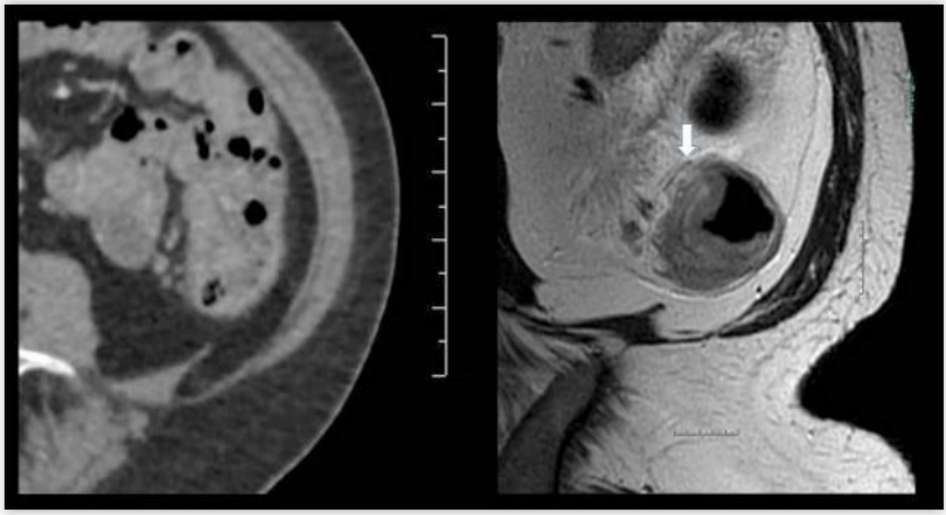


Figure 1: *(left) The CT scan did not identify the colonic tumor, although the request indicated a tumor in the descending colon detected at colonoscopy. (right) The MRI scan showed*

(left) The CT scan did not identify the colonic tumor, although the request indicated a tumor in the dscending colon detected at colonoscopy. (right) The MRI scan showed.

(left) The CT scan did not identify the colonic tumor, although the request indicated a tumor in the descending colon detected at colonoscopy. (right) The MRI scan showed a semicircumscript tumor at the mesenteric side of the descending colon (cT3a, N1,V0), confirmed at the histopathological specimen.

2.2. Endorectal Ultrasonography (ERUS)

The device consists of an ultrasonic transducer that is placed on a 25 cm long rigid probe, can rotate 360 degrees and can make 4 – 6 spins per second. The most important advantage of ERUS is the success of showing the rectal wall layers and thus the depth of invasion of the cancer in the rectal wall. The accuracy rate of T staging of ERUS is between 69 – 91%. Determining lymph node involvement with ERUS is more difficult than determining wall involvement. The accuracy rate in N staging is between 54 – 88%. As a diagnostic method, high accuracy in staging, low cost, and not exposing patients to radiation are advantages, thus it also has some disadvantages such as being dependent on the operator, requiring experience and relatively inadequate in T2 tumors *(11)*. The majority of staging errors in ERUS are the evaluation of T2 tumors as T3 due to surrounding inflammation. However, necrosis, bleeding, exposure to radiotherapy, post-biopsy changes, fibrosis, stool artifacts can be counted among other causes of high staging. ERUS is an appropriate and reliable diagnostic method, especially when it is desired to differentiate between T1 and T2 cancers and in early stage cases where local excision is planned *(9 – 11)*.

2.3. Pelvic Magnetic Resonance Imaging

Although cancer spread around the rectum is evaluated better than computerized tomography *(CT)*, due to the sharp contrast between cancer tissue and adipose tissue in conventional MRI, conventional MRI does not have a significant superiority over CT in local staging. With the introduction of phased array coils in recent years, the staging success of MRI has increased. Phase array MRI has become a useful, non-invasive method for staging both superficial and locally advanced rectal tumors *(12)*.

Its advantages are higher spatial resolution as well as the ability to obtain a wider imaging area, to display the rectal wall layers and to reveal the meso-rectal anatomy in detail. In addition, the location of the tumor and the presence of stenosis are not effective on the method. In the T2W-weighted sequence, three layers can be distinguished in the rectal wall: the innermost hyperintensity indicates the mucosa and submucosa, the outermost hypointensity indicates the muscularis propria, and the outermost hyperintensity indicates the perirectal adipose tissue. In contrast-enhanced dynamic T1W images, the mucosa and muscularis mucosa can be distinguished from the muscularis propria stained in the late stage by contrast in the early stage. In previous literature the importance

of MRI imaging in determining the perioperative margin of peripheral resection in rectal cancer surgery has been emphasized with 100% accuracy in staging of rectal tumors *(9, 13)*.

Although different techniques have been proposed in rectal high-resolution MR imaging, there is still no accepted consensus for the optimal technique. A good rectal cleaning is necessary as residual faeces can cause errors in the evaluation. Rectal lumen distension is still a controversial method. Distension can be created for the evaluation of rectal wall layers, but it has been reported that optimal results can be obtained without luminal distension. Luminal distension can be performed with air or positive/negative contrast material. With air and negative contrast medium, the lumen is hypointense on T2W sequences, and hyperintense on T1W sequences with positive contrast medium. Thus, tumors with different signal characteristics can be distinguished *(14)*.

There are two different approaches in the shooting protocol, such as imaging with only T2W sequences or imaging with both T1W and T2W sequences. T2W images are obtained with breath-holding turbo spin echo sequences. High resolution is obtained with the developing high resolution matrix, thin sections *(< 3 – 4 mm)* and small field of view *(FOV)*. Fat-suppressed T2W imaging can also be used to detect tumor extension into perirectal fatty tissue. T1W images with contrast can also be obtained. T1A turbo spin echo sequences with dynamic contrast have been used with endo-rectal MRI *(ERMRI)*. It is also possible to obtain high-resolution MRI have obtained contrast-enhanced T1W images using conventional spin echo sequences. Intravenous contrast material is essential when taking T1W images, because rectal wall layers cannot be visualized in detail in non-contrast examinations. In contrast-enhanced T1W images, the mucosa and submucosa show early and intense contrast enhancement, while the muscularis propria is not enhanced and the perirectal fatty tissue is hyperintense. It has been shown that contrast-enhanced T1-weighted sequences are not necessary for local staging of rectal cancer *(15)*.

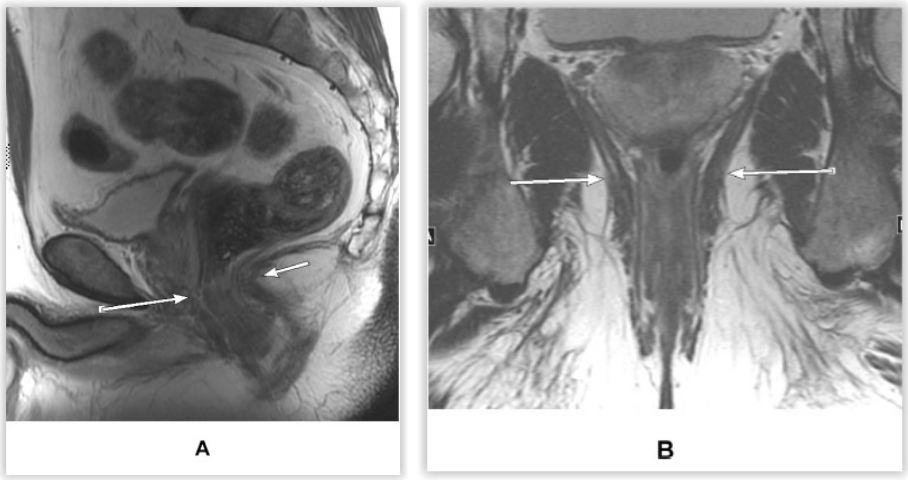


Figure 2: *A, B: Sagittal and coronal T2W MR pelvis images through the pelvic floor in a 52-year-old male with rectal cancer. Arrows indicate top of puborectalis/pubococcygeus muscles denoting the anorectal junction or "ring". MR, magenetic resonance.*

It is reported that the anal canal can also be evaluated during imaging of the rectum. Although its spatial resolution is low compared to ERMRI, it has been reported that the levator ani muscle, internal and external sphincters can be visualized with HRRM *(9)*.

Adipose tissue has high signal and muscular layer has low signal On T2W images, while tumor tissue has moderate signal intensity compared to these structures. In addition, its intensity is higher than that of the mucosa and submucosa. The meso-rectal fascia is a thin, hypointense band surrounding perirectal fatty tissue with a hyperintense appearance *(9)*.

HRRM cannot always distinguish between T1 and T2 tumors, as it is insufficient to distinguish between the mucosal and submucosal layers. In T1 and T2 tumors, the border between the submucosa and the surrounding circular muscle layer cannot be distinguished due to tumoral involvement, but the border between the muscularis propria and the surrounding perirectal adipose tissue is intact. In other words, if the border between muscularis propria and perirectal adipose tissue is clearly observed, the tumor is limited to stage T1 or T2. If this border is not clearly observed and nodular extensions of the tumor are present in this area, the tumor is compatible with stage T3. The definitive criterion for distinguishing between T2 and T3 is perirectal fatty tissue involvement. However, the main problem here is the desmoplastic reaction observed around

the tumor. High staging is therefore an obvious problem. In T4 tumors, muscular structures of the pelvic wall and tumor signal changes are observed in adjacent intrapelvic organs *(9, 13 – 15)*.

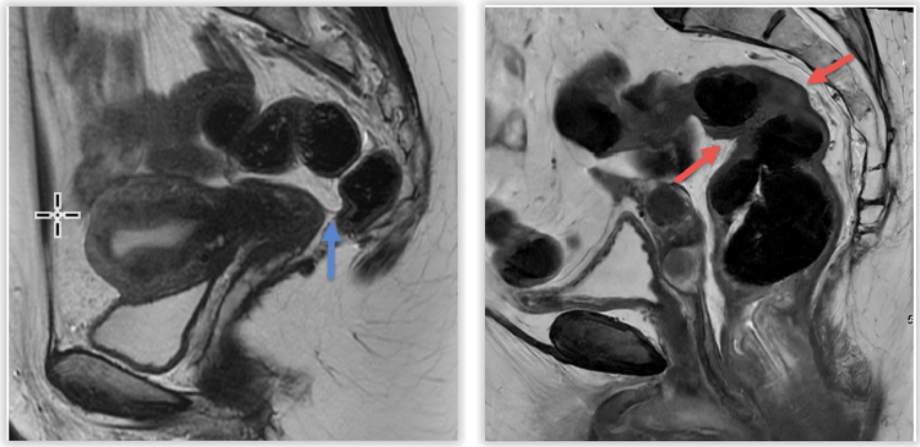


Figure 3: *Sagittal T2W MR of the pelvis in a 33-year-old female with rectal cancer. Blue arrow indicates the thin black line, the anterior peritoneal reflection, inserting onto the rectum at the cul-de-sac. MR, magnetic resonance.*

2.4. Imaging with Diffusion MR

The random thermal motion of molecules, also known as 'brownian motion', is called diffusion. Water molecules move randomly at a distance of tenths or hundredths of a millimeter per second. This movement is a microscopic movement and occurs depending on the temperature of the tissue and from the region of high concentration to the region of low concentration *(16)*.

In DWI, strong magnetic field gradients are activated in certain directions *(x, y, z axes)* and *'water diffusion'* becomes the dominant contrast mechanism and is directly visualized. This mechanism is based on magnetic resonance imaging of the signal loss, which occurs as a result of the interaction of the scattered movements of protons in water molecules in a spatially altered strong magnetic field. Diffusion-weighted MRI technique is sensitive to diffusion and perfusion at the cellular level. Fluid movement at the cellular level can be isotropic or anisotropic. Isotropic motion is equal, randomized motion in all directions. Anisotropic diffusion is the cellular diffusion that occurs at different rates in different directions. Differences in the amount of water inside and outside the

cell reveal the diversity of diffusion properties in tissues. These variations help explain pathological conditions in tissues *(17)*.

The basic physical principle of diffusion-weighted imaging is that magnetic fields changing by random diffusion of molecules cause dephase and signal loss in oscillation phases. This effect is too small to be noticed on standard images. To accentuate this effect of diffusion, strong gradients are used that sensitize an appropriate sequence to diffusion. The intravoxel dephase created by diffusion and the signal loss caused by it are formulated as follows *(9, 18)*:

S/S0:exp(-bD)

S/S0: It is the ratio of the signal obtained with and without diffusion gradient.

D : The value unit is the diffusion coefficient in square millimeters or square centimeters per second. This value depends on the physical properties of the molecules. For example, water molecules and similar small molecules have a large D value due to their fast movement, while larger molecules such as protein have a small D value due to their slow movement. Since other factors such as perfusion, mass movement, and water transport other than diffusion in the biological environment will cause signal loss, the term 'apparent diffusion coefficiant', that is, apparent diffusion coefficient, is used instead of the D value *(18)*.

b: It is the parameter that determines the diffusion weight of the signal. It is expressed in seconds per square millimeter or square centimetre. B values between a few hundred and a thousand sec/mm² are used for diffusion-weighted imaging. High b values reduce the signal-to-noise ratio, but increase the diffusion weight of the image *(18)*.

The b value is affected by several factors formulated below *(9, 18)*:

b = γ2δ2G2 (Δ-δ/3)
γ 2: gyromagnetic ratio
G: amplitude of applied gradient
δ: duration of applied gradient
Δ: time between gradients

Since the molecules are very small, gradients used to create a visible signal record due to diffusion must be very strong or used for a long time. Molecular

movement is affected by physiological movements and this influence is much greater than diffusion. Therefore, diffusion images obtained with conventional magnetic resonance sequences contain too much motion artifact and cannot be evaluated. These artifacts have been reduced by fast magnetic resonance sequences that have been used recently. The most important of these sequences is the single shot echo-planar imaging *(EPI)* sequence. Spin echo EPI *(SE EPI)* or gradient echo EPI *(GRE EPI)* sequences are used in diffusion-weighted imaging. Gradient echo EPI allows shorter TE values compared to SE EPI sequence, thus less T2 effect and higher b values can be obtained. EPI SE T2-weighted sequence adds two extra gradients of equal magnitude but opposite direction. While the first gradient causes the phase distribution *(dephase)* in the protons, the second gradient in the opposite direction provides the phase focusing *(rephase)* in the stationary protons *(9, 19)*.

Since some of the mobile protons have left the section and are not exposed to the second gradient, the phase focusing is partial and the initial T2 signal decreases proportionally to the diffusion coefficient. Protons with fast diffusion on diffusion-weighted images have a low signal due to loss of T2 signal, whereas protons with slow diffusion or at rest have a high signal because there is not much change in T2 signal *(19, 20)*.

2.4.1. Techniques Used in Diffusion-Weighted Imaging

First of all, EPI SE T2-weighted images without diffusion gradient *(b=0)* are obtained in diffusion-weighted images. Then this sequence is repeated 3 times by adding the diffusion gradient *(b= 400–1000 s/mm2)* in the x, y and z directions. The images obtained in the x, y and z directions reveal the differences in the diffusion rate depending on the tissue array, which are called anisotropic images. The direction, magnitude and T2 signal of the diffusion that creates the contrast in these images. The projection of the diffusion vector is calculated by taking the cube root of the product of the signal intensities measured in the x, y and z directions for each voxel. Thus, trace *(isotropic)* diffusion-weighted images are obtained. In these images, the direction-dependent signal change is eliminated. The magnitude of the diffusion and the T2 signal create contrast. As the b value increases, the diffusion weight increases and the dependence on T2 decreases. In practice, a b value over 400 s/mm2 provides sufficient diffusion weight *(21)*.

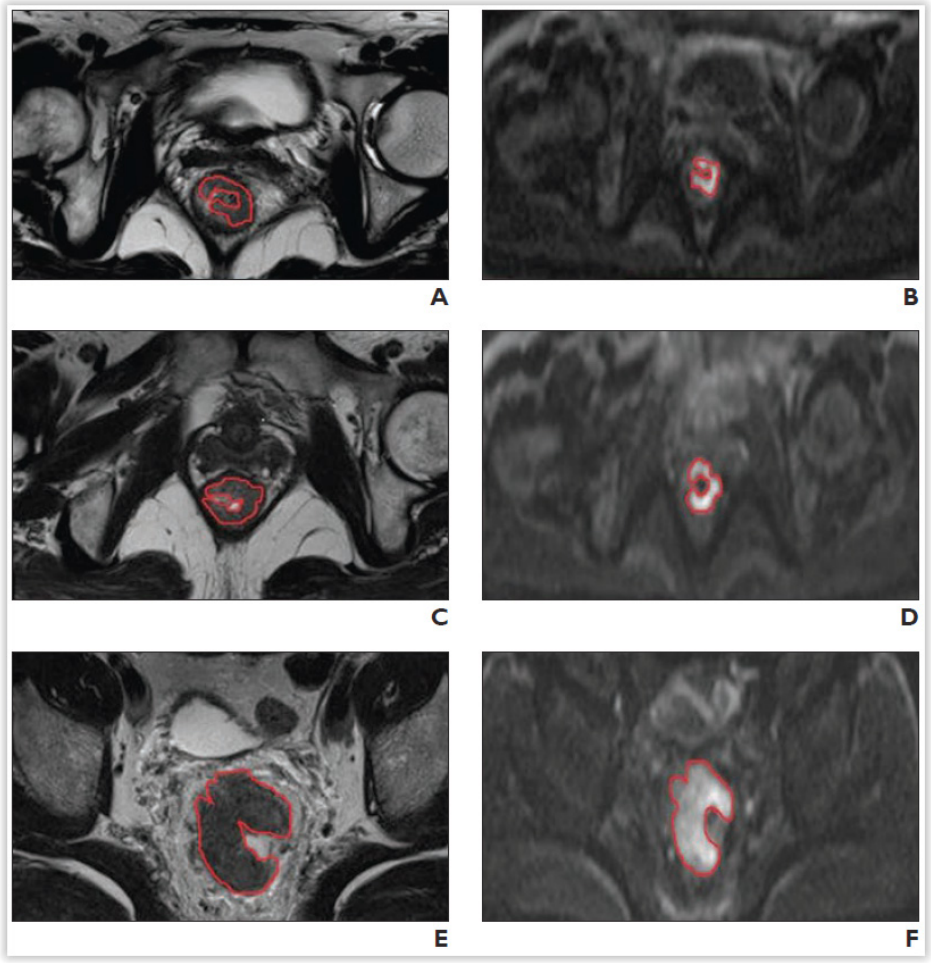


Figure 4: *Calculation of gross tumor volume (GTV) of well-defined rectal tumors. After manual tracing of lesion outer edge on each image (red line), GTV was automatically calculated as sum of cross-sectional volumes. A and B, Oblique axial T2-weighted MR (A) and DW (B) images show well-defined rectal tumor in 51-year-old woman with pathologically proven T1N0 disease but no lymphovascular invasion (LVI). GTV was 8.35 cm3 in A and 7.98 cm3 in B. C and D, Oblique axial T2-weighted MR (C) and DW (D) images show well-defined rectal tumor in 60-year-old woman with pathologically proven T2N1 disease but no LVI. GTV was 15.59 cm3 in C and 14.97 cm3 in D. E and F, Oblique axial T2-weighted (E) and DW (F) image show well-defined rectal tumor in 63-year-old man with pathologically proven T4aN2 disease and LVI. GTV was 42.45 cm3 in E and 39.40 cm3 in F.*

T-stage regression with pre-operative chemo-radiotherapy in locally advanced rectal cancer is an important prognostic factor that determines local recurrence and five-year survival. Although it is the optimal imaging method for staging cancer, it is sometimes insufficient to distinguish between fibrosis and tumor tissue in the evaluation of response to treatment after neoadjuvant therapy. The main goals of the developments in surgical technique, multiple use protocols of chemotherapy and radiotherapy are to prevent local recurrence of primary cancer, increase survival and preserve quality of life. Correct staging is essential before the operation in order to plan the correct treatment *(22)*.

The gradient intensity applied in the diffusion measurement is expressed with the *"b"* value. It is a parameter whose unit is mm²/second, which reflects the strength and duration of the gradient. As the gradient intensity increases, the phase distribution of the mobile protons and thus the signal loss increases. Therefore, the diffusion weights of the selected studies with a high *"b"* value are high. In clinical practice, it is generally recommended to use two *"b"* values, low *(b = 0 s/mm²)* and maximum *(b = 1000 s/mm²)*. Diffusion image with a value of *"b = 0"* provides only T2-weighted information, while *"b=1000"* creates pure diffusion-weighted images in x, y, z axes *(18, 23, 24)*.

In a study conducted by Sun et al. in 37 patients with locally advanced rectal cancer without distant metastases, ADC values *(b=1000 s/mm²)* were measured before treatment and at 1, 2 weeks after treatment and before surgery. While the percentage of ADC increase obtained 1 week after the start of treatment was 24.3% in the group with T-stage regression, it was 3.7% in the group without T-stage regression *(25)*. It was found significantly higher in patients with T-stage regression than in patients without T-stage regression *($p<0.001$)*. In this study, pre-treatment ADC values were found to be lower in the group that responded to treatment than in the group that did not respond to treatment. In addition, the percentages of ADC increase were found to be statistically significant between the two groups with and without regression in T stage with preoperative chemoradiotherapy. Extramural invasion seen in T3 – T4 rectal cancers is a poor prognostic finding *(25)*.

In a prospective study conducted by Kim et al. in 34 patients without distant metastasis and with T3 and T4 rectal tumors according to MRI evaluation, pre-treatment tumor ADC values, tumor volume, ADC increase rates, volume reduction rates were calculated and statistically significant differences were found between the groups that responded and did not respond to treatment. no significant difference was found *($p>0.05$)(26)*. In this study, pre-treatment

ADC values were compared in groups that responded and did not, and it was observed that ADC values were lower in the responding group. The mean ADC value was found to be 0.87±0.03 in the responding group when the T-stage regression was taken as the reference standard, and 0.89±0.06 when Mandard's 5 – point fibrosis grading system was taken as reference. ADC values for b 600 and b 1000 were measured in the study of Kim et al. in 76 patients with locally advanced rectal cancer. Post-treatment ADC values were found to be higher in the group that responded completely to treatment compared to the group that did not respond completely to treatment *(p<0.001)*. Pre-treatment ADC values were not found to be statistically significant in the groups that responded and did not fully respond to treatment *(p=0.40)*. In the neoadjuvant treatment of patients with locally advanced rectal cancer, ADC is accepted as a numeric biomarker to distinguish between T-stage regression and non-regression *(26)*.

3. Treatment of Rectal Cancer in Coordination with MRI Findings

The main method used in the treatment of rectal cancers is surgery. The standard surgical approach in clinically resectable, lower rectal, invasive cancers is abdomino-perineal resection *(APR)*. Despite advances in surgical techniques, the rate of pelvic recurrence is high when rectal cancers are treated with surgery alone. Five-year survival rates are given as 44-60% in T3-T4 rectal cancers that undergo surgery alone, and 25-30% in cases of lymph node involvement. In addition, these rapidly progressing cancers in the pelvis often cause severe pain and sacral plexopathy, negatively affecting the patient's quality of life *(27)*.

Another problem is the high morbidity and mortality after radical resection due to local recurrence in patients who underwent surgery alone especially abdomino-perineal resection. In many series, urinary complications due to APR application, especially sexual dysfunctions occurred more prominently in men, and infection were reported at a rate of 10 – 50%. The mortality rate was too high to be underestimated, and it has been reported to vary between 0 – 6.3% in various studies. In addition, these patients have to carry a permanent colostomy for life *(27)*. Post-operative simultaneous chemo-radiotherapy combination has become the standard treatment option in patients with stage II and III rectal cancer, due to randomized studies showing that post-operative radiotherapy is beneficial in local and regional disease control and chemo-therapy also contributes to survival. Small intestine toxicity increases due to the movement of the small intestines to the pelvis after surgery, and it appears as a factor

limiting the total dose of the applied radiotherapy *(28)*. For these reasons, the pre-operative use of radiotherapy and chemotherapy in locally advanced rectal cancers has come to the fore in recent years. The best treatment results in locally advanced rectal cancers have been obtained with the preoperative use of high-dose pelvic radiotherapy and 5 – Fluorouracil *(5 – FU)*-based chemotherapies. With the use of preoperative chemo-radiotherapy, a decrease in tumor stage and an increase in resectability were observed, and sphincter function-preserving operations were performed *(29)*.

With recent neoadjuvant chemo-radiotherapy applications, the complete response rate to treatment is approximately 20 – 30%. The rate has increased to 60% in reducing tumor stage. MRI is beneficial in the complete and accurate evaluation of the response to treatment before aggressive surgery, especially in the selection of sphincter-sparing surgery with less aggressive resection in cases with complete or almost complete response to chemo-radiotherapy. Although high-resolution rectal MRI *(HRRM)* is highly successful in imaging the primary tumor and meso-rectal fascia, it is insufficient in distinguishing residual tumor from fibrosis *(30)*.

Diffusion within living tissues is due to the random Brownian motion of molecules. Diffusion MRI is the only method to visualize Brownian motion in vivo. Therefore, MRI is significantly different from other morphology-weighted imaging methods. Today, diffusion-weighted MRI is frequently used in the early diagnosis of infarcts. In addition, many studies have shown that diffusion MRI has successfully differentiated benign-malignant pathologies of the breast, liver, kidney, and ovary *(31)*.

It is known that diffusion within the intracellular compartment is relatively slow due to the presence of cellular membranes. Apparent diffusion coefficient *(ADC)* values therefore vary in proportion to the distribution of extracellular and intracellular compartments within the tissue. Especially in malignant lesions, since increased cell density causes an increase in cellular membranes, intracellular organelles, matrix and other macromolecules, these lesions produce a higher signal on diffusion-weighted images due to restriction in diffusion *(32)*. ADC measurements from lesions are observed to be lower than benign ones. It was shown that that diffusion-weighted imaging *(DWI)* is superior to conventional MRI in detecting residual tumor in patients with head and neck cancer. High cellularity and low ADC values have also been reported in studies with malignant breast tumors. This is attributed to the structure and cell density of the tumoral tissue. All these studies show that diffusion techniques can be

used to evaluate individual response to chemotherapy and to guide treatment. It has also been shown in studies with experimental animals that the increase in ADC values can be detected quite early compared to the changes in tumor volume in the evaluation of the response to treatment after the chemotherapeutic agent. DWI also provide additional information such as tissue components such as edema, necrosis, fibrosis and tumor structure and cell density *(18, 33)*.

4. 3 Tesla MRI

Today, whole body MRI scanners and devices with high magnetic field *(3 Tesla)* have been used. In general, high magnetic field increases the signal-to-noise ratio *(SNR)* with it increasing spatial and temporal resolution. In previous studies, it was thought that high spatial resolution might improve outcomes of rectal cancer that could not be expected, especially in T staging. In this context, the anatomical layers of the rectal wall can be evaluated more clearly. Excellent results were obtained in studies with 3 Tesla MR devices. Kim et al. *(34)* have utilized 3 Tesla MRI and phase sequence winding, the accuracy rate in T staging was 92%, and T1 for tumors this rate is 97%. In another study comparing 3 Tesla MRI with endorectal sonography, Chun et al. *(35)* found the sensitivity of muscularis propria invasion to be 100% for both techniques. Although different techniques can be used in high resolution MRI, there is no standardization. Rectal cleaning is required before extraction, as residual faeces may cause errors during the evaluation *(34, 35)*.

Lumen distension can be achieved with air or positive/negative contrast material. Lumen T2-weighted images with air and negative contrast material *(T2AG)* hypointense, with positive contrast medium, luminal T1-weighted images *(T1AG)* appear hyperintense, so tumor with different signal can be distinguished *(9, 18)*.

MRI is insufficient to distinguish the mucosal and submucosal layers and cannot always distinguish T1 and T2 tumors accurately. In T1 and T2 stage tumors, the border between the submucosa and the surrounding circular muscle layer cannot be distinguished due to the extent of the tumor, but the muscularis propria and perirectal adipose tissue are intact. If the border between the propria and perirectal adipose tissue is clearly observed, the tumor is limited to T1 and T2 *(early stage)*. If we cannot clearly trace the border between the muscularis propria and the peri-rectal adipose tissue. If there is tumor extension at this level, the tumor is compatible with stage T3. The criterion in the differentiation

of T2 and T3 stage tumors is the involvement of perirectal adipose tissue, but high staging is frequently observed, as tumor and desmoplastic reaction may be confused. In stage T4 tumors, the tumor extends to the muscular structures of the pelvic wall or adjacent intrapelvic organs *(36)*.

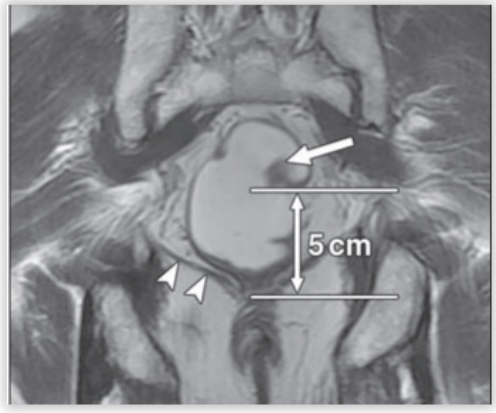


Figure 5: *57-year-old man with T1 well differentiated rectal adenocarcinoma (arrow). Coronal T2-weighted MR image shows distance from lower margin of rectal cancer to upper margin of external sphincter, where levator ani muscle (arrowheads) attached to rectum, was 5 cm (double arrow). Patient underwent sphincter-sparing resection of rectum.*

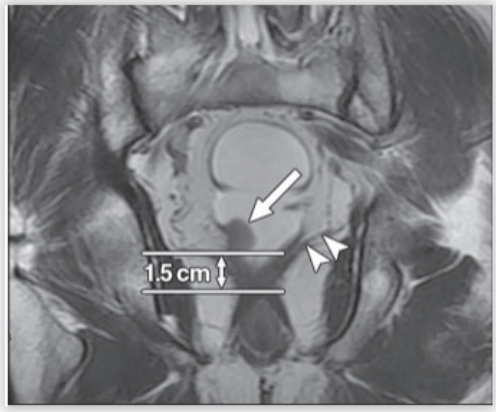


Figure 6: *58-year-old man with T2 moderately differentiated rectal adenocarcinoma (arrow). Coronal T2-weighted MR image shows distance from lower margin of rectal tumor to point where levator ani muscle (arrowheads) attaches to rectum is 1.5 cm (double arrow). Patient underwent internal sphincter resection with prolapsing technique to save external sphincter and anus.*

While 3 Tesla MRI systems provide great advantages to 1.5 Tesla MRI systems in brain and musculoskeletal imaging, they are also widely used for abdominal imaging. The generally accepted advantage is the significant increase in signal-to-noise ratio *(SNR)*, image optimization and the use of special imaging techniques. An increase in SNR increases spatial and temporal resolution hence, the shooting time is reduced. With the shortening of the imaging time, larger body areas such as whole body MRI and DWI can be obtained. With increasing SNR, thinner sections can be taken with higher b values in DWI. In practice, however,

the expected increase is not due to changes in the relaxation time of tissues, different coil designs, magnetic field inhomogeneities, artifacts and specific absorption rate *(SAR)* limitations *(37)*. As a result of the prolonged T1 relaxation time, the T1 contrast of the tissue decreases and the TR value is increased in order to compensate this, which increases the acquisition time and decreases the SNR. Chemical shift artifacts increase 2-fold compared to 1.5 Tesla MRI systems, which reduces SNR. However, the chemical shift effect provides an advantage in MR spectroscopy examination. The SAR value increases, resulting in an increase in body temperature. 3 Tesla MRI systems cause inhomogeneous RF distribution due to dielectric effects in tissues. B1 inhomogeneity causes low signal areas to form in the center of the imaged object *(37, 38)*.

Although 3 Tesla MRI systems increase spatial and temporal resolution, the main problem is understaging and overstaging in local staging. In a study comparing 3 Tesla MRI using superficial phase sequential coil and endorectal sonography in N staging of rectal cancer, *Chun et al. (35)* found the sensitivity for lymph node involvement 63.6% and 57.6%, respectively; specificity 92.3% and 82.1%; They found the accuracy rate as 79.2% and 70.8%. Although statistical data of MRI were higher, no significant difference was found. *Chun et al. (35)* used irregular border and mixed signal intensity instead of size as criteria for malignant lymph node. There are quite different results in the literature on lymph node staging. Diffusion Weighted MRI displays the differences in the motion of water molecules in different tissues. It has recently been used in oncology for tumor detection and characterization and to differentiate metastatic from nonmetastatic lymph nodes *(40, 41)*. When DWI is used together with conventional MRI, it is successful in distinguishing metastatic lymph nodes from non-metastatic ones, and its accuracy rate is higher than CT. The apparent diffusion coefficient (ADC) value of metastatic LNs was found to be lower than LNs without involvement*(39)*. Cho et al. *(40)* evaluated 468 lymph nodes in 34 patients separately with only diameter criteria in T2AG and ADC value in DWI, and after histopathological correlation, the accuracy rate of T2AG was 76%, and the cut-off value in ADC was when the diameter was taken as 3.8 mm. They reported an accuracy rate of 72% when 1.0x10-3 mm^2/sec was taken and reported that ADC could be used to identify metastatic lymph node. Mizukami et al. *(41)* in a study in which 129 patients and 1250 LNs were evaluated in recognizing metastatic lymph node in rectal cancer, in which they compared DWI + conventional MRI and CT, the accuracy rates were 87% and 76%, respectively; reported the sensitivity as 93% and 73%. In this study, it was stated

that DWI + conventional MRI is a superior modality than CT in evaluating metastatic lymph node in order to choose the optimal treatment in rectal cancer *(41)*.

5. Conclusion

Rectal cancer surgery is developing in order to achieve goals such as providing local control, increasing the quality of life, and protecting the sphincter, genitourinary and sexual life. In appropriate patients, minimally invasive methods such as transanal or local excision or transanal endoscopic microsurgery and laparoscopic resection increase the patient's comfort, shorten the hospital stay, and enable an earlier return to preoperative life *(27 – 33)*.

Magnetic resonance imaging has gained increasing importance in the management of rectal cancer over the last two decades. The role of MRI in patients with rectal cancer has expanded beyond the tumor-node-metastasis *(TNM)* system in both staging and restaging scenarios and has contributed to identifying "high" and "low" risk features that can be used to tailor and personalize patient treatment; for instance, selecting the patients for neoadjuvant chemoradiation *(NCRT)* before the total meso-rectal excision *(TME)* surgery based on risk of recurrence *(40)*.

Among those features, the status of the circumferential resection margin *(CRM)*, extramural vascular invasion *(EMVI)*, and tumor deposits have stood out. Moreover, MRI also has played a role in surgical planning, especially when the tumor is located in the low rectum, when the relationship between tumor and the anal canal is important to choose the best surgical approach, and in cases of locally advanced or recurrent tumors invading adjacent pelvic organs that may require more complex surgeries such as pelvic exenteration. As approaches using organ preservation emerge, including transanal local excision and *"watch-and-wait" (9),* MRI may help in the patient selection for those treatments, follow up, and detection of tumor regrowth. Additionally, potential MRI-based prognostic and predictive biomarkers, such as quantitative and semi-quantitative metrics derived from functional sequences like diffusion-weighted imaging *(DWI)* and dynamic contrast-enhanced *(DCE) (41).*

Diffusion-weighted MRI is a non-invasive imaging method used in oncology in the diagnosis and characterization of tumors, as well as in monitoring the response to treatment with chemoradiotherapy. Rapid technological developments have brought new imaging methods to the fore.

Diffusion-weighted MRI has advantages such as being non-invasive, not requiring exogenous contrast material, being safe in patients with renal dysfunction, not containing ionizing radiation, enabling numerical evaluation, and rapid imaging. There are studies showing the effectiveness of diffusion MRI in detecting recurrent cancer in oncology, distinguishing residual active tumor from post-treatment changes, monitoring and staging the response to treatment before and after chemoradiotherapy treatment, and determining lymph node involvement *(9)*.

Abbreviations

ADC : *apparent diffusion coefficient*
APR : *abdomino-perineal resection*
CRM : *circumferential resection margin*
CT : *computerized tomography*
DWI : *diffusion-weighted imaging*
EMVI : *extramural vascular invasion*
EPI : *echo-planar imaging*
ERMRI : *endo-rectal MRI*
ERUS : *endorectal ultrasonography*
FOV : *field of view*
GRE EPI : *gradient echo EPI*
HRMR : *high resolution pelvic MRI*
HRRM : *high-resolution rectal MRI*
MRF : *meso-rectal fascia*
MRI : *magnetic resonance imaging*
NCRT : *neoadjuvant chemoradiation*
PET : *positron emission tomography*
SE EPI : *Spin echo EPI*
SAR : *specific absorption rate*
SNR : *signal-to-noise ratio*
TME : *total meso-rectal excision*
TNM : *tumor-node-metastasis*
USG : Ultrasonography
5 – FU : *5 – Fluorouracil*

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, Ca - Cancer J. Clin. 71 (3) (2021) 209–249.

2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017; 67:7–30

3. You YN, Hardiman KM, Bafford A, Poylin V, Francone TD, Davis K, Paquette IM, Steele SR, Feingold DL, On behalf of the clinical practice guidelines committee of the American society of, S. Rectal, the American society of colon and rectal surgeons clinical practice guidelines for the management of rectal cancer, Dis. Colon Rectum 63 (9) (2020) 1191–1222.

4. Siddiqui MRS, Simillis C, Hunter C, Chand M, Bhoday J, Garant A, Vuong T, Artho G, Rasheed S, Tekkis P, Abulafi AM, Brown G, A meta-analysis comparing the risk of metastases in patients with rectal cancer and MRI-detected extramural vascular invasion (mrEMVI) vs mrEMVI-negative cases, Br. J. Cancer 116 (12) (2017) 1513–1519.

5. Beets-Tan RGH, Lambregts DMJ, Maas M, Bipat S, Barbaro B, Curvo-Semedo L, Fenlon HM, Gollub MJ, Gourtsoyianni S, Halligan S, Hoeffel C, Kim SH, Laghi A, Maier A, Rafaelsen SR, Stoker J, Taylor SA, Torkzad MR, Blomqvist L, Magnetic resonance imaging for clinical management of rectal cancer: updated recommendations from the 2016 European Society of Gastrointestinal and Abdominal Radiology (ESGAR) consensus meeting, Eur. Radiol. 28 (4) (2018) 1465–1475.

6. Glynne-Jones R, Wyrwicz L, Tiret E, Brown G, Rodel C, Cervantes A, Arnold D, Committee, Rectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Ann. Oncol. 29 (Suppl 4) (2018), iv263

7. Brown G, Davies S, Williams GT, Bourne MW, Newcombe RG, Radcliffe AG, Blethyn J, Dallimore NS, Rees BI, Phillips CJ, MaughanTS, Effectiveness of preoperative staging in rectal cancer: digital rectal examination, endoluminal ultrasound or magnetic resonance imaging? Br. J. Cancer 91 (1) (2004) 23–29.

8. Maizlin ZV, Brown JA, So G, Brown C, Phang TP, Walker ML, Kirby JM, Vora P, Tiwari P, Can CT replace MRI in preoperative assessment of the circumferential resection margin in rectal cancer? Dis. Colon Rectum 53 (3) (2010) 308–314.

9. Fernandes MJ, Brown GG, The importance of MRI for rectal cancer evaluation, Surgical Oncology 43 (2022) 101739

10. Schaefer O , Langer M . Detection of recurrent rectal cancer with CT, MRI and PET/CT . Eur Radiol 2007 ; 17 (8): 2044 – 2054 .

11. Akasu T, Kondo H, Moriya Y, et al. Endorectal ultrasonography and treatment of early stage rectal cancer. World J Surg 2000;24: 1061–1068.

12. Kang JH, Kim YC, Kim H, et al. Tumor volüme changes assessed by three-dimensional magnetic resonance volumetry in rectal cancer patients after preoperative chemoradiation: the impact of the volume reduction ratio on the prediction of pathologic complete response. Int J Radiat Oncol Biol Phys 2010; 76:1018–1025

13. Suppiah A, Hunter IA, Cowley J, et al. Magnetic resonance imaging accuracy in assessing tumour down-staging following chemoradiation in rectal cancer. Colorectal Dis 2009;11: 249–253.

14. Nougaret S, Reinhold C, Mikhael HW, Rouanet P, Bibeau F, Brown G. The use of MR imaging in treatment planning for patients with rectal carcinoma: have you checked the 'DISTANCE'? Radiology 2013; 268: 330–344

15. Bipat S, Glas AS, Slors FJ, Zwinderman AH, Bossuyt PM, Stoker J. Rectal cancer: local staging and assessment of lymph node involvement with endoluminal US, CT, and MR imaging—a metaanalysis. Radiology 2004;232:773–783.

16. Lambregts DM, Vandecaveye V, Barbaro B, Bakers FC, Lambrecht M, Maas M, Diffusion weighted MRI for selection of complete responders after chemoradiation for locally advanced rectal cancer: a multicenter study. Ann Surg Oncol. 2011; 18(8):2224–31.

17. Sassen S, de Booij M, Sosef M, Berendsen R, Lammering G, Clarijs R, Locally advanced rectal cancer: is diffusion weighted MRI helpful for the identification of complete responders (ypT0N0) after neoadjuvant chemoradiation therapy? Eur Radiol. 2013; 23(12):3440–9

18. Song I, Kim SH, Lee SJ, Choi JY, Kim MJ, Rhim H. Value of diffusion-weighted imaging in the detection of viable tumour after neoadjuvant chemoradiation therapy in patients with locally advanced rectal cancer: comparison with T2 weighted and PET/CT imaging. Br J Radiol. 2012; 85(1013):577–86.

19. Beets GL, Figueiredo NL, Habr-Gama A, van de Velde CJ. A new paradigm for rectal cancer: Organ preservation: Introducing the International Watch & Wait Database (IWWD). Eur J Surg Oncol. 2015; 41(12):1562–4.

20. Martens MH, Maas M, Heijnen LA, Lambregts DM, Leijtens JW, Stassen LP, Long-term Outcome of an Organ Preservation Program After Neoadjuvant Treatment for Rectal Cancer. J Natl Cancer Inst. 2016;108(12)

21. Hotker AM, Garcia-Aguilar J, Gollub MJ. Multiparametric MRI of rectal cancer in the assessment of response to therapy: a systematic review. Dis Colon Rectum. 2014; 57(6):790–9

22. Akashi M, Nakahusa Y, Yakabe T, Egashira Y, Koga Y, Sumi K, Assessment of aggressiveness of rectal cancer using 3-T MRI: correlation between the apparent diffusion coefficient as a potential imaging biomarker and histologic prognostic factors. Acta Radiol. 2014; 55(5):524–31

23. Carbone SF, Pirtoli L, Ricci V, Venezia D, Carfagno T, Lazzi S, Assessment of response to chemoradiation therapy in rectal cancer using MR volumetry based on diffusion-weighted data sets: a preliminary report. Radiol Med. 2012; 117(7):1112

24. Padhani AR, Liu G, Koh DM, Chenevert TL, Thoeny HC, Takahara T, et al. Diffusion-weighted magnetic resonance imaging as a cancer biomarker: consensus and recommendations. Neoplasia. 2009; 11 (2):102–25.

25. Sun YS, Zhang XP, Tang L, Locally advanced rectal carcinoma treated with preoperative chemotherapy and radiation therapy: preliminary analysis of diffusion-weighted MR imaging for early detection of tumor histopathologic downstaging. Radiology. 2010 Jan;254(1):170-8.

26. Kim SH, Lee JY, Lee JM, Han JK, Choi BI. Apparent diffusion coefficient for evaluating tumour response to neoadjuvant chemoradiation therapy for locally advanced rectal cancer. European radiology 2011;21:987-995.

27. Lu JY, Lin GL, Qiu HZ, Xiao Y, Wu B, Zhou JL. Comparison of transanal endoscopic microsurgery and total mesorectal excision in the Treatment of T1 Rectal Cancer: A Meta-Analysis. PLoS One. 2015;10(10):e0141427.

28. Sajid MS, Farag S, Leung P, Sains P, Miles WF, Baig MK. Systematic review and meta-analysis of published trials comparing the efectiveness of transanal endoscopic microsurgery and radical resection in the management of early rectal cancer. Colorectal Dis. 2014;16(1):2–14.

29. Borstlap WA, Coeymans TJ, Tanis PJ, Marijnen CA, Cunningham C, Bemelman WA, Meta-analysis of oncological outcomes after local excision of pT1-2 rectal cancer requiring adjuvant (chemo)radiotherapy or completion surgery. Br J Surg. 2016;103(9):1105–16.

30. Pericay C, Serra-Aracil X, Ocana-Rojas J, Mora-Lopez L, Dotor E, Casalots A, Further evidence for preoperative chemoradiotherapy and transanal endoscopic surgery (TEM) in T2–3s, N0, M0 rectal cancer. Clin Transl Oncol. 2016;18(7):666–71.

31. Garcia-Aguilar J, Renfro LA, Chow OS, Shi Q, Carrero XW, Lynn PB, Organ preservation for clinical T2N0 distal rectal cancer using

neoadjuvant chemoradiotherapy and local excision (ACOSOG Z6041): results of an open-label, single-arm, multiinstitutional, phase 2 trial. Lancet Oncol. 2015;16(15):1537–46.

32. Serra-Aracil X, Pericay C, Golda T, Mora L, Targarona E, Delgado S, et al. Non-inferiority multicenter prospective randomized controlled study of rectal cancer T2–T3s (superfcial) N0, M0 undergoing neoadjuvant treatment and local excision (TEM) vs total mesorectal excision (TME). Int J Colorectal Dis. 2018;33(2):241–9.

33. Stornes T, Wibe A, Nesbakken A, Myklebust TA, Endreseth BH. National early rectal cancer treatment revisited. Dis Colon Rectum. 2016;59(7):623–9

34. Kim CK, Kim SH, Chun HK, Preoperative staging of rectal cancer: accuracy of 3-Tesla magnetic resonance imaging. Eur Radiol. 2006; 16:972–980.

35. Chun HK, Choi D, Kim MJ, et al. Preoperative staging of rectal cancer: comparison of 3- Tesla high filed MRI and endorectal sonography. AJR Am J Roentgenol 2006;187:1557-1562

36. Laghi A, Ferri M, Catalano C, Baeli I, et al. Local staging of rectal cancer with MRI using a phased array body coil. Abdom imaging. 2002;27:425-31.

37. Taylor FG, Quirke P, Heald RJ, Moran B, Blomqvist L, Swift I, Sebag-Montefiore DJ, Tekkis P, Brown G. Preoperative High-resolution Magnetic Resonance Imaging Can Identify Good Prognosis Stage I, II, and III Rectal Cancer Best Managed by Surgery Alone: A Prospective, Multicenter, European Study. Ann Surg. 2011; 253:711–719

38. Feng Q, Yan YQ, Zhu J, Xu JR. T staging of rectal cancer: accuracy of diffusion-weighted imaging compared with T2-weighted imaging on 3.0 tesla MRI. J Dig Dis. 2014;15:188–194.

39. Chang K, Kamel I, Macura K, Bluemke D, 3.0-T MR Imaging of the Abdomen: Comparison with 1.5 T. Radiographics 2008;28:1983-1998.

40. Cho EY, Kim SH, Yoon JH, Lee Y, Lim YJ, Kim SJ, et al. Apparent diffusion coefficient for discriminating metastatic from non-metastatic lymph nodes in primary rectal cancer. Eur J Radiol 2013; 82: e662–8.

41. Mizukami Y, Ueda S, Mizumoto A, et al. Diffusion-weighted magnetic resonance imaging for detecting lymph node metastasis of rectal cancer. World J Surg. 2011; 35:895–899.

CHAPTER XX

IMAGING FINDINGS OF NON-TRAUMATIC ACUTE HEPATOBILIARY AND PANCREATIC DISEASES

Burcu Akman

(Asst. Prof,), Department of Radiology, Amasya University, Faculty of Medicine, Amasya, Turkey
E-mail: burcuakman80@gmail.com
ORCID: 0000-0002-1067-9008

1 IMAGING METHODS AND FINDINGS OF Gallbladder and BIIIary Tract Stones and Acute Cholecystitis

1.1 Ultrasonography Findings of Acute Cholecystitis

Acute cholecystitis often occurs because of stones localized in the gallbladder neck or cystic duct, causing obstruction in 95% of patients (1). Ultrasonography (US) is the first imaging method used in the examination of patients with acute Murphy findings since it does not contain ionizing radiation, its easy accessibility, and its low cost. The sensitivity and specificity of the US in the visualization of gallstones are very high(2). In order to evaluate the gallbladder in the US, 12 hours of fasting is required. Otherwise, the gallbladder is contracted and optimal evaluation cannot be made. In the US, gallstones appear as echogenity with posterior acoustic shadows that may displace during patient movement (**Fig 1**)(3). But, US examination is limited in detecting complications of acute cholecystitis and is dependent on the experience of the radiologist performing US. Magnetic resonance imaging (MRI) and computed tomography(CT) provide useful information in evaluating and localization of these complications and detecting other accompanying pathologies (4).The “sonographic Murphy sign” is a significant superiority of ultrasound in the examination of acute cholecystitis. This sign indicates acute cholecystitis with an accuracy of 92% (5).

Ultrasonography imaging findings of acute cholecystitis:

- Increased thickness of the gallbladder wall (> 3 mm) and edema
- Increased diameter of gallbladder (> 40 mm)
- Presence of "sonographic Murphy sign"
- Pericholecystic and perihepatic mai(6).

While the US provides useful information in the evaluation of the hepatic bile ducts, especially the middle and distal parts of the common bile duct (CBD) may not be evaluated due to gastrointestinal gases in the midline (Fig 2).

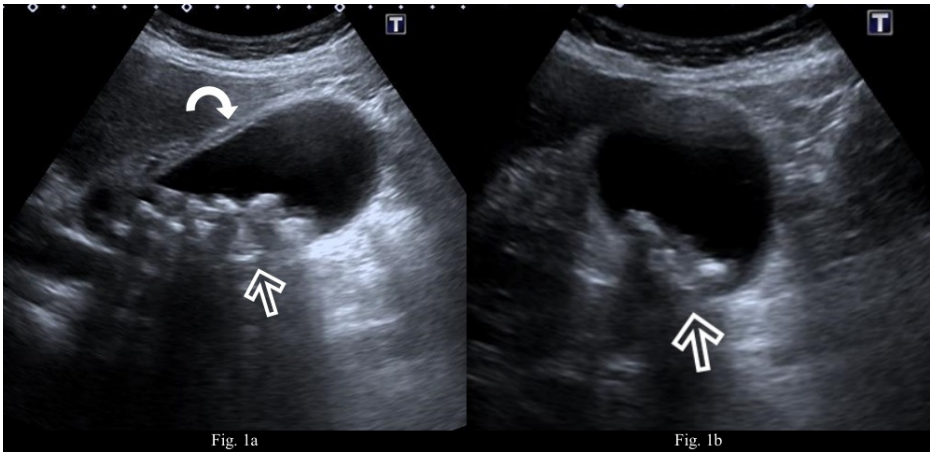


Fig 1a,b. Ultrasonography images of a patient with acute cholecystitis show (a), (b) multiple stones with posterior acoustic shadows in the gallbladder (hollow arrows) and(a) thickening of the wall (curved arrow) and an increase in the diameter of the gallbladder.

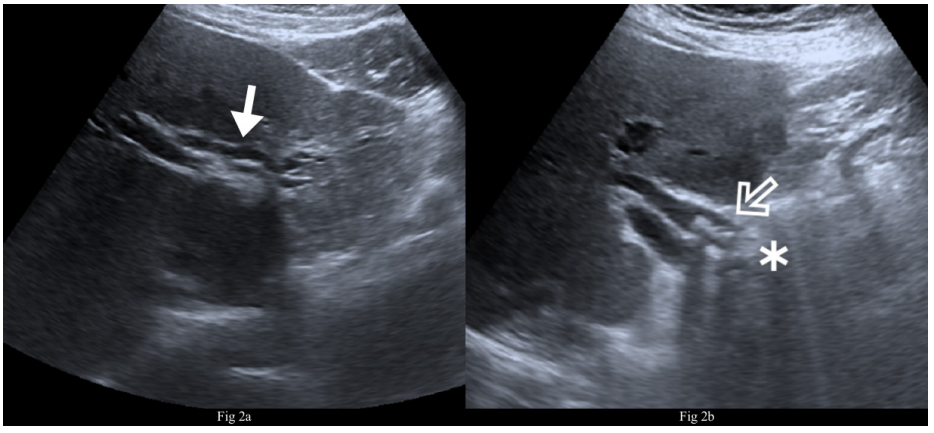


Fig 2a,b. (a) Ultrasonography shows dilated left hepatic bile ducts (white arrow) and(b) dilatation of the CBD and stones in the proximal part of CBD (hollow arrow). The distal part of the CBD could not be visualized due to gastric and intestinal gases (asteriks).

1.2 CT Findings of Acute Cholecystitis

Acute cholecystitis findings on CT are:

- increased thickness of the gallbladder wall (> 3mm);
- increased mural or mucosal enhancement;
- hypo-hyperdense stones in the gallbladder;
- stranding in the pericholecystic adipose tissue secondary to inflammation and pericholecystic fluid;
- hyperattenuating in the hepatic gallbladder fossa, which is called "temporary hepatic attenuation difference" (6,7).

CT provides very important informations in the detection of the complications of acute cholecystitis. The most important complications are; emphysematous cholecystitis, gallstone ileus, gangrenous cholecystitis, bleeding, and gallbladder perforation(8). The fundus is the most perforated part of the gallbladder(9).

1.3 MRI and MR Cholangiopancreatography (MRCP) Findings of Acute Cholecystitis

In emergency situations, MRCP with MRI provides a non-invasive, rapid, reliable diagnosis or exclusion for acute cholecystitis and concomitant choledocholithiasis.On MRI, biliary sludge and stones are seen as hyperintense leveling in the lumen on T2weighted (W) images and hypointense foci of different sizes on the T1W sequence.MRI findings of acute cholecystitis were enlargement of the gallbladder (diameter ≥4 cm), increased wall thickness (>3 mm), and hyperintense signal in T2W due to inflammation of the gallbladder wall and pericholecystic and perihepatic liquid. Gallbladder neck stones and cystic duct stones may cause obstruction and they are observed as a round hypointense filling defect on MRI (Fig 3) (10). While ultrasound has limited sensitivity (38%) for the diagnosing of stones in the CBD, the sensitivity (89–100%) and specificity (83–100%) of MRCP are very high in the detection of the CBD stones. In MRCP, the CBD stones are observed as hypointense filling defects and can be detected even very small (≤3 mm) (11,12).MR provides comprehensive examination of complications associated with cholecystitis, such as gallbladder perforation, gangrenous cholecystitis, pericholecystic-perihepatic abscess, and fistulization(10).

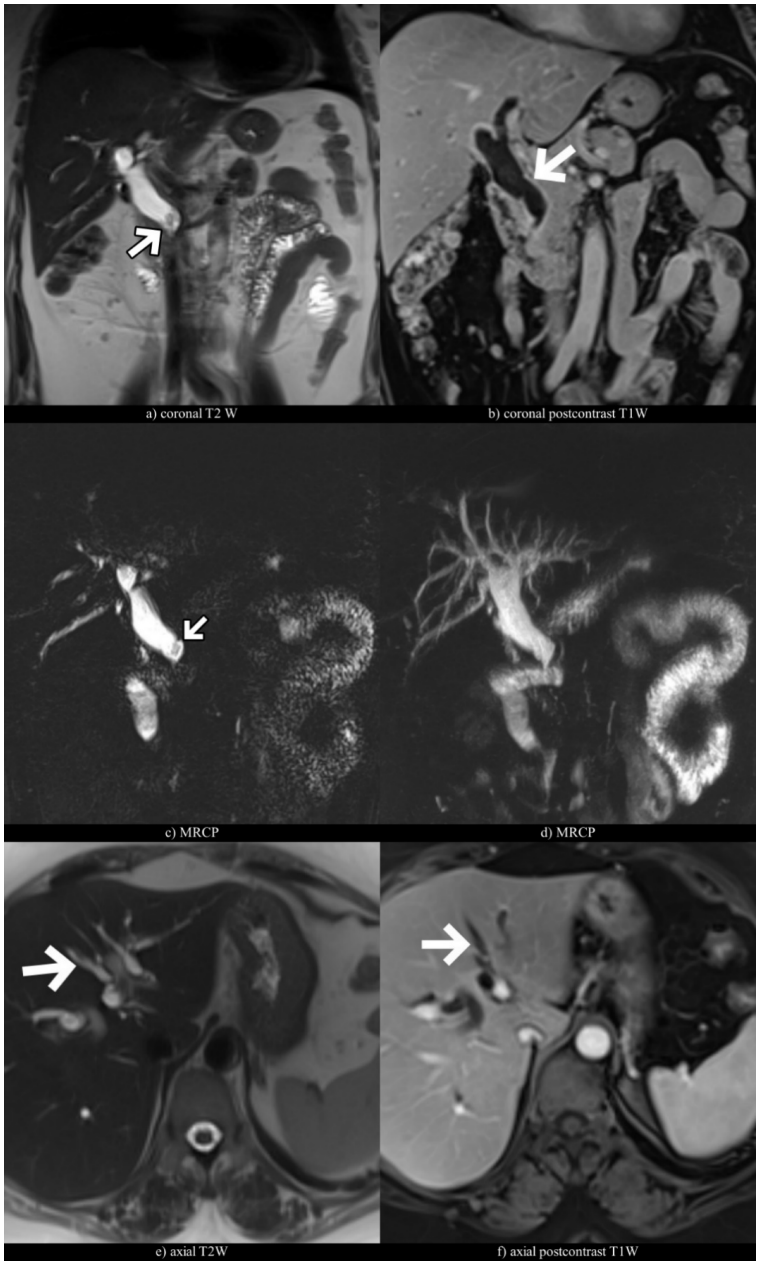


Fig 3 a-f. MRI and MRCP images of the patient with intra and extrahepatic bile ducts dilatation due to a stone in the common bile duct (CBD). Coronal T2W (**a)** and post contrast T1W (**b)** images show a stone (arrows) leading to enlargement of the CBD. MRCP (**c), (d)** images show marked dilatation of the intrahepatic bile ducts and CBD and a stone (arrow) in the CBD. Axial T2W (**e)** and postcontrast T1W (**f)** show dilatation of left and right hepatic bile ducts(arrows).

2 IMAGING METHODS AND FINDINGS OF ACUTE PANCREATITIS

Acute pancreatitis (AP) is called the inflammation of pancreatic parenchymal areas and the surrounding tissue. AP is the most common pancreatic disease in adults and children(13). In addition, AP is one of the common gastrointestinal diseases leading to hospitalization. It requires high costs for the health system due to the need for long-term treatment(14). The findings of the AP were pain in the upper abdomen that may spread to the back, increased serum lipase and amylase levels; and typical AP imaging findings on transabdominal US, contrast-enhanced CT (CECT) or MRI (15).

Radiologic imaging findings are very important in the diagnosis of acute pancreatitis and in the evaluation of its complications and in guiding interventional treatment. In addition, it provides the detection of stones in the gallbladder, bile duct obstruction, or structural abnormalities, leading to the formation of pancreatitis. CECT is generally the most commonly used imaging method due to good image quality, shorter duration of the examination, and more accessibility. But, MRI has some advantages over CT, such as no exposure to ionizing radiation and better soft tissue resolution(13).

AP is divided into two subtypes according to the radiological findings resulting from pathophysiological mechanisms. They are interstitial edematous pancreatitis (IEP) (85%) and necrotizing pancreatitis (NP)(15%). The mortality rate in IEP is about 3% and in NP, it ranges from 17% to 30%. Especially superinfection of necrotic collections adversely affects the prognosis of the patients with NP(16–18). Therefore, the diagnosis of acute pancreatitis in the early stage and initiation of treatment in the early period are very important.

2.1 Ultrasound Findings of Acute Pancreatitis

Ultrasound is the first radiologic imaging modality that is frequently applied at the time of patient admission. Although it provides limited information for the acute pancreatitis, it may show the gallstones and dilatation in the biliary tract that cause pancreatitis.

In the US examination, especially the pancreatic parenchyma structure and distal CBD stones may not be evaluated due to obesity, gastrointestinal gases, and inexperience of the radiologist who performs the US (13,19). The advantages of US are that it does not contain radiation, not used contrast material, and allows the patient to be evaluated at the bedside. Fluid collections resulting from pancreatitis can be detected in the US.

2.2 CT Findings of Acute Pancreatitis

CECT may not be needed, especially in patients with mild acute pancreatitis. CT should be used to diagnose patients with complaints consistent with severe pancreatitis (20). The most important disadvantages of CECT are that it contains ionizing radiation and cannot be used in pregnant women. Also CT is not sensitive as US in showing gallstones and especially in patients with kidney disease or contrast agent allergy, contrast material cannot be used (21,22).

CT findings of interstitial edematous pancreatitis are focal or diffuse increase in pancreatic size due to inflammatory edema, stranding in the peri-pancreatic areas and increased density of the peri-pancreatic fatty tissue(23). In the early stage of AP, edema and increased glandular size of the pancreas are observed on CT images. Complications such as necrotic collections develop on CT in the late stage of AP (24,25). In the first four weeks of the IEP, acute peri-pancreatic fluid collections (APFCs) are homogeneous and have no wall and solid components (**Fig 4**). These fluid collections usually occur in the lesser sac and anterior pararenal space. In this early period, APFCs are usually sterile, and regress spontaneously in approximately 50% of cases. If they stay longer than four weeks, they usually transform into pseudo cysts with a circumscribed wall (26). Complications such as bleeding and infection may occur in 50% of cases after pseudo cyst formation (27). In the early stage of necrotizing pancreatitis, necrotic collections of cellular debris without a wall are formed. Acute necrotic collections turn into necrotic fluid collections with a wall similar to pseudo cysts but they have partly solid content, after four weeks (**Fig 5**)(27). In pancreatitis, CECT is very useful in showing the stage of pancreatitis and demonstrating the complications with a risk of mortality, such as infected necrosis or vascular hemorrhage (23,28).

CT scan should be performed in two phases if acute pancreatitis is suspected: late arterial phase (pancreatic phase) and portal venous phase. Images are taken from the top of the diaphragm to the whole abdomen(27). Maximum parenchymal enhancement of the pancreas is obtained between 35-45 seconds after bolus injection of a nonionic iodinated contrast agent(29). In particular, the biphasic approach is very useful in the detecting of local complications of necrotic collections such as suspected bleeding, and characterization of vascular lesions(28,30). Areas with a density of less than 30 HU in the arterial phase in the pancreatic parenchyma are considered as necrosis (28).

Balthazar, in 1985, reported the most widely used acute pancreatitis scoring system worldwide in terms of peripancreatic inflammation and the presence of collections (31) (**Table 1**).

Table 1: Grading of pancreatitis on CT (Balthazar score)		
A	Normal pancreas size and parenchyma	0
B	Focal or diffuse diameter increase of the pancreas	1
C	Inflammatory findings in pancreatic parenchyma and peripancreatic fatty tissue	2
D	Single irregularly circumscribed peripancreatic collection	3
E	Two or more peripancreatic fluid collections, pancreatic or retroperitoneal gas	4

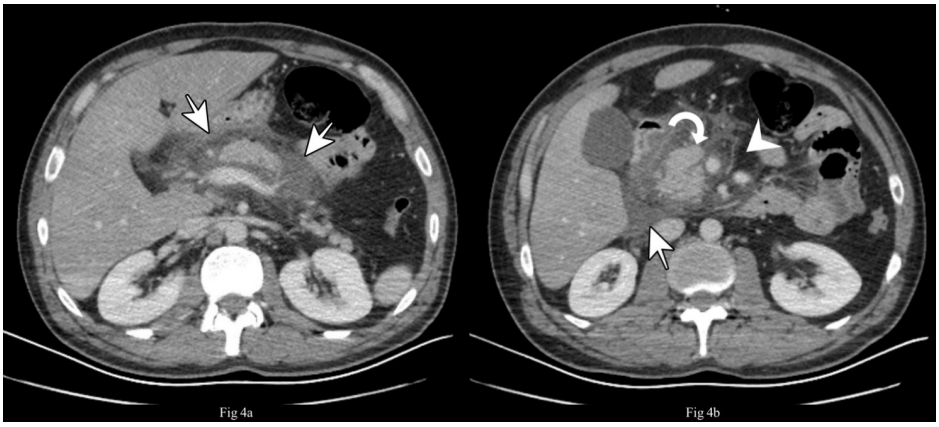


Fig 4a,b. Axial abdominal CECT images with show (a), (b) peripancreatic fluid (white arrows) and(b) peripancreatic fat stranding (arrowhead) and increased pancreatic size (curved arrow) consistent with acute pancreatitis.

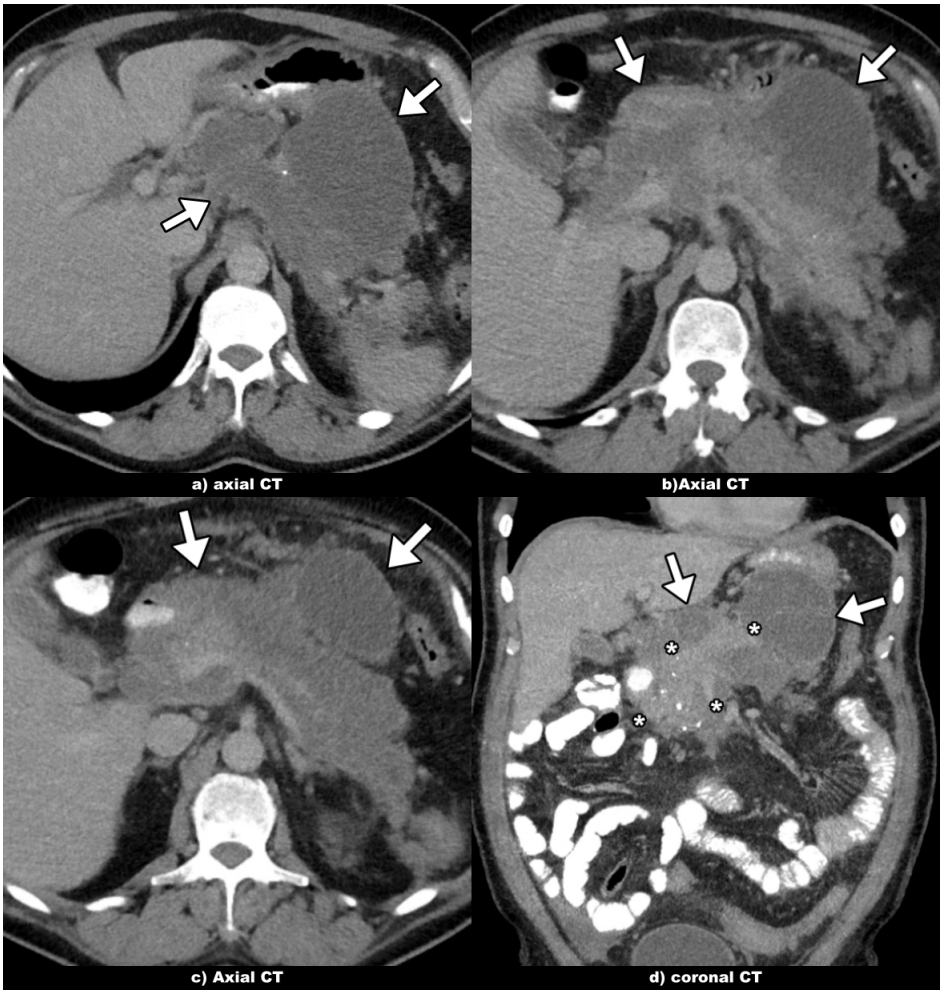


Fig. 5 (a), (b), (c) Axial abdominal non-contrast CT images and (d) a coronal CT image of a patient with necrotizing pancreatitis. Non-contrast CT images show multiple low-density areas compatible with necrosis in the pancreatic parenchyma and multiple peripancreatic fluid collections with walls (arrows). (d) The coronal CT image shows heterogeneous pancreatic parenchyma (asterisks).

2.3 MRI Findings of Acute Pancreatitis

T1W and T2 W sequences, and post-contrast T1W sequences were the routinely used pulse sequences of abdominal MRI. MRCP should be added to the protocol to evaluate for pancreatic duct and obstruction, biliary tract dilatation, and biliary stones (32,33). MRI provides more information than CT

in the diagnosis of acute pancreatitis, especially in the early stage. In particular, minor peripancreatic inflammatory changes are not visible on CT but can be detected with MRI. CT has been reported as normal in some (approximately 15-30%) of patients clinically consistent with acute pancreatitis (31).

References

1. Kimura Y, Takada T, Kawabata Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreatic Surg. 2007; 14(1):15-26.

2. Pinto A, Reginelli A, Cagini L, et al. Accuracy of ultrasonography in the diagnosis of acute calculous cholecystitis: review of the literature. Crit Ultrasound J. 2013;5(1):1-4.

3. Bortoff GA, Chen MYM, Ott DJ, Wolfman NT, Routh WD. Gallbladder stones: imaging and intervention. Radiographics. 2000;20(3):751-766.

4. Chawla A, Bosco JI, Lim TC, Srinivasan S, Teh HS, Shenoy JN. Imaging of acute cholecystitis and cholecystitis-associated complications in the emergency setting. Singapore Med J. 2015;56(8):438.

5. Ralls PW, Colletti PM, Lapin SA, et al. Real-time sonography in suspected acute cholecystitis. Prospective evaluation of primary and secondary signs. Radiology. 1985;155(3):767-771.

6. Smith EA, Dillman JR, Elsayes KM, Menias CO, Bude RO. Cross-sectional imaging of acute and chronic gallbladder inflammatory disease. Am J Roentgenol. 2009;192(1):188-196.

7. Fidler J, Paulson EK, Layfield L. CT evaluation of acute cholecystitis: findings and usefulness in diagnosis. AJR Am J Roentgenol. 1996;166(5):1085-1088.

8. O'Connor OJ, Maher MM. Imaging of cholecystitis. AJR-American J Roentgenol. 2011;196(4):W367.

9. Watanabe Y, Nagayama M, Okumura A, et al. MR imaging of acute biliary disorders. Radiographics. 2007;27(2):477-495.

10. Tonolini M, Ravelli A, Villa C, Bianco R. Urgent MRI with MR cholangiopancreatography (MRCP) of acute cholecystitis and related complications: diagnostic role and spectrum of imaging findings. Emerg Radiol. 2012;19(4):341-348.

11. Yeh BM, Liu PS, Soto JA, Corvera CA, Hussain HK. MR imaging and CT of the biliary tract. Radiographics. 2009;29(6):1669-1688.

12. Kim YJ, Kim MJ, Kim KW, et al. Preoperative evaluation of common bile duct stones in patients with gallstone disease. Am J Roentgenol. 2005;184(6):1854-1859.

13. Busireddy KK, AlObaidy M, Ramalho M, et al. Pancreatitis-imaging approach. World J Gastrointest Pathophysiol. 2014;5(3):252.

14. Crockett SD, Wani S, Gardner TB, et al. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. Gastroenterology. 2018;154(4):1096-1101.

15. Zhao K, Adam SZ, Keswani RN, Horowitz JM, Miller FH. Acute pancreatitis: revised Atlanta classification and the role of cross-sectional imaging. Am J Roentgenol. 2015;205(1):W32-W41.

16. Banks PA, Freeman ML, Gastroenterology PPC of the AC of. Practice guidelines in acute pancreatitis. Off J Am Coll Gastroenterol ACG. 2006;101(10):2379-2400.

17. Gregucci F, Fiorentino A, Mazzola R, et al. Radiomic analysis to predict local response in locally advanced pancreatic cancer treated with stereotactic body radiation therapy. Radiol Med. 2022;127(1):100-107.

18. Karmazanovsky G, Gruzdev I, Tikhonova V, Kondratyev E, Revishvili A. Computed tomography-based radiomics approach in pancreatic tumors characterization. Radiol Med. 2021;126(11):1388-1395.

19. Megibow AJ, Ralls PW, Balfe DM, et al. Acute pancreatitis. American College of Radiology. ACR Appropriateness Criteria. Radiology. 2000;215:203-207.

20. Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology. 2012;262(3):751-764.

21. Anderson SW, Lucey BC, Varghese JC, Soto JA. Accuracy of MDCT in the diagnosis of choledocholithiasis. Am J Roentgenol. 2006;187(1):174-180.

22. Anderson SW, Rho E, Soto JA. Detection of biliary duct narrowing and choledocholithiasis: accuracy of portal venous phase multidetector CT. Radiology. 2008;247(2):418-427.

23. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-111.

24. Porter KK, Zaheer A, Kamel IR, et al. ACR Appropriateness Criteria® acute pancreatitis. J Am Coll Radiol. 2019;16(11):S316-S330.

25. Srisajjakul S, Prapaisilp P, Bangchokdee S. CT and MR features that can help to differentiate between focal chronic pancreatitis and pancreatic cancer. Radiol Med. 2020;125(4):356-364.

26. De Muzio F, Cutolo C, Granata V, et al. CT study protocol optimization in acute non-traumatic abdominal settings. Eur Rev Med Pharmacol Sci. 2022;26(3):860-878.

27. Brizi MG, Perillo F, Cannone F, Tuzza L, Manfredi R. The role of imaging in acute pancreatitis. Radiol Med. 2021;126(8):1017-1029.

28. Balthazar EJ. Acute pancreatitis: assessment of severity with clinical and CT evaluation. Radiology. 2002;223(3):603-613.

29. Agostini A, Borgheresi A, Bruno F, et al. New advances in CT imaging of pancreas diseases: a narrative review. Gland Surg. 2020;9(6):2283.

30. Leung VJ, Godfrey EM, Biddle DJ, Al-Khatib A. Split-bolus single-pass CT for vascular complications in acute pancreatitis: assessment of radiation dose and multi-phasic contrast enhancement compared to single-bolus multi-pass CT. Clin Radiol. 2020;75(8):644-e1.

31. Balthazar EJ. CT diagnosis and staging of acute pancreatitis. Radiol Clin North Am. 1989;27(1):19-37.

32. Soto JA, Barish MA, Yucel EK, et al. Pancreatic duct: MR cholangiopancreatography with a three-dimensional fast spin-echo technique. Radiology. 1995;196(2):459-464.

33. Takehara Y, Ichijo K, Tooyama N, et al. Breath-hold MR cholangiopancreatography with a long-echo-train fast spin-echo sequence and a surface coil in chronic pancreatitis. Radiology. 1994;192(1):73-78.

CHAPTER XXI

IMAGING OF PERIANAL FISTULAS AND ABSCESS

Ayşegül Öz Özcan

(MD, Radiologist), aoz.ayseguloz@gmail.com
ORCID: 0000-0002-5797-5066

1. Definition, Etiology and Pathogenesis

Perianal fistula, is a tract, extending from the anal canal to the skin. These fistulas can be simple and isolated or associated with accompanying perianal abscess (1,2). Infected fistula and abscess require urgent surgical intervention (3). Perianal fistulas which occur 2 to 4 times more frequently in men, are often idiopathic, but many factors can be involved in the etiology. The main etiologic factors are; Crohn's disease, pelvic inflammations-infections, tuberculosis, pelvic and hematologic malignancies, birth trauma/episiotomies, radiotherapy (2, 4). It is known that there is a lifetime risk of 20-50% perianal fistula development in inflamatory bowel disease -Crohn's disease- patients (5-7).

Particularly in idiopathic cases, cryptoglandular inflammation that develops with the obstruction of the anal gland ducts opening to the dentate-pectinate line is the main factor in the pathophysiology. Inflammation begins with infection of the intersphincteric gland. This inflammation causes the formation of an intersphincteric fistula. At this point, a drainage tract develops, and if this tract is obstructed, abscess formation occurs. Continuation of intersphincteric chronic inflammation causes persistent fistulas and recurrent abscess formation. Majority of the anal glands are located superficially in the subepithelial area. Some are located deep in the longitudinal layer of the internal sphincter. Some of them are located near to the external sphincter. When an abscess forms from the superficial part, it often drains automatically into the anal canal. But if the abscess forms in the deep part of the internal sphincter, the sphincter forms a natural block and with the burst of the abscess, the infected content extends

into the intersphincteric space which is a potential low resistant space. If this infected content opens into the skin an intersphincteric fistula occurs. Perianal or intersphincteric abscess may accompany this fistula. A transsphincteric fistula develops if the infection progresses beyond the external sphincter, in this case inflammation and abscess develop in the ischiorectal fossa (2, 4, 8, 9).

2. Anatomy

2.1. Macro and microanatomy

The anal sphincter has 2 muscular layers. The inner part is internal sphincter which consists of involuntarily contracting smooth muscles and is continuous with the circular muscle layer of the rectum. The internal sphincter provides 85% of the resting tone of the anal canal. The external sphincter can make voluntary contractions with its striated musculature. It extends back to the coccyx with the anococcygeal ligament and anteriorly to the urogenital diaphragm. It joins with the pelvic floor muscles. Provides 15% of resting tone and prevents involuntary defecation (10). While external sphincter damage causes anal incontinence, this is not expected in internal sphincter damage (2).

Between internal and external sphincters there is an intersphincteric area where the resistance is lower and therefore the contents of the fistula and abscess can easily pass. In this area, fat, connective tissue and longitudinal muscles are located (4). The muscles in this region are continuous with the lower rectal muscles without contributing to the anal tone (4, 11).

The distal half of the anal canal is covered by squamous epithelium and the proximal half by columnar epithelium. The distal part of the transition zone in between is the dentate-pectinate line. It is 2 cm to the anal opening (anal verge).

2.2. Anal Clock Anatomy

Surgically and radiologically with magnetic resonance imaging (MRI), anal fistulas are described according to the clock dials in the supine lithotomy position. 12 o'clock indicates anterior midline perineal cut, 6 o'clock indicates posterior midline gluteal segment. 3 o'clock describes the left, 9 o'clock right lateral cut (2).

3. Classification

There are several reasons why perianal fistulas should be evaluated with MRI preoperatively. First; The aim is to identify the secondary fistula tracts

adjacent to the abscess cavities to be operated urgently, thus preventing relapse. Another reason is to identify the contuguity of the fistulas with the sphincter and to shape the operation accordingly. MRI is the method that best detects the anatomy of the anal and perianal region, the course of the fistula tract, and accompanying abscess formations with high soft tissue resolution.

There are 2 most commonly used perinal fistula classifications.

3.1. Parks Classification

It is a classification developed by Parks et al. in 1976 with 400 patients. It references the external sphincter. It is based on the evaluation of the connection and involvement of the perianal fistula and the sphincter complex in the coronal plane. It defines 4 types of perianal fistula (12).

3.1.1. Intersphincteric Fistulas

It is the most common type (45%). The fistula opens into the anal canal. It passes between the longitudinal muscle planes in the internal sphincter and the intersphincteric area, opening to the perianal skin or adjacent to the subcutaneous external sphincter. It does not cross the external sphincter (Figure 1).

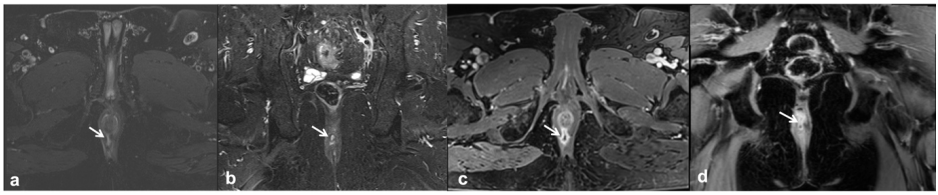


Figure 1. Intersphincteric fistula, 64 year old male patient, 1,5T perianal MR imaging with i.v. contast media injection. **a**. axial T2W FS image, hyperintense lineer fistula tract (arrow) at 6 o'clock position, **b**. coronal T2W FS image, hyperintense fistula tract (arrow) **c.** axial postcontrast T1W FS image, peripheral rim enhancement (arrow) and anal canal opening is best distinguished in this sequence, **d.** coronal postcontrast T1W FS image, fistula tract with peripheral hyperintense rim enhacement (arrow). W:weighted, FS: fat saturated

3.1.2. Transsphincteric Fistulas

It is the second most common type (30%). Tract traverses the external sphincter, passes through the intersphincteric space and reaches the ischiorectal/ ischioanal fossa (Figure 2 and 3).

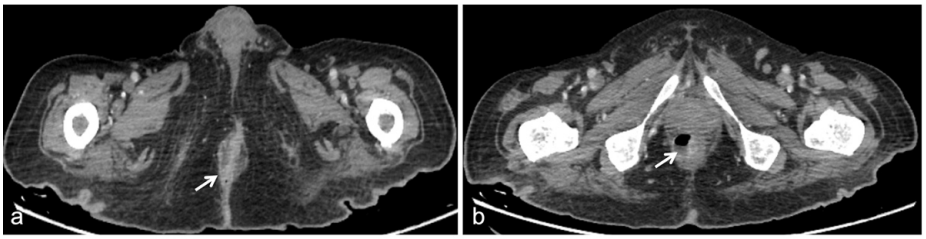


Figure 2. 74 years old male admitted to the emergency room with pelvic pain. On contract enhanced axial CT images a. perianal fistula and b. perianal abscess with air-fluid level is detected (arrows). CT: computed tomography

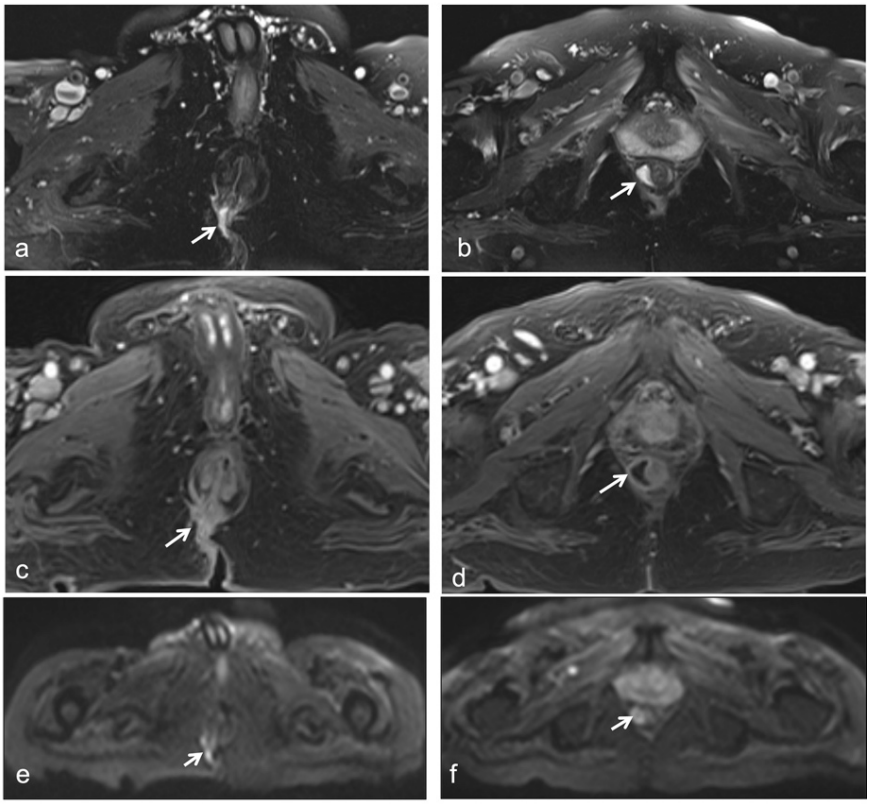


Figure 3. 1,5T perianal MR imaging with i.v. contast media injection of the same patient. a and b; axial T2W FS images a. hyperintense transphincteric fistula tract at 6o'clock position (arrow), b. accompanying perianal abscess in the intersphincteric space (arrow). c and d; axial postcontrast T1W FS images c. hyperintense transphincteric fistula tract (arrow) with lateral minimal irregular extensions, d. intersphincterperianal abscess (arrow) with rim enhancement, e and f; hyperintense fistula and abscess on DWI.

3.1.3. Suprasphincteric Fistulas

It is the third most common type (20%). The tract goes upward in the intersphincteric area, extends over the musculus puborectalis, passes through the levator plate and opens into the skin from the ischiorectal fossa (Figure 4).

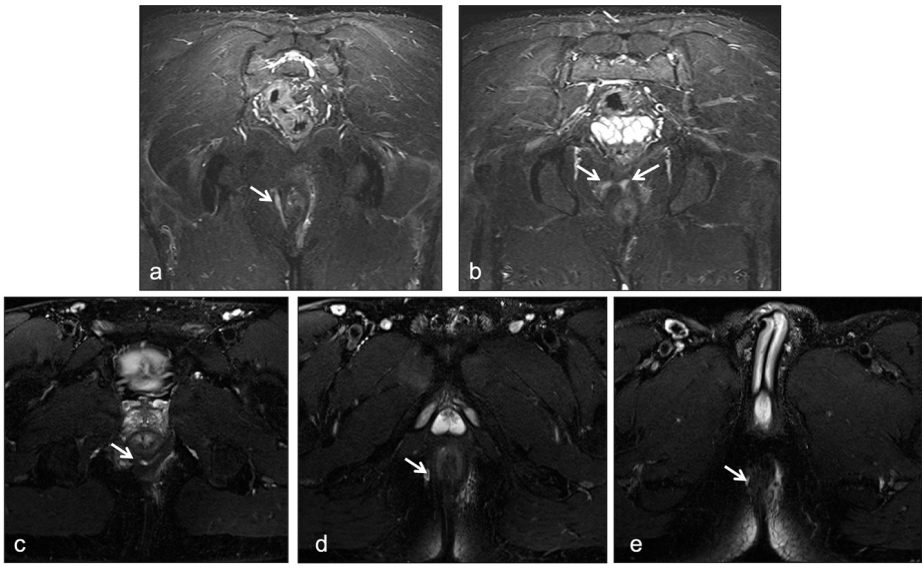


Figure 4. Suprasphincteric fistula, 37 year old male patient, 1,5T perianal MR imaging with i.v. contast media injection. a. and b. coronal T2W FS images, lineer hyperintense fistula tract extends superiorly in the intersphincteric space c, d and e. tractus ascends and opens to the skin.

3.1.4. Extrasphincteric Fistulas

It is the rarest type (5 %). The internal aperture of this type of fistula is in the rectum. It extends through the levator plate and the ischiorectal fossa and opens into the perianal skin. It is totally outside of the anal sphincters. In the presence of such fistulas, it is recommended to think Crohn's disease or primary rectal malignancies in the differantial diagnosis (12).

Superficial and complex fistula definitions, which are not involved in the Parks classification, were also added over time. Superficial fistulas describe the fistulas that are not related to the anal canal. Complex fistulas; used for primary fistula and accompanying secondary tracts and/or abscesses. Secondary tracts usually extend bilaterally, enveloping the internal sphincter or continuing as horseshoe branches or abcesses in the intersphincteric space (12, 13).

3.2. St James University Hospital Classification

In 2000, Morris et al. developed a MRI-based classification system. In this system, axial anatomy is used, which provides convenience to radiologists. It allows to identify both primary and secondary tracts and abscesses. Five subtypes are identified (2).

3.2.1. Grade 1: Simple Linear Intersphinteric Fistula

The fistula tract begins in the anal canal, passes through the intersphincteric area, and opens into the perianal skin. Intersphincteric, ischioanal-rectal secondary fistula is not accompanied by fistula extension or abscess. The intersphincteric tract is completely bounded by the external sphincter.

3.2.2. Grade 2: Intersphinteric Fistula with an Abscess or Secondary Tract

In the intersphincteric space, there is a primary tract and one or more secondary tracts or abscesses. Secondary tracts or abscesses may be horseshoe type. The external sphincter is not traversed.

3.2.3. Grade 3: Transsphincteric Fistula

It crosses the external and internal sphincter, traverses the ischoanal/ischiorectal fossa and opens into the perineal skin. Its internal opening is usually at the dentate-pectinate line. It can be best distinguished in the coronal section. There is no additional accompanying tract or abscess.

3.2.4. Grade 4: Transsphincteric Fistula with an Abscess or Secondary Tract in the Ischiorectal/Ischioanal Fossa

In addition to Grade 3, extension or abscess is accompanied at the level of the ischioanal/ischiorectal fossa.

3.2.5. Grade 5: Supralevator and Translevator Disease

Infrequently, the fistula expands superiorly to the levator ani muscle. It passes superiorly over the intersphincteric area, and progresses into the ischiorectal fossa. This type is usually associated with primary pelvic disease (2).

4. MRI Assesment of Perianal Fistulas and Abscess

MRI is the gold standard technique in the detection and assesment of perianal fistula and abscess. It has an important role in emergency surgery

planning. Especially detecting extensions is one of the most important factors in reducing postoperative recurrence.

Although the recommended protocol may vary from device to device: axial TSE/FSE T2-weighted (W), axial TSE/FSE T2W with fat suppression (FS), coronal or sagittal TSE/FSE T2-W, axial diffusion weighted imaging (DWI), axial T1W FS pre and postcontrast, coronal and/or sagittal T1W FS sequences are preferred (1, 8).

T2W images are the basic sequences that allow to distinguish abscess and fistula. Abscesses, fistulas and fluids are selected as hyperintense in this sequence. DWI is superior in distinguishing the fistula tract, especially when i.v. contrast administration is not possible. Sphincter complex and muscles are iso-hypointense on T2W sequences. High resolution, TSE T2W, thin slice sequences are very informative in evaluating anatomy.

While evaluating anatomy on precontrast T1W sequences, hemorrhagic changes can be discerned in precontrast FS T1W sequences. On postcontrast FS T1W sequences, primary fistulous tracts, extensions, abscess, and granulation tissue, if present, are distinguished as markedly hyperintense. The fistula sphincter relationship is clarified. Abscesses show a circumferential, circular pattern of enhancement in postcontrast sequences. It is important not to confuse vascular structures with fistula tracts in postcontrast images. Fibrotic chronic fistula tracts have low signal on T1W and T2W sequences and do not show significant increase in signal on postcontrast images (1, 2, 8, 14, 15).

It has been shown that DWI/apperent diffusion coefficient (ADC) and dynamic contrast-enhanced MRI can be useful in demonstrating the activity of perianal fistula (16,17).

There are certain points that need to be clarified radiologically, that will change the emergency approach, and that need to be reported in MRI. First of all, it is necessary to detect the perianal fistula and determine its internal and external openings. Fistula location should be defined according to the anal clock. Whichever classification is used in the internal common language between departments with surgical correlation, fistula and abscess should be described according to this classification and anal sphincter relationship should be evaluated. If there is a secondary fistula, extensions should be added. Surrounding organ pathologies, anogenital, rectovaginal fistula should be noted. For the presence of additional findings suggestive of Crohn's disease, the detection of stenotic segment and wall thickening included in the imaging area should be checked (2, 8, 18).

Detection and grading of perianal fistulas and abscesses with MRI contributes significantly to planning the treatment, reducing the recurrence with correct planning, preventing unnecessary sphincter damage, determining the emergency approach and predicting the prognosis (19, 20).

References

1. MR Imaging of Perianal Fistulas. Jhaveri KS, Thipphavong S, Guo L, Harisinghani MG. Radiol Clin North Am. 2018;56(5):775-789.

2. Morris J, Spencer JA, Ambrose NS. MR imaging classification of perianal fistulas and its implications for patient management. Radiographics. 2000;20(3):623-35.

3. Sarofim M, Ooi K. Reviewing perianal abscess management and recurrence: lessons from a trainee perspective. ANZ J Surg. 2022;92 (7-8):1781-1783.

4. Eisenhhammer S. A new approach to the anorectal fistulous abscess based on the high intermuscular lesion. Surgical Gynecol Obstet. 1958;106(5):595-9.

5.Szurowska E, Wypych J, Izycka-Swieszewska E. Perianal fistulas in Crohn's disease: MRI diagnosis and surgical planning. Abdom Imaging 2007;32:705-18.

6. Schwartz DA, Loftus EV Jr, Tremaine WJ, et al. The natural history of fistulizing Crohn's disease in Olmsted County, Minnesota. Gastroenterology 2002;122:875–80.

7. Eglinton TW, Barclay ML, Gearry RB, et al. The spectrum of perianal Crohn's disease in a population based cohort. Dis Colon Rectum 2012; 55:773–7.

8. de Miguel Criado J, del Salto LG, Rivas PF, et al. MR imaging evaluation of perianal fistulas: spectrum of imaging features. Radiographics. 2012;32(1):175-94

9. Parks AG. Pathogenesis and treatment of fistuila-in-ano. Br Med J. 1961;1(5224):463-9

10. Milligan ET, Morgan CN. Surgical anatomy of the anal canal: with special reference to anorectal fistula. Lancet 1934;224:1150-1156

11. Lunniss PJ, Phillips RK. Anatomy and function of the anal longitudinal muscle. J Surg. 1992;79(9):882-4.

12. Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. Br J Surg 1976;63:1-12.

13. Halligan S, Stoker J. Imaging of fistula in ano. Radiology 2006;239:18-33.

14. Spencer JA, Ward J, Beckingham IJ, Adams C, Ambrose NS. Dynamic contrast-enhanced MR imaging of perianal fistulas. AJR Am J Roentgenol. 1996;167(3):735-41.

15. Bartram C, Buchanan G. Imaging anal fistula. Radiol Clin North Am. 2003 Mar;41(2):443-57.

16. T, Wada A, Takahara T, et al. Diffusion weighted MRI for evaluating perianal fistula activity: feasibility study. Eur J Radiol 2012;81:2049–53.

17. Ziech ML, Lavini C, Bipat S, et al. Dynamic contrast enhanced MRI in determining disease activity in perianal fistulizing Crohn disease: a pilot study. AJR Am J Roentgenol 2013;200:W170–7.

18. Andreani SM, Dang HH, Grondona P, et al. Rectovaginal fistula in Crohn's disease. Dis Colon Rectum. 2007;50:2215–22.

19. Spencer JA, Chapple K, Wilson D, Ward J, Windsor AC, Ambrose NS. Outcome after surgery for perianal fistula: predictive value of MR imaging. AJR Am J Roentgenol. 1998;171(2):403-6.

20. Gould SW, Martin S, Agarwal T, Patel B, Gedroyc W, Darzi AJ. Image-guided surgery for anal fistula in a 0.5T interventional MRI unit. Magn Reson Imaging. 2002;16(3):267-76.

CHAPTER XXII

IMAGING FINDINGS OF NON-TRAUMATIC ACUTE INTESTINAL DISEASES

Burcu Akman

(Asst. Prof,), Department of Radiology, Amasya University, Faculty of Medicine, Amasya, Turkey
E-mail: burcuakman80@gmail.com
ORCID: 0000-0002-1067-9008

1 ACUTE APPENDICITIS

Acute appendicitis is a disease that causes acute onset of abdominal pain and often requires emergency surgery. In the United States, the incidence of cases has been reported to be 250,000 annually (1). Patients with fever, nausea, vomiting, abdominal right lower quadrant pain, and laboratory findings including leukocytosis should be investigated for acute appendicitis. The rate of appendix perforation was reported as 16-39% in the literature (2). As a result of perforation, serious complications like peritonitis, intra-abdominal abscess, and sepsis may develop(3).

Since ultrasound (US) does not contain radiation, it is used as a screening method for appendicitis in pediatrics and pregnant women. If the US is non-diagnostic, magnetic resonance imaging (MRI) can be applied to pregnant patients. The widely accepted imaging method to evaluate appendicitis in the general population is computed tomography (CT) (4).

1.1 Ultrasonography Findings of Acute Appendicitis

In acute appendicitis, an incompressible enlarged appendix (diameter>6 mm), increased wall thickness, and echogenicity in the lumen compatible with appendicolith can be seen in US. Fluid in the pericecal area, inflammation in the surrounding fatty tissue, and a frank abscess are the other imaging findings of appendicitis (**Fig 1**) (4).

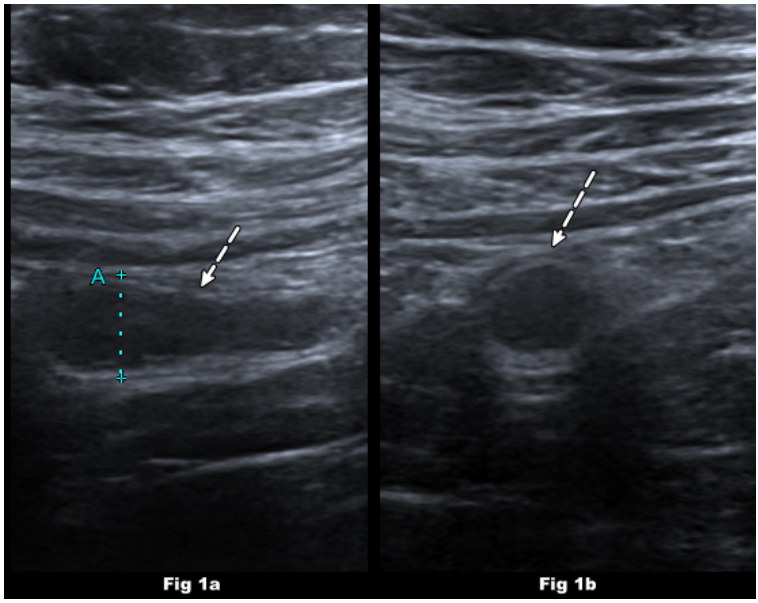


Fig 1 a,b. The ultrasound images of a 12-year-old boy with complaints of nausea and right lower quadrant pain show an aperilstaltic appendix with an increased diameter (10 mm) (arrows) and inflammation in the surrounding fatty tissue. US findings are compatible with acute appendicitis.

1.2 Computed Tomography Findings of Acute Appendicitis

CT is used for imaging in cases where the appendix cannot be visualized in the US due to intestinal gases, obesity, and patient incompatibility.

- Increased diameter of the appendix,
- Thickening of its wall,
- Appendicolith,
- Thickening of the mesoappendix,
- Peri-appendiceal fat stranding, and/ or phlegmon are the CT findings of acute appendicitis (5).

Intravenous (IV) contrast agents can be used to rule out acute vascular conditions such as ischemia of the bowel, bleeding and renal infarction (4). In CT, the diameter of the appendix, the presence of inflammation or abscess in the tissues adjacent to the appendix are investigated. Free fluid and free abdominal air indicate perforation of the appendix. The disadvantages of CT compared

to the US are radiation exposure, contrast material side effects and a more expensive examination.

1.3 MRI Findings of Acute Appendicitis

In pregnant patients with clinical symptoms, MRI is performed in cases where the diagnosis of appendicitis cannot be made by US. MRI's sensitivity and specificity in detecting acute appendicitis are high in pregnant patients with clinical symptoms (6). MRI is an alternative cross-sectional imaging method in patients for whom tomography cannot be applied for the diagnosis of appendicitis.

2 INTUSSUSCEPTION

Intussusception occurs when the proximal segment of the intestinal loop telescope within the distal intestinal lumen. Invagination is frequently observed in childhood. 5% of total cases occur in adults and approximately 1-5% of the total cases cause intestinal obstruction (7). Ultrasonography is particularly useful in children and thin adult patients. The "target sign" in the axial view and "pseudo-kidney sign" in the longitudinal view are typical for intussusception (8). In the US, it can be determined that the mesentery and lymph nodes have entered into the intestine lumen with the adjacent intestine.

Abdominal CT is the imaging method with the highest sensitivity in the diagnosis of intussusception. Also, localization and causes of intussusception can be detected on CT. In these patients, typically inhomogeneous "target" signs are detected in CT scans (7) (**Fig 2**).

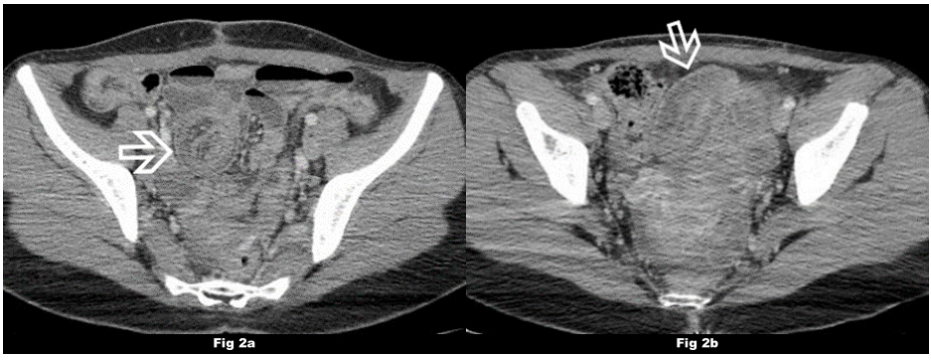


Figure 2 a,b. Patient with ileo-ileal intussusception. Axial CT images show the proximal segment of the ileum is telescoping within the lumen of the distal ileal segment. (a) "Target" sign (b) "pseudo-kidney" sign (hollow arrows).

3 ACUTE BOWEL OBSTRUCTION

We can categorize intestinal obstruction into two groups as small and large bowel obstruction. The reasons of small and large bowel obstruction are summarized in Table 1.

Table 1. Causes of Small and Large Bowel Obstruction (9,10)

Frequency	**Small-Bowel Obstruction**	**Large-Bowel Obstruction**
Common (>80%)	Adhesion (70%) Hernia Malignancy	Neoplasm (60%–80%) Volvulus (11%–15%) Acute diverticulitis (4%–10%)
Uncommon	Inflammatory bowel disease İntussusception Volvulus Gallstones Intraluminal bezoars Intraluminal foreign body Trauma	Invagination Hernia Inflammatory bowel disease External compression to bowels from abscess or other masses Intraluminal fecaloid or bezoars Intestinal foreign body

3.1 Small-Bowel Obstruction

3.1.1 Abdominal Radiography Findings of Small-Bowel Obstruction

- Dilatation of small bowel loops (diameter>3 cm)
- Multiple air-fluid levels in different areas
- Absence of rectal gas
- Gasless abdomen
- Increased small-bowel to large-bowel ratio (4,9).

3.1.2 Ultrasonography Findings of Small-Bowel Obstruction

Ultrasound has limitations in the evaluation of the intestines due to the gas in the intestines. Dilated small bowel loops (>3 cm) and hyperperistalsis are observed in small-bowel obstruction (SBO) in US. Fluid-filled, distended, and aperistaltic bowel with wall thickening could represent infarction (4).

3.1.3 CT Findings of Small-Bowel Obstruction

Computed tomography is a very useful imaging method for evaluating the location and cause of SBO. CT with IV contrast is recommended to evaluate

SBO. The oral contrast material usage may vary according to the tolerability of the patient. If contrast enhancement in the intestinal wall is to be evaluated, oral contrast material is not used (4).

CT findings of SBO;

- Dilated small bowel loops (diameter >2.5-3 cm)
- Presence of transition-point between dilated and non-dilated small intestine
- Air-fluid levels
- Non-dilate or decompressed colon

Adhesions occurred during surgery are the most common cause of SBO. Generally, it is not possible to see the adhesions on CT. However, acute angulation or well-circumscribed external compression in the short segment of the bowel can be seen as secondary signs of adhesions (4).

3.1.4 MRI Findings of Small-Bowel Obstruction

MRI is useful imaging method for detecting the causes of bowel obstructions and differentiating malignant from benign conditions. In some patients, adhesions can be seen in the form of hypointense soft tissue bands passing through the mesenteric adipose tissue on T2-weighted (W) MR images (4).

3.2 Large-Bowel Obstruction

Acute total large bowel obstruction (LBO) usually requires surgery and has high rates of morbidity and mortality if treatment is delayed. The frequency of obstruction of colon segments is 4 to 5 times higher than SBO and the reasons for LBO were significantly different from SBO (Table 1) (10).

3.2.1 Abdominal radiography findings of Large-Bowel Obstruction

It is the first imaging technique that should be used in patients with suspected colonic obstruction. Supine, upright, or left lateral decubitus radiographs can be performed for the diagnosis of LBO and to evaluate the complications. Dilatation in the colon is considered if the diameter of the cecum is greater than 9 cm and the diameter of the other colon is greater than 6 cm (10).

Abdominal radiography findings of LBO (10)

- Dilated colon
- Air-fluid levels in the dilated colon (in the acute phase of LBO)
- Absence of gas distal to the obstruction

Findings showing ischemic colon in the late period

- Pneumatosis coli
- Gas in the portal veins
- Pneumoperitoneum

3.2.2 CT findings of Large-Bowel Obstruction

CT is the most useful imaging technique showing the localization, causes, and complications of LBO. The CT imaging's sensitivity and specificity in detecting colonic obstruction have been reported as 96% and 93% (11,12). The diagnosis of LBO is made by visualization of a transition point, dilatation of the proximal bowel, and decompressed distal bowels on CT (12,13). The IV contrast agent is useful for detecting the presence of a neoplasm and bowel inflammation and ischemia. The usage of oral contrast agents in acute abdominal pain is controversial and their use is highly variable (10).

3.2.3 Major causes of Large-Bowel Obstruction

Colon neoplasm is the first most common cause of colonic obstruction (60%) (10). CT findings of colonic neoplasm were asymmetric, irregularly circumscribed thickening of the colon wall in a short segment or an irregularly circumscribed mass lesion with IV contrast enhancement leading to narrowing of the lumen originating from the colon (10).

Volvulus has been reported as the second most common cause of colonic obstruction (10%–15%) (13). The volvulus is described as an intestinal loop that twists around itself causing an obstruction. Sigmoid volvulus (60%–75%) and cecal volvulus (25%–33%) were common (14). "Inverted U sign" is a typical finding seen only in sigmoid volvulus. It is seen on abdominal X-ray in 25-78% of patients with sigmoid volvulus (15). Also, a very enlarged sigmoid colon that looks like a "coffee bean" may be seen in cases with sigmoid volvulus (15). The most useful radiological imaging technique in detecting volvulus is CT. On CT, the "whirl sign" is detected, which shows the turning of the mesenteric vessels when the intestine rotates around its mesentery (16). The whirl sign provides information about the localization of the volvulus on CT (**Fig 3**).

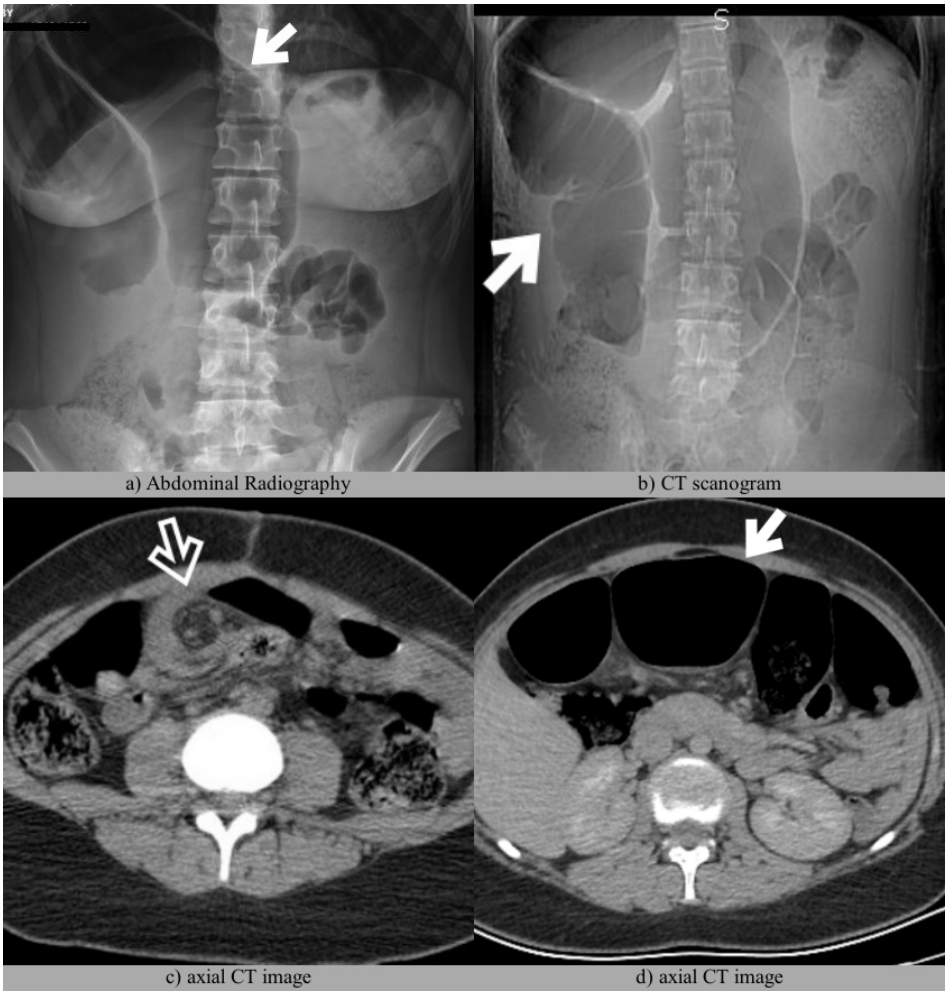


Figure 3 a-d (a) Abdominal radiography, (b) CT scanogram, and (c), (d) axial CT images of a patient with complaints of abdominal pain.

Radiography, and CT scanogram show marked dilatation of the sigmoid colon that looks like a "coffee bean" or "inverted U" (white arrows) consisting of sigmoid volvulus. **(c)** The turning of the mesenteric vessels which is called the "whirl sign" (hollow arrow) is seen in the axial CT image **(d)** Marked distention of the sigmoid colon is seen in the axial CT image (white arrow).

Diverticulitis is the cause of about 10% of all LBO cases. In cases of acute diverticulitis, intestinal wall edema and pericolic inflammation may cause LBO (13). The prevalence of diverticulosis increases with advancing age and occurs in 5-10% of persons >45 years of age. Acute diverticulitis occurs as a result of

inflammation of the diverticulum and surrounding tissues. Abscess, phlegmon formation, fistulization, obstruction or perforation, and bleeding may occur as complications of acute diverticulitis (4). Most patients with acute diverticulitis usually have a fever, pain in the left lower abdomen, and laboratory findings including leukocytosis (17). Ultrasound can show bowel wall thickening and inflammation in the surrounding tissue, which is indirect findings of acute diverticulitis. Contrast-enhanced CT is the most sensitive radiologic imaging method for the detection of acute diverticulitis and its complications. In CT scans, diverticulitis is observed as a segmental, symmetrical increase in intestinal wall thickness and is characterized as including a longer segment (≥10 cm) unlike malignancy (18).

4 ACUTE MESENTERIC ISCHEMIA

Bowel ischemia results in high mortality (exceeding 60%) and morbidity rates (19). The etiology of acute mesenteric ischemia includes multiple conditions that cause decreasing mesenteric blood flow to the intestine. There are two main etiological groups: occlusive and non-occlusive mesenteric ischemia. Occlusive-based mesenteric ischemia occurs secondary to vascular occlusion (venous or arterial) and causes ischemic damage in the bowel wall. Non-occlusive mesenteric ischemia results from systemic hypoperfusion due to hypovolemia, heart failure, hypotension, intestinal obstruction, inflammatory conditions, and trauma (20,21).

The most important imaging method for diagnosing acute mesenteric ischemia is CT angiography (CTA). The sensitivity and specificity of CTA in detecting the cause of mesenteric ischemia is very high (22). CTA may show atherosclerosis, arterial or venous thrombus, occlusion, invasion or compression by tumors or other masses. In addition, mesenteric stranding or fluid, increased intestinal wall thickness, increase in bowel wall enhancement in the early phase of mesenteric ischemia or decrease in bowel wall enhancement in the late phase, or perforation may be seen in CT (4). Pneumatosis intestinalis is seen as air in the intestinal wall in CT, which indicates intestinal necrosis and is related with poor prognosis and high rate of mortality (21) (fig 4). Portal venous air is related to the advanced level of mesenteric infarction (9–36%) (**Fig 4**) (4).

5 INTESTINAL PERFORATION

Intestinal perforation may be thought in a patient with sudden and severe pain in the abdomen and a rigid abdomen on examination. Abdominal X-ray

is the first imaging method to be applied. Pneumoperitoneum is a finding suggestive of gastrointestinal perforation, which often requires surgery (23). However, it may detect 50-70% extraluminal air and cannot show a minimal free air and localization of the intestinal perforation (24). Free air under the diaphragm is a classic sign of pneumoperitoneum on the upright chest and abdominal radiographies. CT is very sensitive to detecting very little free intra-abdominal air, and the lung parenchyma window is useful for detecting free air (**Fig 4).** CT findings of gastrointestinal perforation are free air in the abdomen, discontinuity in the intestinal wall, and extravasation of oral contrast material outside the intestinal lumen (23).

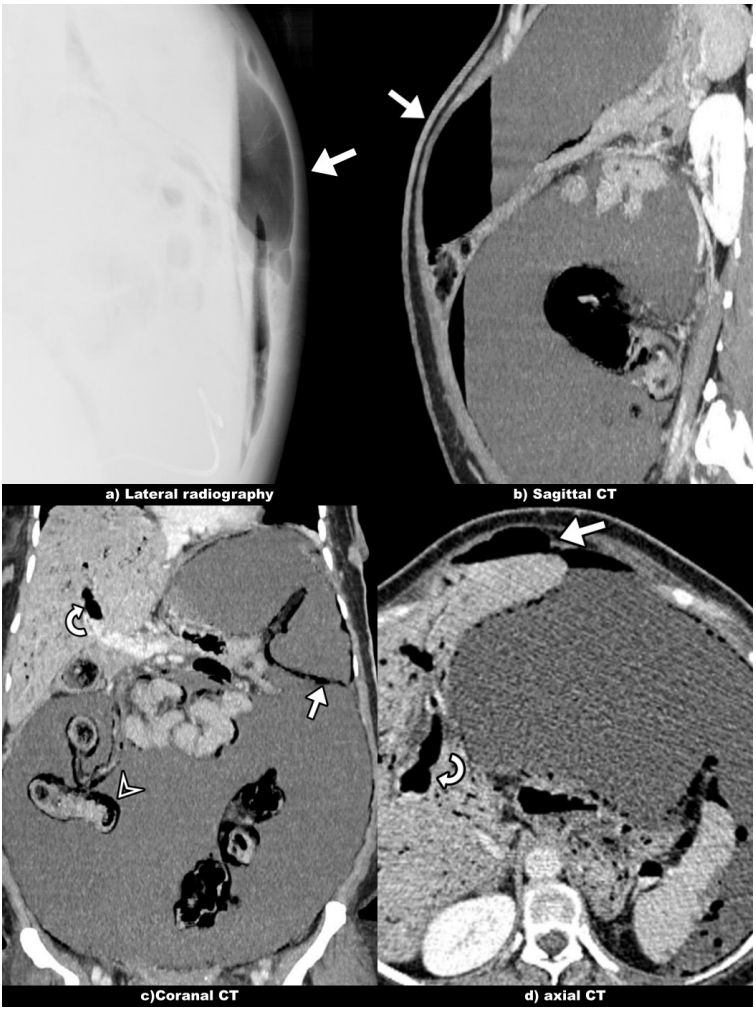


Figure 4 a-d. A 55-year-old female patient with a history of ovarian carcinoma (CA) who died despite emergency surgery.

(a) Lateral radiography and (b) sagittal CT images show multiple intra-abdominal free air (straight arrows) compatible with intestinal perforation. There were also diffuse ascites due to ovarian CA. (c) Coronal CT images show multipl airs in the intestinal walls (pneumatosis intestinalis) due to intestinal necrosis (arrowhead) and gas in the portal venous system (curved arrow). (d) axial CT shows gas in the portal venous system (curved arrow) and free abdominal air (straight arrow).

REFERENCES

1. Deng Y, Chang DC, Zhang Y, Webb J, Gabre-Kidan A, Abdullah F. Seasonal and day of the week variations of perforated appendicitis in US children. Pediatr Surg Int. 2010;26(7):691-696.

2. Addiss DG, Shaffer N, Fowler BS, Tauxe R V. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol. 1990;132(5):910-925.

3. Storm-Dickerson TL, Horattas MC. What have we learned over the past 20 years about appendicitis in the elderly? Am J Surg. 2003;185(3):198-201.

4. Gangadhar K, Kielar A, Dighe MK, et al. Multimodality approach for imaging of non-traumatic acute abdominal emergencies. Abdom Radiol. 2016;41(1):136-148.

5. Raman SS, Lu DSK, Kadell BM, Vodopich DJ, Sayre J, Cryer H. Accuracy of nonfocused helical CT for the diagnosis of acute appendicitis: a 5-year review. Am J Roentgenol. 2002;178(6):1319-1325.

6. Birchard KR, Brown MA, Hyslop WB, Firat Z, Semelka RC. MRI of acute abdominal and pelvic pain in pregnant patients. AJR Am J Roentgenol. 2005;184(2):452-458.

7. Marinis A, Yiallourou A, Samanides L, et al. Intussusception of the bowel in adults: a review. World J Gastroenterol WJG. 2009;15(4):407.

8. Boyle MJ, Arkell LJ, Williams JT. Ultrasonic diagnosis of adult intussusception. Am J Gastroenterol. 1993;88(4):617-618.

9. Paulson EK, Thompson WM. Review of small-bowel obstruction: the diagnosis and when to worry. Radiology. 2015;275(2):332-342.

10. Jaffe T, Thompson WM. Large-bowel obstruction in the adult: classic radiographic and CT findings, etiology, and mimics. Radiology. 2015;275(3):651-663.

11. Beattie GC, Peters RT, Guy S, Mendelson RM. Computed tomography in the assessment of suspected large bowel obstruction. ANZ J Surg. 2007;77(3):160-165.

12. Godfrey EM, Addley HC, Shaw AS. The use of computed tomography in the detection and characterisation of large bowel obstruction. Clin Corresp. Published online 2009.

13. Taourel P, Kessler N, Lesnik A, Pujol J, Morcos L, Bruel JM. Helical CT of large bowel obstruction. Abdom Radiol. 2003;28(2):267.

14. Gore RM, Levine MS. Textbook of Gastrointestinal Radiology. Saunders/Elsevier; 2008.

15. Levsky JM, Den EI, DuBrow RA, Wolf EL, Rozenblit AM. CT findings of sigmoid volvulus. Am J Roentgenol. 2010;194(1):136.

16. Frank AJ, Goffner LB, Fruauff AA, Losada RA. Cecal volvulus: the CT whirl sign. Abdom Radiol. 1993;18(3):288-289.

17. De Muzio F, Cutolo C, Granata V, et al. CT study protocol optimization in acute non-traumatic abdominal settings. Eur Rev Med Pharmacol Sci. 2022;26(3):860-878.

18. Chintapalli KN, Chopra S, Ghiatas AA, Esola CC, Fields SF, Dodd III GD. Diveriticulitis versus colon cancer: differentiation with helical CT findings. Radiology. 1999;210(2):429-435.

19. Lee R, Tung HKS, Tung PHM, Cheung SCW, Chan FL. CT in acute mesenteric ischaemia. Clin Radiol. 2003;58(4):279-287.

20. Gandhi SK, Hanson MM, Vernava AM, Kaminski DL, Longo WE. Ischemic colitis. Dis colon rectum. 1996;39(1):88-100.

21. Paolantonio P, Rengo M, Ferrari R, Laghi A. Multidetector CT in emergency radiology: acute and generalized non-traumatic abdominal pain. Br J Radiol. 2016;89(1061):20150859.

22. Cangemi JR, Picco MF. Intestinal ischemia in the elderly. Gastroenterol Clin. 2009;38(3):527-540.

23. Rodríguez LC, de Gracia MM, Galán NS, Dueñas VP, Arrieta LS, Moll GG. Use of multidetector computed tomography for locating the site of gastrointestinal tract perforations. Cirugía Española (English Ed. 2013;91(5):316-323.

24. Kothari K, Friedman B, Grimaldi GM, Hines JJ. Nontraumatic large bowel perforation: spectrum of etiologies and CT findings. Abdom Radiol. 2017;42(11):2597-2608.

CHAPTER XXIII

MULTIMODALITY IMAGING APPROACH TO ACUTE ABDOMEN

Abdullah Enes Ataş

(MD.), Konya City Hospital, Department of Radiolog, Konya, Turkiye
aenesatas@gmail.com
ORCID: 0000-0001-6623-3024

1. INTRODUCTION

"Acute abdomen" refers to a clinical situation marked by the development of severe abdominal discomfort that must be treated quickly, either medically or surgically. Acute abdominal pain is a common symptom among patients who visit the emergency room, and it can result from either trauma or non-traumatic diseases. The most important imaging technique for assessing patients with severe abdominal injuries and those with nontraumatic acute abdominal illness is widely acknowledged to be computed tomography (CT). Unenhanced CT scans are not commonly performed in cases of acute abdominal pain. Contrast-enhanced CT can be obtained in the arterial and portal phase. The excretory phase can be added in terms of urinary tract pathologies. To use ultrasonography (US) as the starting approach in patients with acute abdominal pain and to refer patients with negative US to CT. The current use of conventional radiography is limited to bowel obstruction and subdiaphragmatic free gas. In the evaluation of acute abdomen, magnetic resonance imaging (MRI) offers an alternative to CT and does not expose the ionizing radiation.

However, CT is indispensable in imaging acute abdomen in terms of both cost effectiveness and diagnostic sensitivity.

2. ABDOMINAL TRAUMA

Abdominal discomfort is a frequent complaint made by trauma victims who visit the emergency room. Some of them need medical or surgical treatment

in the early period. The essential relevance of sonography in the early assessment of patients with hemodynamic instability is also well acknowledged, even though computed tomography is commonly regarded as the primary imaging method for the evaluation of severe trauma patients. Because it is repeatable, non-invasive, non-irradiating, and affordable, US has acquired widespread recognition as a viable triage tool to assess trauma patients with probable abdominal injuries. US is employed as a quick diagnostic test in the current clinical approach to show intra-abdominal free fluid in traumatic abdominal injuries (1).

When CT was first used in clinical practice, acquisition times were long and image quality was poor. Its role in trauma patients has grown in importance since the introduction of new technologies such as multidetector CT (MDCT) (2). The use of CT allows for 3D reformatting with a flexibility, allowing for a thorough analysis of vascular and visceral structures. Modern technology has reduced the time required for CT scans and made it possible to detect small injuries that were previously missed. The quickest imaging technique that allows multitrauma patients to have their entire body examined effectively is computed tomography.

In order to find solid and visceral organs as well as vascular injury during abdominal and pelvic scans, it is advised to perform CT with contrast agent. Rapid acquisition techniques allow for multiphasic imaging on the CT. To assess arterial structures, one uses arterial phase imaging. The portal phase is useful for identifying injury to abdominal organs. In the case of urinary tract injuries, late phase evaluation is advised.

Coronal and sagittal images obtained through multiplanar reconstruction are particularly useful in evaluating vertebrae and other structures. MIP (maximum intensity projection) and VR (volume rendered) reconstruction are also used in cases of vascular injuries, spinal or pelvic fractures.

Whole-body CT scanning for multi-trauma patients in emergency departments is becoming more common. Radiation exposure is another topic that has come up as a result of this situation(3). The development of dose modulation techniques by CT manufacturers to lower radiation to the ideal dose was motivated by the detection of the deterministic and stochastic effects of radiation(4). Furthermore, trauma CTs are mostly used in the emergency department on children. The long-term effects of radiation on this population continue to be a source of concern.

The ALARA principle (as low as reasonably achievable) should not be overlooked when doing an ideal assessment on the relevant patient in

the emergency services while taking radiation safety considerations into consideration.

Benefiting from dose modulation in the devices is required to lower the radiation dose in CT scans. By regulating the tube current and voltage in this way, the patient can receive the least amount of radiation feasible without the image quality suffering.

Some studies using low-dose CT and lower tube current have demonstrated satisfactory images(5,6).

There have been very few studies done on the use of MRI in hemodynamically stable trauma patients. In fact, there aren't many MRI indications for trauma patients, and patient compliance is challenging.

Therefore, despite the need for caution due to radiation exposure, CT plays a crucial role in trauma. It is crucial not only for the injury's detection but also for getting multi-trauma patients the right surgical treatment as quickly as feasible.

3. NON-TRAUMATIC ABDOMINAL EMERGENCIES

One of the most frequent reasons for admission to the emergency room is acute abdominal pain. Acute abdominal pain can also be caused by disorders necessitating immediate surgery, even though the etiology may be vast and self-limiting. With just a medical history, physical exam, and lab results, some situations are challenging to diagnose. Diagnostic imaging methods are routinely employed as a result (7). Direct radiography's function has diminished as cross-sectional imaging has grown in popularity. For children, the most common imaging technique is ultrasound. It can also be used to assess the pelvic organs and hepatobiliary system. Computed tomography, however, is the most useful imaging technique for orienting patients with severe abdominal discomfort (8-11).

Contrast-enhanced CT is the most appropriate imaging method in the approach to non-localized acute abdominal pain according to the American College of Radiology (ACR) appropriateness criteria. Direct radiography, ultrasonography and non-contrast CT have a more limited place in these cases.

3.1. Acute right upper quadrant pain

Acute calculous cholecystitis is a common condition in patients presenting with right upper quadrant pain. In these cases, it would be more appropriate to prefer ultrasonography.

Finding gallstones is the main evaluation focus. The sonographic Murphy sign, gallbladder wall thickening, and pericholecystic fluid are examples of secondary findings (Figure 1). A gallstone often blocks the cystic duct in acute cholecystitis. Due to the limited blood supply, gallbladder perforation and the accompanying pericholecystic abscess frequently occur close to the fundus of the gallbladder. CT might be helpful for sonographic diagnosis and complications(12).

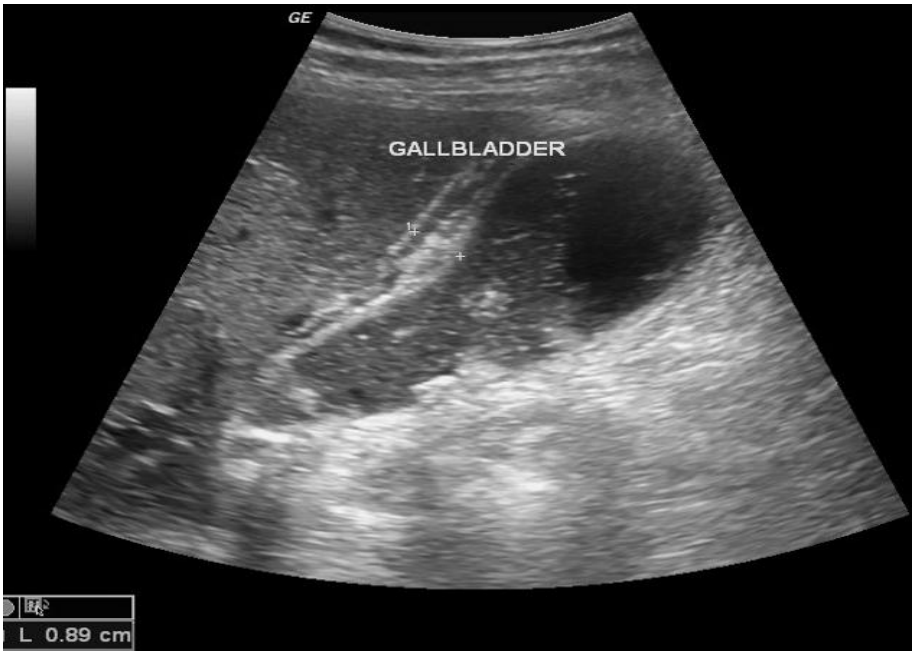


Figure 1. Sonographic image of acute cholecystitis.

3.2. Acute left upper quadrant pain

Rare cases of acute left upper quadrant discomfort exist. The cause may include a peptic ulcer, spleen infarction, or abscess. CT is typically utilized, and US is rarely. In the diagnosis of stomach diseases, endoscopy might also be a solution.

3.3. Acute right lower quadrant pain and approach to acute appendicitis

It is well known that acute right lower quadrant discomfort frequently leads to admission to the emergency room. Its clinical etiology is complex, and therapy options are numerous.

In addition to being the most frequent cause of acute abdominal pain, acute appendicitis is also the most common cause of right lower quadrant pain. Terminal ileitis, pelvic inflammatory disease, hemorrhagic cyst rupture, ovarian torsion, and ectopic pregnancy are further disorders that cause right lower quadrant pain. The preoperative diagnosis of these patients has been made easier by recent developments in cross-sectional imaging (13).

US is mostly used to assess acute appendicitis, particularly in children. The fact that it is not compressible and has a diameter greater than 7 mm is significant for the diagnosis. On US, it can be challenging to distinguish normal appendix. When inflamed, it becomes apparent.

Utilizing the US needs user-dependent competence, and obese patients have challenging imaging. When sonographic results are unclear or a patient is suspected of having a complicated appendicitis, computed tomography is used as a diagnostic tool (Figure 2).

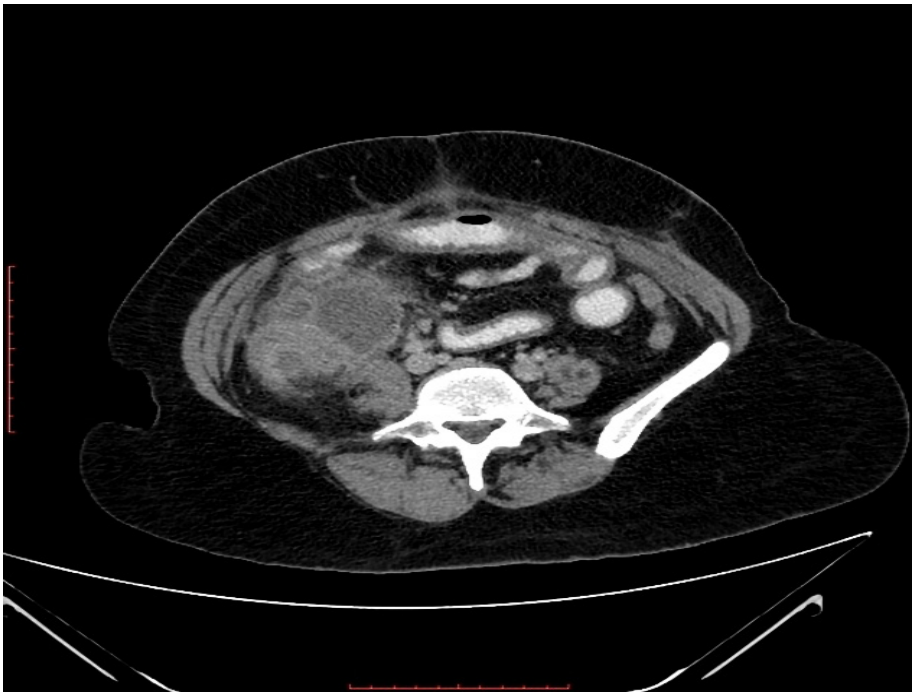


Figure 2. Complicated acute appendicitis with abscess formation.

3.4. Acute left lower quadrant pain

The sigmoid colon diverticulosis is the most typical cause of left lower quadrant pain. About one-fourth of instances involve inflammation. In its

diagnosis and exclusion, CT is crucial(14). On radiographic examination of the intestinal wall, diverticula, wall thickening, and stranding in paracolic fat planes are visible(15).

When found on a CT scan, an abscess or extraluminal free air implies complicated diverticulitis (Figure 3). Fistulas and intestinal obstruction might also be considered complications(16).

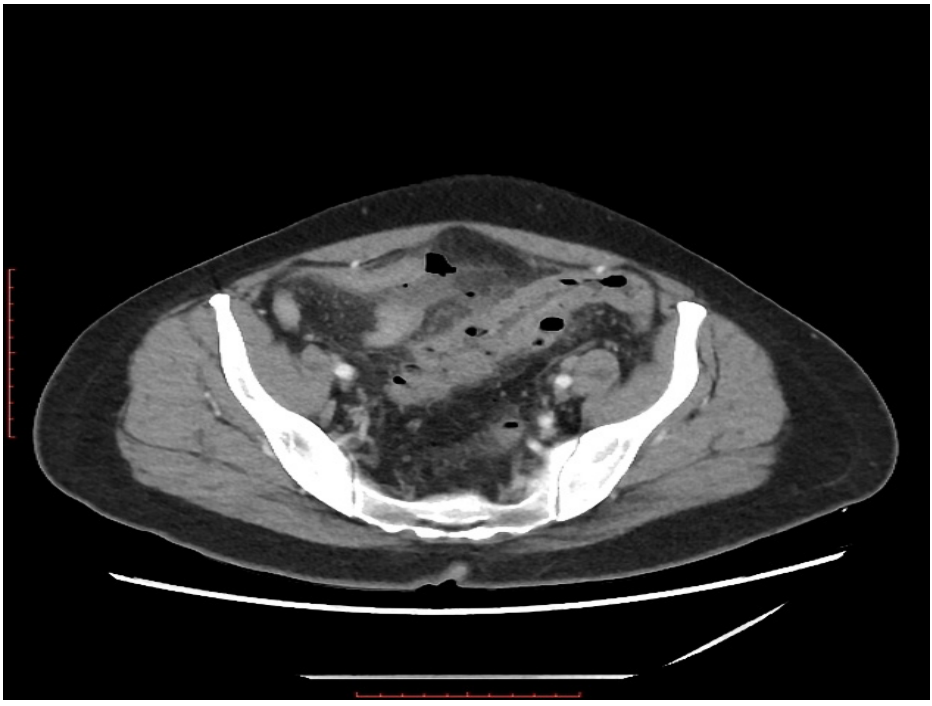


Figure 3. Perforated sigmoid diverticulitis with pneumoperitoneum.

3.5. Approach to intestinal obstruction

There are many conditions that can produce acute diffuse abdominal pain, including those that involve the gastrointestinal system or peritoneum. Bowel obstruction is known to be the most common cause of surgical hospitalizations, despite the fact that gastroenteritis is highly common(12).

While malignancies predominate in colonic obstructions, adhesions are the primary cause of small bowel obstructions. Conventional radiography and clinical examination can both identify bowel blockage (Figure 4). However, computed tomography is the primary imaging technique that establishes the cause and degree of obstruction and establishes the surgical course of action(17,18).

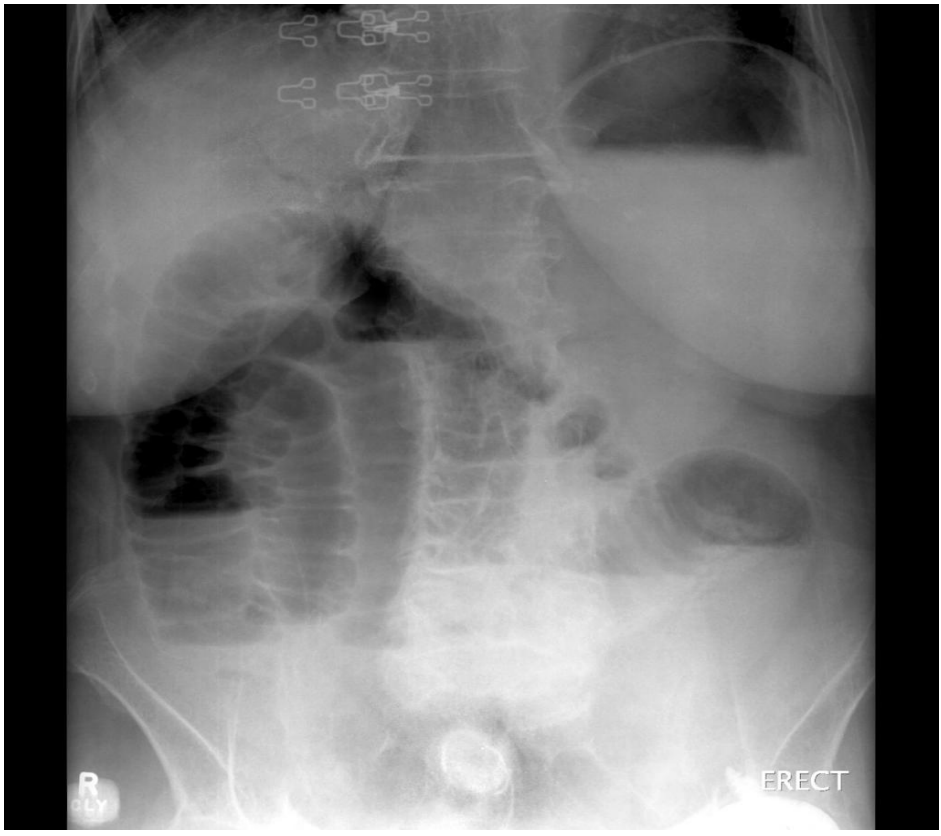


Figure 4. Air-fluid levels in distended small bowel segments consistent with intestinal obstruction.

3.6. Approach to mesenteric ischemia

Ischemic bowel disease should be considered in the differential diagnosis in circumstances where there is insufficient mesenteric blood flow. Acute mesenteric ischemia is brought on by arterial blockage, hypotension, and venous circulation issues. In these situations, CT is routinely used, and CT angiography can be used to visualize the mesenteric arteries. Radiological signs of intestinal ischemia include edema and a lack of enhancement in the intestinal wall(7) . Ascites, intraperitoneal free air, and air-fluid levels are among findings that show the condition has gotten more complicated. There may also be additional abnormalities, such as intestinal pneumatosis and air in the portal vein. The lung window is useful for clearly displaying the pneumoperitoneum. Patients are swiftly referred for surgical therapy when these indicators are found using CT.

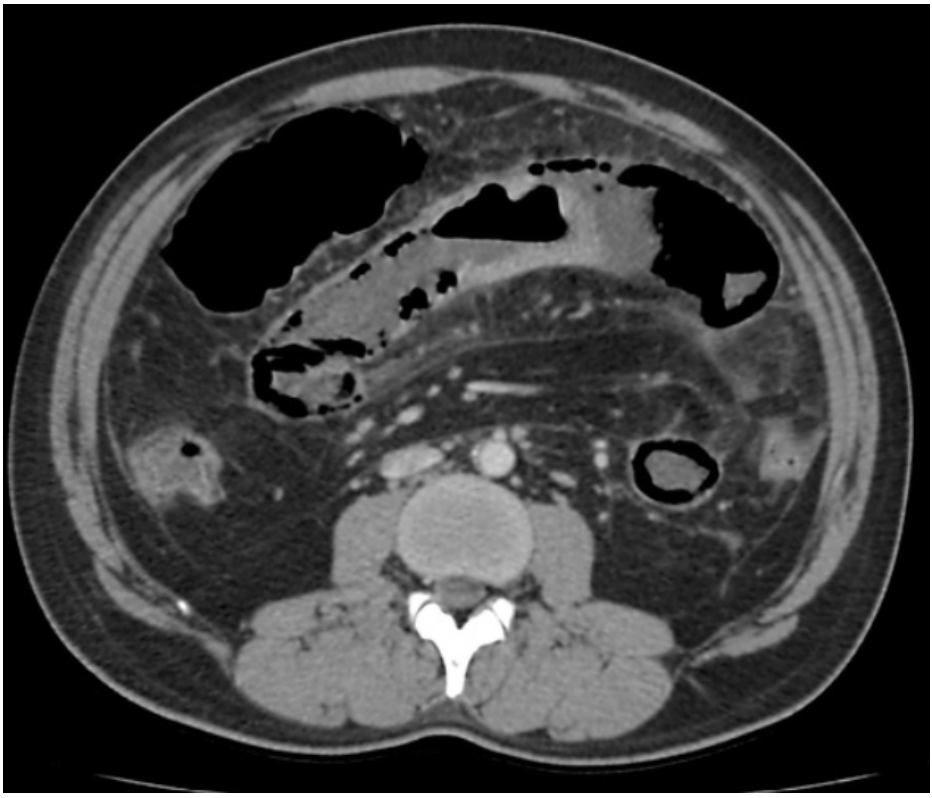


Figure 5. Ischemia in the small bowel segment is indicated by presence of pneumatosis intestinalis.

3.7. Approach to urinary colic

Urinary colic is a frequent illness that produces severe flank pain. Although US can identify hydronephrosis, CT without contrast is the essential imaging technique for urinary system stone(19). Without the use of intravenous contrast, the ureters and renal collecting system can be examined in this procedure. CT is useful for determining the grade of dilatation, the location of the occlusive stone, and the best approach to take.

3.8. Approach to acute pancreatitis

Acute pancreatitis is a significant cause to epigastric discomfort. Acute pancreatitis' etiology includes gallstones and detectable with US. However, in circumstances like the degree of inflammation, the presence of complications, or the presence of collections, CT is required to be beneficial. This disease, which

manifests as pancreatic edema, frequently has complications. By resulting in necrosis, hemorrhage and thrombosis in nearby vessels, it may be lethal (12) (Figure 6).

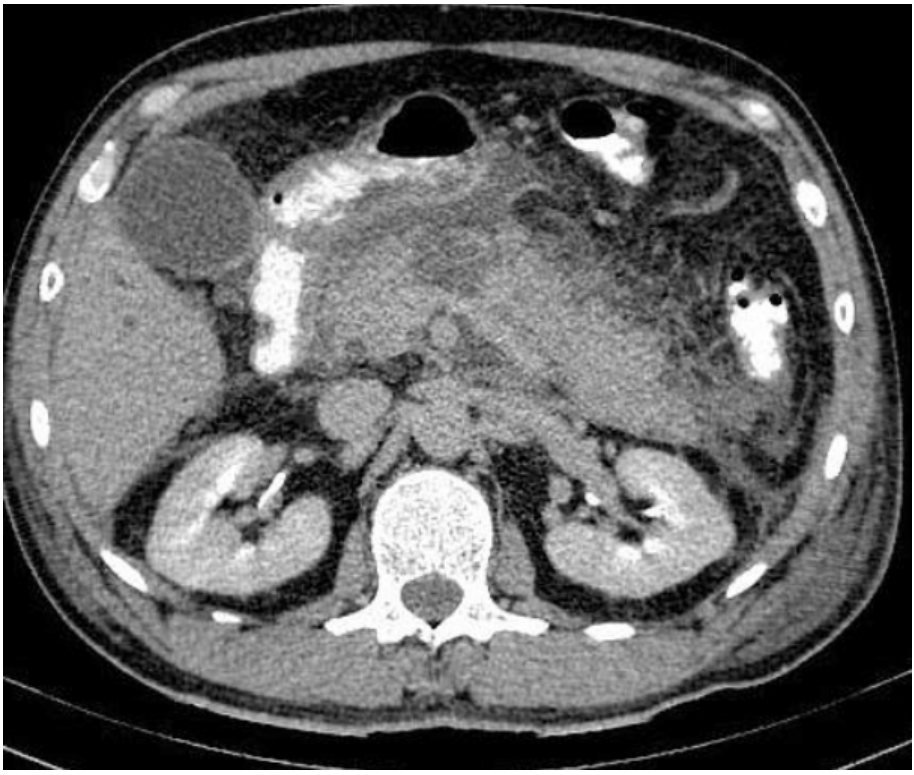


Figure 6. Acute pancreatitis causes necrosis and peripancreatic inflammation in the pancreatic body part.

One of the reasons of acute abdomen that might be fatal is acute aortic syndrome. Hemodynamic stability needs to be attained right away in cases where an abdominal aortic aneurysm rupture is suspected. Then, using CT angiography, an aortic aneurysm and bleeding in the paraaortic region are found.

3.9. Role of MRI in abdominal and pelvic emergencies

When evaluating abdominal and pelvic emergencies, magnetic resonance imaging falls short of CT and US. Because it doesn't contain radiation, it is recommended for pregnant patients as an alternative to CT (20). However, MRI has a great sensitivity in detecting gynecological diseases and acute pelvic pain. The drawbacks of MRI include prolonged imaging time and a relatively challenging availability in emergency rooms.

There is not a lot of scientific data on the utility of MRI in acute abdomen cases. However, the higher cost also has a disadvantage. For MRI optimization and diagnostic accuracy to be maximized, suitable protocol establishment is crucial. Although it is being explored as a substitute owing to radiation exposure, there is yet insufficient data to support its routine use.

REFERENCES

1. Shackford SR. Focused ultrasound examinations by surgeons: the time is now. J Trauma. 1993;35(2):181-182.

2. Milia DJ, Brasel K. Current use of CT in the evaluation and management of injured patients. Surg Clin North Am. 2011;91(1):233-248.

3. Ptak T, Rhea JT, Novelline RA. Radiation dose is reduced with a single-pass whole-body multi-detector row CT trauma protocol compared with a conventional segmented method: initial experience. Radiology. 2003;229(3):902-905.

4. Fanucci E, Fiaschetti V, Rotili A, Floris R, Simonetti G. Whole body 16-row multislice CT in emergency room: effects of different protocols on scanning time, image quality and radiation exposure. Emerg Radiol. 2007;13(5):251-257.

5. Prasad SR, Wittram C, Shepard JA, McLoud T, Rhea J. Standard-dose and 50%-reduced-dose chest CT: comparing the effect on image quality. AJR Am J Roentgenol. 2002;179(2):461-465.

6. Hagtvedt T, Aalokken TM, Notthellen J, Kolbenstvedt A. A new low-dose CT examination compared with standard-dose CT in the diagnosis of acute sinusitis. Eur Radiol. 2003;13(5):976-980.

7. Stoker J, van Randen A, Lameris W, Boermeester MA. Imaging patients with acute abdominal pain. Radiology. 2009;253(1):31-46.

8. Mindelzun RE, Jeffrey RB. Unenhanced helical CT for evaluating acute abdominal pain: a little more cost, a lot more information. Radiology. 1997;205(1):43-45.

9. Novelline RA, Rhea JT, Rao PM, Stuk JL. Helical CT in emergency radiology. Radiology. 1999;213(2):321-339.

10. Gore RM, Miller FH, Pereles FS, Yaghmai V, Berlin JW. Helical CT in the evaluation of the acute abdomen. AJR Am J Roentgenol. 2000;174(4):901-913.

11. Rosen MP, Sands DZ, Longmaid HE, 3rd, Reynolds KF, Wagner M, Raptopoulos V. Impact of abdominal CT on the management of patients

presenting to the emergency department with acute abdominal pain. AJR Am J Roentgenol. 2000;174(5):1391-1396.

12. Marincek B. Nontraumatic abdominal emergencies: acute abdominal pain: diagnostic strategies. Eur Radiol. 2002;12(9):2136-2150.

13. Birnbaum BA, Jeffrey RB, Jr. CT and sonographic evaluation of acute right lower quadrant abdominal pain. AJR Am J Roentgenol. 1998;170(2):361-371.

14. Rao PM. CT of diverticulitis and alternative conditions. Semin Ultrasound CT MR. 1999;20(2):86-93.

15. Pradel JA, Adell JF, Taourel P, Djafari M, Monnin-Delhom E, Bruel JM. Acute colonic diverticulitis: prospective comparative evaluation with US and CT. Radiology. 1997;205(2):503-512.

16. Destigter KK, Keating DP. Imaging update: acute colonic diverticulitis. Clin Colon Rectal Surg. 2009;22(3):147-155.

17. Caoili EM, Paulson EK. CT of small-bowel obstruction: another perspective using multiplanar reformations. AJR Am J Roentgenol. 2000;174(4):993-998.

18. Furukawa A, Yamasaki M, Furuichi K, et al. Helical CT in the diagnosis of small bowel obstruction. Radiographics. 2001;21(2):341-355.

19. Smith RC, Rosenfield AT, Choe KA, et al. Acute flank pain: comparison of non-contrast-enhanced CT and intravenous urography. Radiology. 1995;194(3):789-794.

20. Heverhagen JT, Klose KJ. MR imaging for acute lower abdominal and pelvic pain. Radiographics. 2009;29(6):1781-1796.

CHAPTER XXIV

IMAGING FINDINGS OF EMERGENCY GENITAL PATHOLOGIES IN MALE PATIENTS

Ahmet Turan Kaya

(Asst. Prof,), Department of Radiology, Amasya University, Sabuncuoğlu Şerefeddin Research and Education Hospital, Amasya, Turkey
E-mail: hmttrnky.62@gmail.com
ORCID: 0000-0001-9803-453X

1 Scrotal EmergencIes

Scrotal pain is one of the emergencies that require careful attention in the differential diagnosis and early diagnosis is important. Imaging is required for causes of scrotal pain. Ultrasonography (US) and color Doppler US (CDUS) is the first preferred imaging modalities since there is no ionizing radiation and it is fast and easily accessible (1–3). The use of magnetic resonance imaging (MRI) is limited compared to the US due to its longer imaging time, not being easily accessible, and not being available in every health center. However, it can be helpful in the differential diagnosis when US and CDUS are not sufficient (4). While a linear high-frequency (7.5–12.0 MHz) transducer is used in US and CDUS, low-frequency convex probes can help examine deep fascia in infectious pathologies with extra-scrotal spread such as "Fournier Gangrene". CDUS is required to demonstrate vascularity in patients with suspected infection or torsion. However, US and CDUS depend on the experience of the operator, and the "absence of pseudo-flow" may occur due to incorrect adjustment of the blood flow echo to the transducer reaching angle. In such cases, "Power Doppler US", which is not affected by the doppler angle, can be applied (5).

1.1 Non-Traumatic Conditions

1.1.1 Epididymitis

The most common cause of acute scrotal pain is epididymitis. If epididymitis is left untreated, infarction may develop in the testicular parenchyma. Due to the retrograde spread of infectious pathogens, the epididymal tail is affected first and then the other parts are affected, so the first imaging findings appear inthe epididymal tail region (6). In the US, due to inflammation in the epididymis, the echogenicity is decreased compared to the testis, its diameter is increased, and it has a heterogeneous appearance (6). Increased vascularity is detected in CDUS (7). If epididymitis is not treated early, it becomes complicated. In US and CDUS, especially the central part of the tail is hypoechoic and vascularity is reduced or absent, while a significant increase in vascularity can be seen in its periphery (7). These findings are indicative of an abscess developing due to delayed diagnosis or unsuccessful treatment (8).

1.1.2 Epididymo-orchitis

It is a co-infection of the epididymis and testis and is seen in 20-40% of patients with epididymitis (2). The most common cause of emergency scrotal pain is testicular torsion. Pain associated with epididymo-orchitis decreases or improves with testicular elevation (Prehn's sign), whereas pain does not decrease with elevation in testicular torsion (6). Edema occurring in the testis may prevent venous return, leading to increased intraparenchymal pressure and disruption of arterial circulation, resulting in necrosis (9). Unsuccessful treatment of epididymo-orchitis may cause pyocele or intra-testicular abscess (10). In US and CDUS, the parenchyma is hypoechoic, heterogeneous, and noticeably increased vascularity compared to the normal epididymis and testis (6).

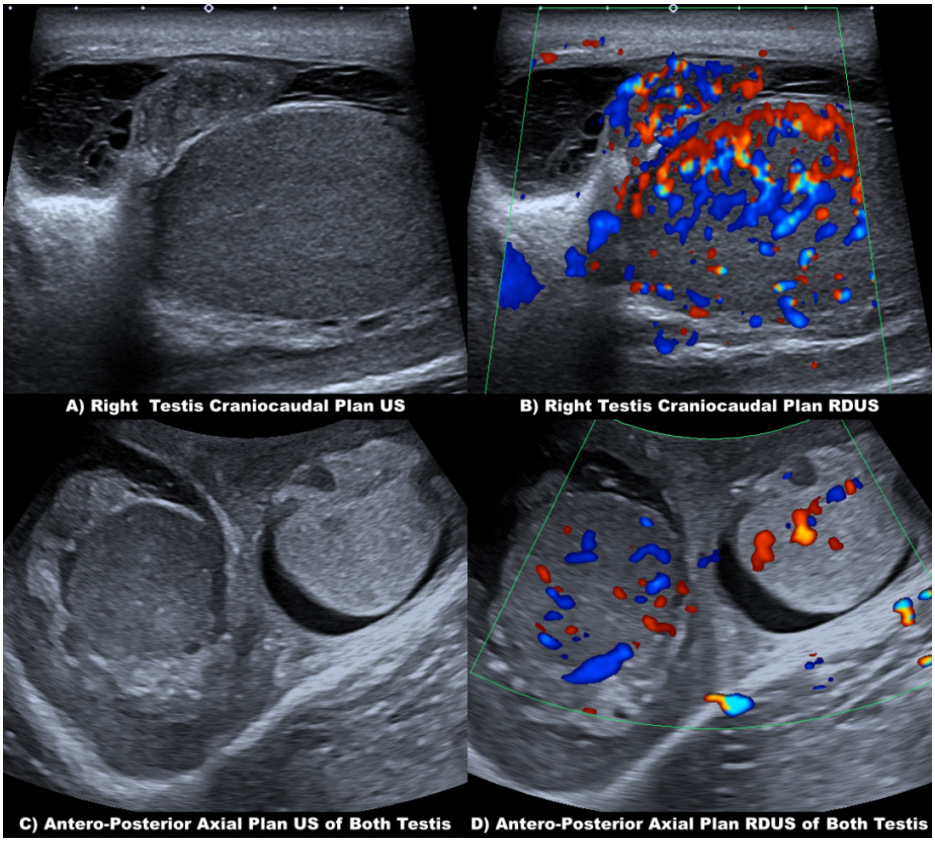


Figure 1A-D) A 57-year-old male patient complained of scrotal pain, swelling, and redness. US and CDUS were performed. A-D) In US and CDUS imaging with high-frequency linear and low-frequency convex transducers, the right testis and epididymal parenchyma appear hypoechoic heterogeneous compared to left testis and epididymis, and their vascularity is noticeably increased. On the right, the intrascrotal fluid is increased and contains echogenic septa. Control US and CDUS were performed on the patient diagnosed with epididymo-orchitis because his complaints increased 2 weeks after the treatment was started. MRI was applied to the patient with a fistulous collection under the skin.

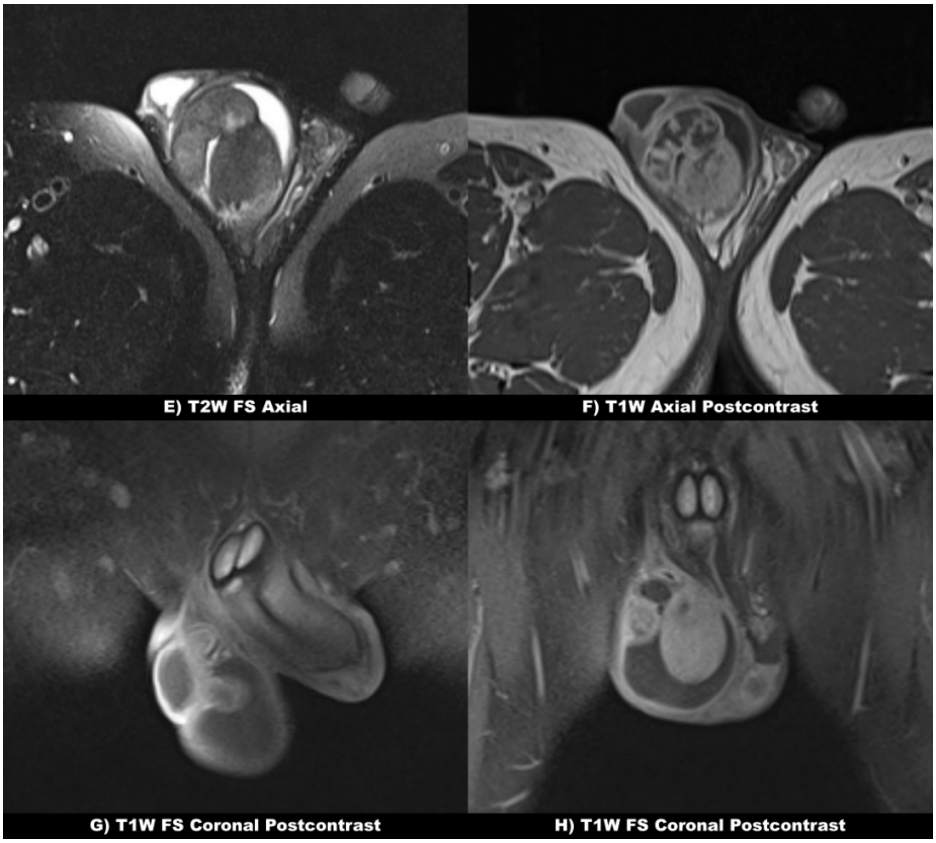


Figure 1 E-H) In the same patient;E) In the T2W FS image, the parenchyma of the right testis and epididymis was heterogeneous, sizes of the epididymis increased, the intrascrotal fluid increased, and a hyperintense collection under the skin was observed. F-H) On postcontrast images, increased contrast enhancement was observed around the epididymis and subcutaneous collection. The collection was evaluated as an abscess and drained.

1.1.3 Fournier Gangrene

It is a urological emergency that is rarer in women (male/female ratio= 10/1), can spread to the deep fascial layers, includes widespread necrosis, and has a mortality of 15% to 50%.(11–14)Comorbidities, especially diabetes mellitus and alcoholism, that impair the immune system are the main factors (13). Although the US can be used in the diagnosis because it shows subcutaneous gas echogenicity and collections, it may be insufficient in determining the spread of the infection (6). In addition, performing pressure with the transducer during the US application may increase the patient's pain. Therefore, contrast-enhanced CT

(CECT), which covers the abdomen, pelvis, scrotum, and penis, is the imaging modality that should be the first choice in patients with Fournier's gangrene, as it can show the focus of infection and its relationship with the surrounding tissues (11). On CT, minimal or diffuse gas densities and fluid collections can be seen in the subcutaneous and deep soft tissues (6,11–14). However, the US can be performed in the emergency room and intensive care units (6).

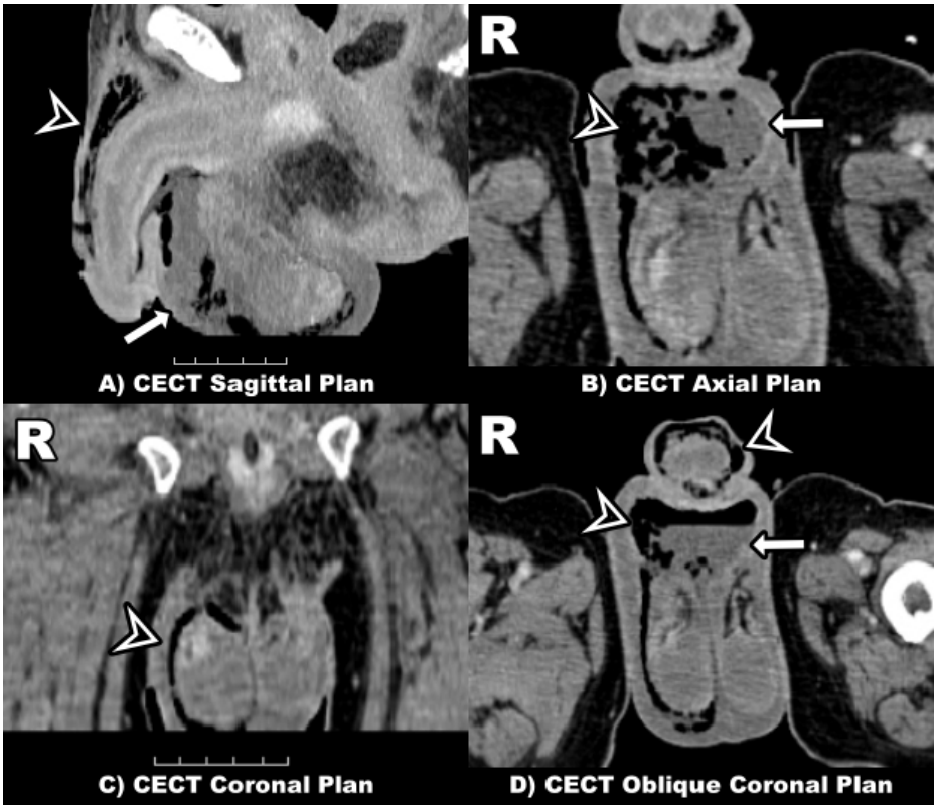


Figure 2 A 59-year-old male patient presented with severe scrotal pain, swelling, and redness extending to the perineal and penile region in addition to abdominal pain. The patient had a history of colon cancer with metastases to the liver and bones. Contrast enhancement CT was applied to the patient. A-D) Subcutaneous air densities (arrowheads) were observed in both intrascrotal areas and around the penis, more prominently in the right intrascrotal area. In addition, there was an increase in leveling fluid (white arrows) containing air densities in the right intrascrotal space(This figure was obtained from Assoc. Prof. Dr. Leyla KARACA's archive with her permission. Department of Radiology, MedicalFaculty, Inönü University, Malatya, Turkey)

1.1.4 Testicular torsion

Testicular torsion is a surgical emergency that is most frequently seen in adolescent boys and should be early diagnosed (2). US scan of the testis with torsion in the early period may be normal (15). In CDUS, the absence of vascularity on the torsioned side compared to the normal testis is diagnostic (15). In the late period due to ischemic changes, testicular size increases and the parenchyma is hypoechoic and heterogeneous (15,16). These findings indicate that the testis has begun to lose vitality (16).

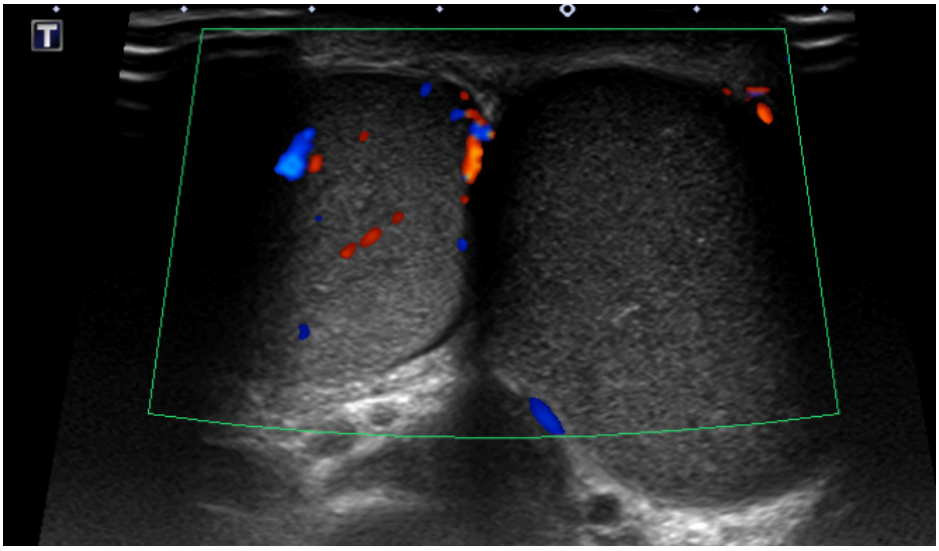


Figure 3 A 22-year-old male patient presented with the complaint of sudden onset and increasing scrotal pain. In the US, left testis distances were increased compared to the right, and parenchymal echogenicity was decreased. While vascularity was observed in the right testicular parenchyma in CDUS, there was no vascularity in the left. The patient with a diagnosis of testicular torsion was performed surgically detorsion.

1.2 Traumatic Conditions

Scrotal trauma is seen in less than 1% of trauma (blunt and penetrating) (17). Emergency surgery is required as testicular ischemia may develop after trauma (15). US and CDUS are successful in the diagnosis of scrotal trauma and are the first-choice imaging method. Depending on the severity of scrotal trauma, contusion, rupture or infarction may develop. In the US, heterogeneity in the parenchyma and irregularities in the testicular contour can be observed. Hematocele in the scrotum and rupture lines in the testicular tissue can be observed (17–21). The presence of an intrascrotal hematocele (US > 5 cm) or

interruption of the continuity of the tunica albuginea is an indication for surgical exploration for testicular rupture (22,23). MRI may be helpful in cases where the US is inadequate (15). Normal testes are both T1W (intermediate signal intensity) and T2W (highsignal intensity) homogeneous (24). Heterogeneous hypointense areas can be observed in T2W in trauma patients (25,26).

2 PenIle EmergencIes

Penile emergencies are often due to traumatic causes although acute penile diseases are rare. US and CDUS are the first-choice modalities, as in the scrotum (15). MRI can be used to show facial lacerations in the penis, especially in patients with blunt penile trauma (15). There are two corpora cavernosa on the dorsal penis and a corpus spongiosum on the ventral (27). The corpora cavernosa, which plays a role during erection, consists of sinusoids that fill with blood (27). In addition, superficial fascia tunica albuginea and deep fascia Buck's fascia contribute to the rigidity of the penis after erection by wrapping the corpora cavernosa (28). Venous return in these caverns is prevented, resulting in the erection of the penis (15,28). Injury to the caverns and fascia causes erectile dysfunction. For this reason, grayscale imaging of the penis with a high-frequency (7.5–12.0 MHz) linear transducer, which provides high-resolution images, and blood flow evaluation with CDUS should be performed (29,30). MR imaging of the penis is used in suspicious cases or for pre-surgical evaluation.

2.1 Priapism

It is a prolonged erection due to disruption of normal venous return, unrelated to sexual pleasure (31,32). Prolonged priapism may lead to permanent erectile dysfunction due to persistent ischemic changes (31). CDUS may indicate increased blood flow in the cavernosal artery, arterial-lacunar fistula, or pseudoaneurysm (15,31). Digital subtracted angiography (DSA) visualizes fistula and pseudoaneurysm more clearly and can be treated with DSA-guided embolization (33,34).

2.2 Penile Fracture

Penile fracture is a blunt traumatic injury, mostly caused by sudden bending of the erect penis (35). It is caused by the rupture of the tunica albuginea or one or both of the corpora cavernosa (36). As a result of the rupture, pain, swelling, and hematoma occur. The US can show irregularity in the tunica albuginea and hematoma in the corpora cavernosa (29,30). If air echogenicity is present within the caverns, injury of the urethra should also be suspected, and retrograde

urethrography should be performed as the US will be insufficient (37). MRI better demonstrates disruption of the tunica albuginea and changes in signal on T1W and T2W images according to the stage of the hematoma (35,37).

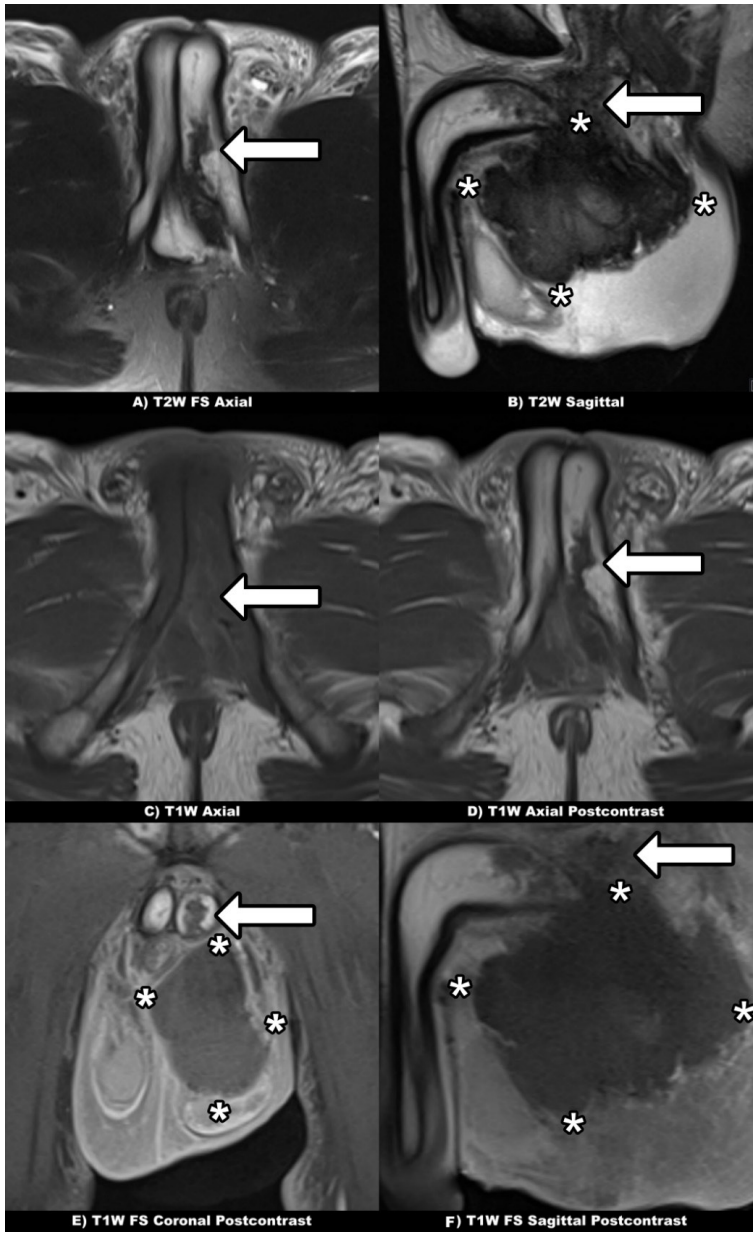


Figure 4 A 41-year-old male patient had pain and swelling, especially in the proximal part of the penis, due to the sudden torsion of his erect penis. After 6 days, US (not shown) and MRI were performed because the swelling increased

and extended into the scrotum. A-C) A hypointense, irregular fracture line (white arrows) extending from the middle part of the left corpus cavernosum to the proximal was observed. A lobulated contoured hypointense hematoma (asterisks) in the T2W image, extending from the proximal of the penis to the left intrascrotal area was observed. D-F) In postcontrast T1W images, the right corpus cavernosum is normally seen as hyperintense due to enhancement. On the left corpus cavernosum, full-thickness, non-enhancing, irregular fracture line (white arrows), and hypointense, lobulated contoured hematoma (asterisks) was observed in the left intrascrotal area.(This figure was obtained from Assoc. Prof. Dr. Leyla KARACA's archive with her permission. Department of Radiology, Medical Faculty, Inönü University, Malatya, Turkey)

Acknowledgments: I would like to thank Assoc. Prof. Dr. Leyla KARACA for her contributions to figures 2 and 4. (Department of Radiology, Medical Faculty, Inönü University, Malatya, Turkey)

References

1. Sung EK, Setty BN, Castro-Aragon I. Sonography of the pediatric scrotum: Emphasis on the Ts - Torsion, trauma, and tumors. Am J Roentgenol. 2012;198(5):996-1003.

2. Dogra VS, Gottlieb RH, Oka M, Rubens DJ. Sonography of the scrotum. Radiology. 2003;227(1):18-36.

3. Remer EM, Casalino DD, Arellano RS, et al. ACR Appropriateness Criteria ® acute onset of scrotal pain--without trauma, without antecedent mass. Ultrasound Q. 2012;28(1):47-51.

4. Parenti GC, Feletti F, Brandini F, et al. Imaging of the scrotum: role of MRI. Radiol Med. 2009;114(3):414-424.

5. Hamper UM, DeJong MR, Caskey CI, Sheth S. Power Doppler Imaging: Clinical Experience and Correlation with Color Doppler US and Other Imaging Modalities. Radiographics. 1997;17(2):499-513.

6. Avery LL, Scheinfeld MH. Imaging of penile and scrotal emergencies. Radiographics. 2013;33(3):721-740.

7. Horstman WG, Middleton WD, Melson GL, Siegel BA. Color Doppler US of the scrotum. Radiographics. 1991;11(6).

8. Konicki PJ, Baumgartner J, Kulstad EB. Epididymal abscess. Am J Emerg Med. 2004;22(6):505-506.

9. Muttarak M, Na Chiangmai W, Kitirattrakarn P. Necrotising epididymo-orchitis with scrotal abscess. Biomed Imaging Interv J. 2005;1(2):e11.

10. Slavis SA, Kollin J, Miller JB. Pyocele of scrotum: consequence of spontaneous rupture of testicular abscess. Urology. 1989;33(4):313-316.

11. Levenson RB, Singh AK, Novelline RA. Fournier gangrene: role of imaging. Radiographics. 2008;28(2):519-528.

12. Safioleas M, Stamatakos M, Mouzopoulos G, Diab A, Kontzoglou K, Papachristodoulou A. Fournier's gangrene: exists and it is still lethal. Springer. 2006;38(3-4):653-657.

13. Morpurgo E, Galandiuk S. Fournier's gangrene. Surg Clin North Am. 2002;82(6):1213-1224.

14. Ferreira PC, Reis JC, Amarante JM, et al. Fournier's gangrene: a review of 43 reconstructive cases. Plast Reconstr Surg. 2007;119(1):175-184.

15. Iraha Y, Okada M, Iraha R, et al. CT and MR imaging of gynecologic emergencies. Radiographics. 2017;37(5):1569-1586.

16. Kaye JD, Shapiro EY, Levitt SB, et al. Parenchymal Echo Texture Predicts Testicular Salvage After Torsion: Potential Impact on the Need for Emergent Exploration. J Urol. 2008;180(4 SUPPL.):1733-1736.

17. Deurdulian C, Mittelstaedt CA, Chong WK, Fielding JR. US of acute scrotal trauma: optimal technique, imaging findings, and management. Radiographics. 2007;27(2):357-369.

18. Guichard G, El Ammari J, Del Coro C, et al. Accuracy of ultrasonography in diagnosis of testicular rupture after blunt scrotal trauma. Urology. 2008;71(1):52-56.

19. Bhatt S, Radiographics VD, 2008 undefined. Role of US in testicular and scrotal trauma. pubs.rsna.org. 2008;28(6):1617-1629.

20. Buckley JC, McAninch JW. Use of ultrasonography for the diagnosis of testicular injuries in blunt scrotal trauma. J Urol. 2006;175(1):175-178.

21. Guichard G, El Ammari J, Del Coro C, et al. Accuracy of ultrasonography in diagnosis of testicular rupture after blunt scrotal trauma. Urology. 2008;71(1):52-56.

22. Buckley JC, McAninch JW. Diagnosis and management of testicular ruptures. Urol Clin North Am. 2006;33(1):111-vii.

23. Kim SH, Park S, Choi SH, Jeong WK, Choi JH. The efficacy of magnetic resonance imaging for the diagnosis of testicular rupture: a prospective preliminary study. J Trauma. 2009;66(1):239-242.

24. Kim W, Rosen MA, Langer JE, Banner MP, Siegelman ES, Ramchandani P. US–MR imaging correlation in pathologic conditions of the scrotum. pubs.rsna.org. 2007;27(5):1239-1253.

25. Kubik-Huch RA, Hailemariam S, Hamm B. CT and MRI of the male genital tract: radiologic-pathologic correlation. Eur Radiol. 1999;9(1):16-28.

26. Cramer BM, Schlegel EA, Thueroff JW. MR imaging in the differential diagnosis of scrotal and testicular disease. Radiographics. 1991;11(1):9-21.

27. Gray's Anatomy, 39th Edition: The Anatomical Basis of Clinical Practice. Am J Neuroradiol. 2005;26(10):2703 LP - 2704.

28. Lee J, Singh B, Kravets FG, Trocchia A, Waltzer WC, Khan SA. Sexually acquired vascular injuries of the penis: a review. J Trauma. 2000;49(2):351-358.

29. Older R, ultrasound LWJ of clinical, 1996 undefined. Ultrasound anatomy of the normal male reproductive tract. Wiley Online Libr. 1996;24:389-404.

30. Wilkins CJ, Sriprasad S, Sidhu PS. Colour Doppler ultrasound of the penis. Clin Radiol. 2003;58(7):514-523.

31. Pautler SE, Brock GB. Priapism. From Priapus to the present time. Urol Clin North Am. 2001;28(2):391-403.

32. McAninch, J. (2008). Smith's general urology. McGraw-Hill Companies, Incorporated.

33. Kawakami M, Minagawa T, Inoue H, et al. Successful treatment of arterial priapism with radiologic selective transcatheter embolization of the internal pudendal artery. Urology. 2003;61(3):645.

34. Abujudeh H, Mirsky D. Traumatic high-flow priapism: Treatment with super-selective micro-coil embolization. Emerg Radiol. 2005;11(6):372-374.

35. Sawh SL, O'Leary MP, Ferreira MD, Berry AM, Maharaj D. Fractured penis: a review. Int J Impot Res. 2008;20(4):366-369.

36. Bitsch M, Kromann-Andersen B, Schou J, Sjøntoft E. The elasticity and the tensile strength of tunica albuginea of the corpora cavernosa. J Urol. 1990;143(3):642-645.

37. Kawashima A, Sandler CM, Wasserman NF, LeRoy AJ, King BF Jr, Goldman SM. Imaging of urethral disease: a pictorial review. Radiographics. 2004;24 Suppl 1:S195-S216.

CHAPTER XXV

CROSS-SECTIONAL IMAGING IN HEPATOPANCREATOBILIARY EMERGENCIES

Mustafa Orhan Nalbant

(MD.), University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Radiology Department
e-mail: musnalbant88@hotmail.com
ORCID: 0000-0002-5277-9111

1. Introduction

Acute abdominal symptoms are among the most frequent reasons people attend the emergency room. Disorders of the biliary system and pancreas account for the majority of these diseases. Cross-sectional imaging helps clinicians diagnose and assess patients with acute abdominal disorders. Due to technological advancements over the past several years, notably in terms of enhanced acquisition speed and lower radiation dosage, MDCT (multidetector computed tomography) has emerged as the preferred imaging modality for emergency abdominal imaging. MDCT's extensive value in abdominal crises is well established.

MRI (magnetic resonance imaging) may be necessary for the assessment of specific clinical circumstances. MRI has the particular benefit of avoiding ionizing radiation as compared to MDCT. MR cholangiopancreatography (MRCP) has evolved into an indispensable imaging technique for the biliary system and pancreasHeavy T2-weighted images provide a quick, noninvasive assessment of the biliary tree and pathological localization. Moreover, MRI may provide pertinent information to individuals being assessed for biliary or pancreatic injuries, bile leakage, acute pancreatitis, cholecystitis, or an obstructed biliary tract.

This article describes the cross-sectional imaging characteristics, diagnostic criteria, and consequences of pancreaticobiliary emergencies that are

regularly seen. This includes a discussion of acute cholecystitis, cholangitis, and pancreatitis. There are also other categories of problems that can happen with these diseases, as well as artifacts that can look like pathology.

2. Common Hepatopancreatobiliary Emergency Pathologies

2.1. Acute Cholecystitis and Associated Complications

A stone blocking the cystic duct or gallbladder neck causes mainly acute cholecystitis (1). Due to its inexpensive cost, convenient accessibility, quick test duration, and minimal ionizing radiation exposure, ultrasonography is the ideal initial imaging method for acute cholecystitis (2). Ultrasound is restricted to evaluating acute cholecystitis complications. For precise localization and surgical planning, such problems may need CT or MR imaging. CT and MR imaging can examine or exclude alternative upper right quadrant pain causes.

CT scans show an enlarged gallbladder, mural enhancement, thickness, pericholecystic fat stranding, and fluid in acute cholecystitis without sequelae (3). Gallbladder neck or cystic duct calculus. Due to gallstones' variable composition, CT has limited ability to identify them. Isodense gallstones may not be visible on CT (4). MRI is equally effective as ultrasonography and CT in detecting acute cholecystitis **(Figure 1).** On the MRCP, a gallbladder neck or cystic duct stone may present as an oval filling defect. The US detects cholelithiasis more sensitively and can identify gallstones in some patients. The most common but least specific observation is the wall thickness of the gallbladder. This is seen in hepatitis, hypoproteinemia, heart failure, and acute pyelonephritis (5, 6).

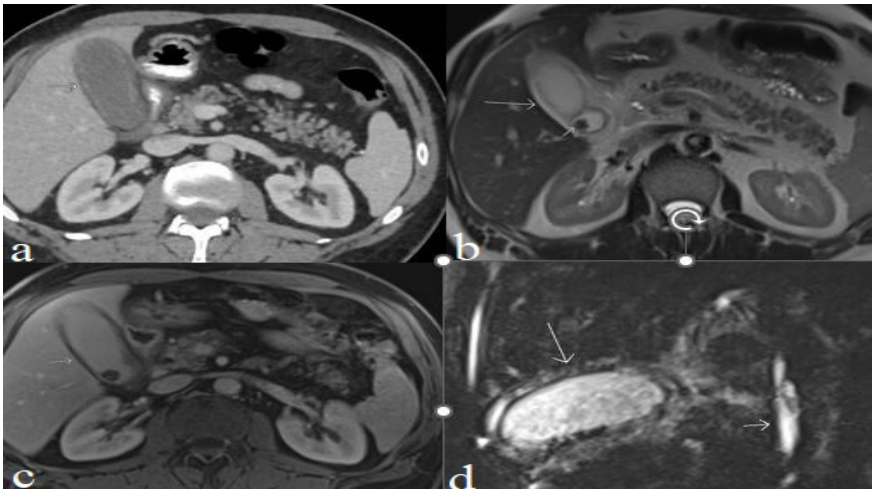


Figure 1: Acute cholecystitis in a 38-year-old female patient. The gallbladder demonstrates an increase in wall thickness (white arrow) on axial CT (a) and

T2-weighted (b) images. On axial MRI scans, a hypointense gallstone is visible (b, c). In the MRCP image (d), the increased wall thickness, pericholecystic fluid, and normal common bile duct are observed.

Gangrenous cholecystitis is a complication that can arise following acute calculous cholecystitis and affects up to 40% of patients. This complication can be fatal (7). CT findings of intraluminal membranes, isolated mural defects, weakly enhanced walls, diminished mural enhancement, and pericholecystic abscesses are specific for gangrenous cholecystitis (8). A focal defect next to pericholecystic fluid is alarming and indicative of gallbladder perforation, which may lead to an intrahepatic abscess, pericholecystic abscess **(Figure 2)**, or peritonitis (9). Serial CT or US scans that show a fast rise in the amount of pericholecystic fluid are a good sign of a perforated gallbladder.

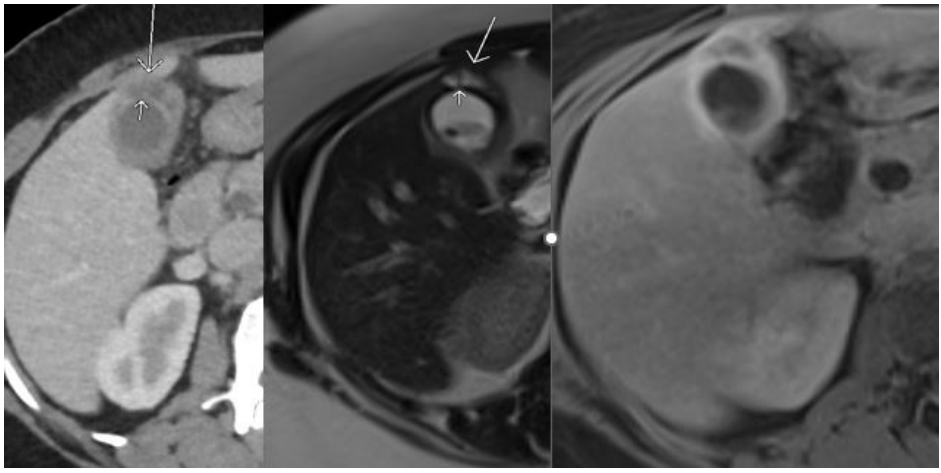


Figure 2: Gallbladder perforation in a 42-year-old male patient. A pericholecystic abscess (long arrow) is seen as a focal defect in the gallbladder wall (short arrow) on axial CT (a) and T2-weighted (b) images (long arrow). In the contrast-enhanced MRI sequence, contrast enhancement is observed in the gallbladder wall and around the abscess.

Emphysematous cholecystitis is caused by gas-forming organism infections. Patients with diabetes have a higher probability and may exhibit less severe symptoms. The CT is diagnostic, demonstrating cholecystitis characteristics and intramural gas **(Figure 3)**. Emphysematous cholecystitis is more likely to progress to perforated cholecystitis than simple cholecystitis (10).

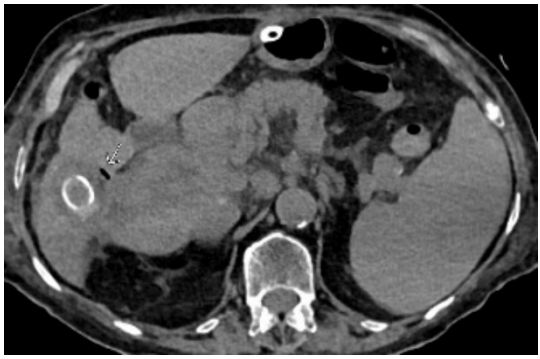


Figure 3: A female patient of 66 years old with emphysematous cholecystitis. The CT axial image reveals intramural gas in the gallbladder wall.

Gallstones in the cystic duct or gallbladder neck contribute to extrinsic compression of the common hepatic duct, resulting in Mirizzi syndrome **(Figure 4)**. Recurrent inflammation can cause cholecystocholedochal fistula. Without a pathognomonic pattern, stomach discomfort, fever, and jaundice are common symptoms, making a clinical diagnosis challenging (11). CT can detect intrahepatic bile duct dilation alongside a common bile duct of normal size. MRCP gives extra information on the precise location of the obstacle (12).

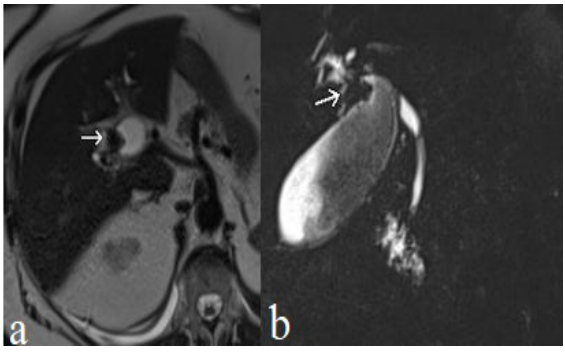


Figure 4: A female patient with Mirizzi syndrome, 45 years old. A T2-weighted axial scan (a) reveals a hypointense gallstone within the cystic duct. The impact of the gallbladder stone on the intrahepatic bile ducts and bile duct dilatation is evident in the MRCP image (b). The calibration of the common bile duct is within normal ranges.

Patients with acute cholecystitis and its accompanying consequences report nonspecific symptoms. Clinical severity may not reflect underlying issues. Cross-sectional imaging identifies acute cholecystitis complications. The emergency radiology staff must be familiar with these imaging findings.

2.2. Imaging of Acute Cholangitis

Cholangitis is an inflammatory disease of the bile ducts that may or may not be accompanied by infection (13). Using the patient's clinical features, medical records, and basic laboratory tests, cholecystitis is evaluated. When hepatobiliary symptoms cannot be pinpointed, cross-sectional imaging is suggested. Ultrasound is the imaging technique of choice for patients with colicky abdominal pain (14–16).

Cancer, trauma, and postoperative patients benefit greatly from CT (17). Magnetic resonance cholangiopancreatography is favored for identifying acute biliary problems because it offers an extensive morphological overview and, if gadoxetic acid is provided, functional and morphological data on the hepatobiliary system (18–20) **(Figure 5)**. Endoscopic ultrasonography and/or retrograde cholangiography are done if brush cytology, peripapillary duct assessment, stenting, or stricture dilatation are needed. Percutaneous transhepatic cholangiography can be utilized when the previous options are not applicable (21).

Imaging is performed to evaluate the location and cause of biliary blockage in addition to the presence of hepatic complications. By demonstrating biliary obstruction, CT imaging can validate the clinical diagnostic criteria for acute cholecystitis. CT is presently a viable imaging modality with high diagnostic performance for biliary obstruction as a result of hardware and software advancements (22–24).

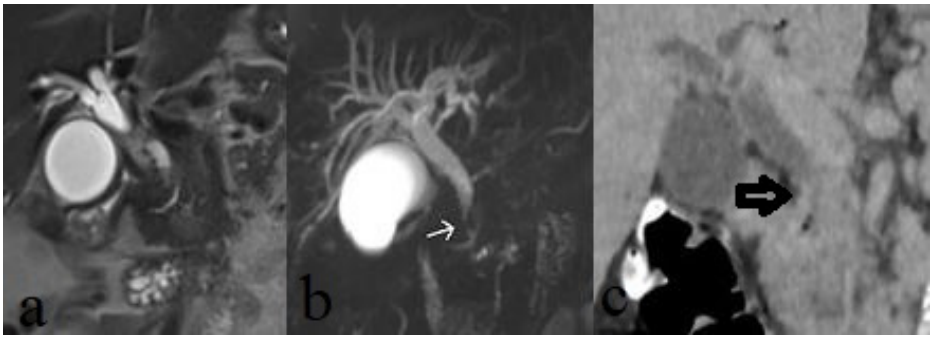


Figure 5: A male patient, age 56, with acute cholangitis. Coronal T2-weighted (a) and MRCP (b) images demonstrate an increase in wall thickness (white arrow) in the distal common bile duct in conjunction with intrahepatic bile duct dilation. In coronal contrast-enhanced CT (c), an increase in thickness and accompanying contrast enhancement (black arrow) are detected at the distal end of the common bile duct.

T2-weighted images reveals an increase in periductal signal intensity, an abscess, thrombosis, transient periductal signal variation, and a ragged duct in acute cholangitis. Biliary ductal dilatation with wall thickening is also a frequent observation in individuals with cholangitis. On contrast-enhanced MRI, increased enhancement is often seen **(Figure 6)**. Due to the prevalence of hepatic occlusion and periportal inflammation in acute cholangitis, they can produce portal vein compression and peribiliary plexus dilatation. With these changes in blood flow, the flow in the hepatic artery may go up, causing an uneven early phase enhancement (25). In patients with cholangitis, MRI reliably detects the source of biliary abnormalities and is particularly effective for predicting acute cholangitis.

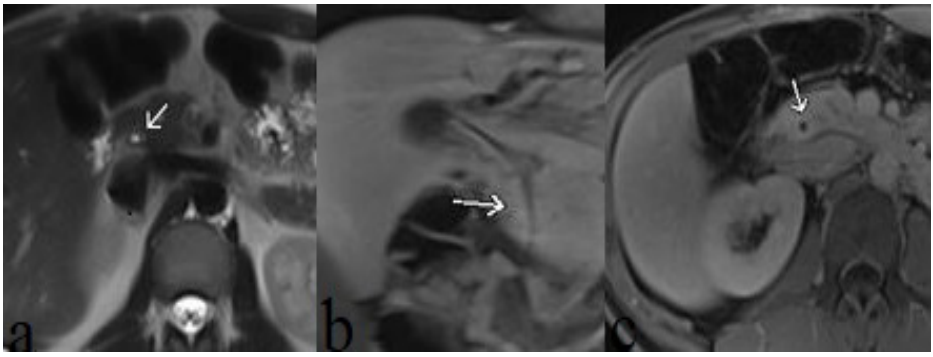


Figure 6: A male patient, age 35, was diagnosed with acute cholangitis. The axial T2-weighted (a) image shows an increased periductal signal intensity with wall thickening (white arrow). On contrast-enhanced coronal (b) and axial (c) MRI sequences, increased enhancement is seen (white arrows).

2.3. Acute Pancreatitis and Corresponding Complications

Acute pancreatitis is a common reason for ER visits, ranging from moderate interstitial to severe types with local and systemic effects (26, 27).

Acute pancreatitis can be necrotizing or interstitial edematous based on its pathologic characteristics. Interstitial edematous pancreatitis is more frequent and is characterized by non-necrotizing inflammation of the pancreas. Inflammatory edema causes diffuse pancreatic enlargement in the majority of individuals **(Figure 7)**. Occasionally, the enlargement is limited to a single area. There are no non-enhanced regions on contrast-enhanced CT scans of pancreatic parenchyma. Peripancreatic fat often exhibits inflammatory alterations such as haziness or minor stranding; peripancreatic fluid may also be present (28).

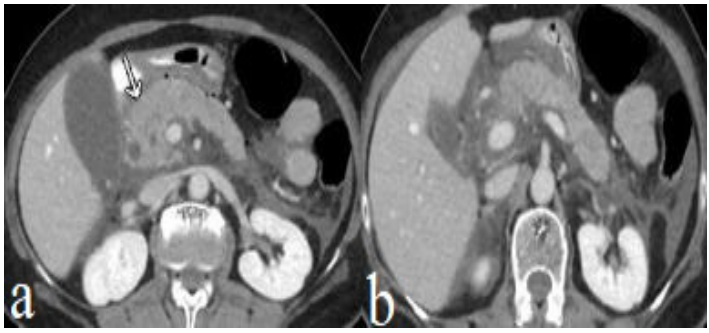


Figure 7: A female patient with acute pancreatitis, 61 years old. Axial CT images reveal pancreatic head enlargement (a) and peripancreatic fluid (b).

Necrotizing pancreatitis frequently manifests as pancreatic and peripancreatic tissue necrosis. The mixed subtype is characterized by non-enhancing pancreatic parenchyma and diverse peripancreatic collections (29).

Interstitial edematous pancreatitis patients might develop acute peripancreatic fluid accumulation within the first four weeks. It becomes more structured and forms a capsule after four weeks that enhances on CT, keeping only fluid and no necrosis. This is a pseudocyst, a well-defined collection enclosed by a capsule **(Figure 8)**.

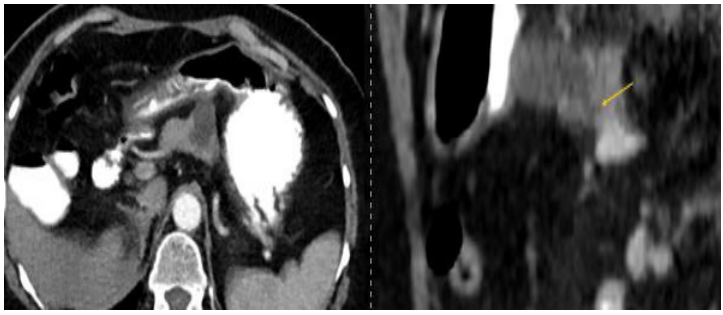


Figure 8: A female patient of 72 years old with a pseudocyst. The axial CT image shows a well-defined hypodense collection, and it is observed that the cystic lesion communicates with the pancreatic duct (arrow).

In the first four weeks of necrotizing pancreatitis, acute necrotic collection occurs, which consists of disorganized necrotic collections. On CT, it lacks a distinct wall that encloses the collection. Four weeks of necrotizing pancreatitis results in the development of WON (walled of necrosis). On CT, it may be

distinguished from a pseudocyst by the presence of interior solid components (30, 31).

Late-phase MRI is more common, has stronger soft tissue contrast resolution, and delivers a more accurate biliary and pancreatic channel examination. On T1-weighted, fat-suppressed images, the pancreas is hyperintense due to pancreatic acinar proteins (32). On T2-weighted images, the pancreatic parenchyma is hypointense **(Figure 9)**. Necrotizing pancreatitis has a hypointense T1WI, a hyperintense T2WI, and no contrast agent-induced enhancement (33) **(Figure 10)**.

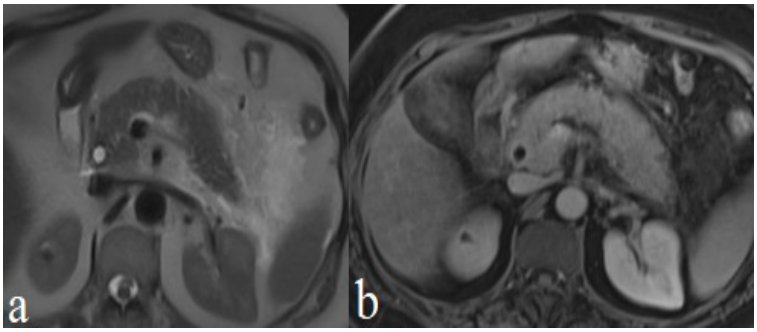


Figure 9: A male patient with acute pancreatitis, age 58. An axial T2-weighted image demonstrates pancreatic expansion and peripancreatic effusion (a). Contrast-enhanced MRI, homogenous enhancement is noticed.

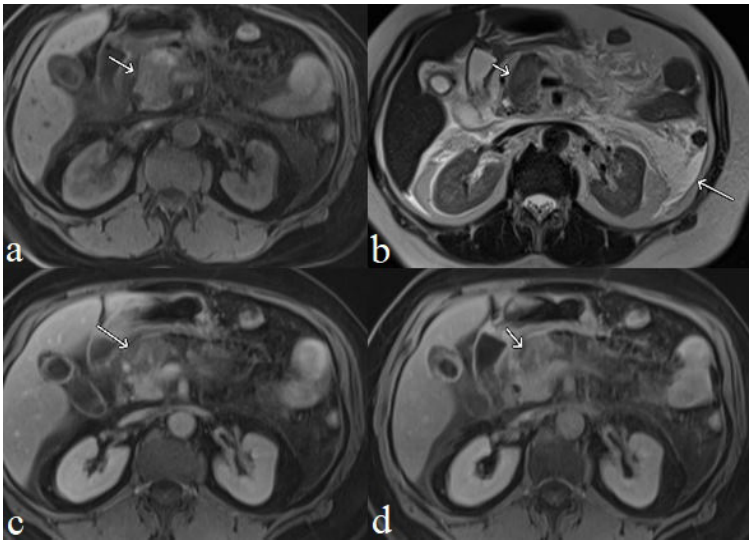


Figure 10: Male patient, 38 years old, with necrotizing pancreatitis. The necrotic zone demonstrates hypointensity on T1WI (a), hyperintensity on T2WI (b), and no contrast agent-induced enhancement (c, d).

Acute peripancreatic collections are uniformly hyperintense and hypointense on T2WIs and T1WIs, respectively. On MRI, pancreatic pseudocysts have a smooth wall, homogeneous fluid intensity on T1WIs and T2WIs, and no debris (34) **(Figure 11)**. MR with MRCP can help plan a pseudocystomy by analyzing the internal composition and showing the link with the stomach or duodenum.

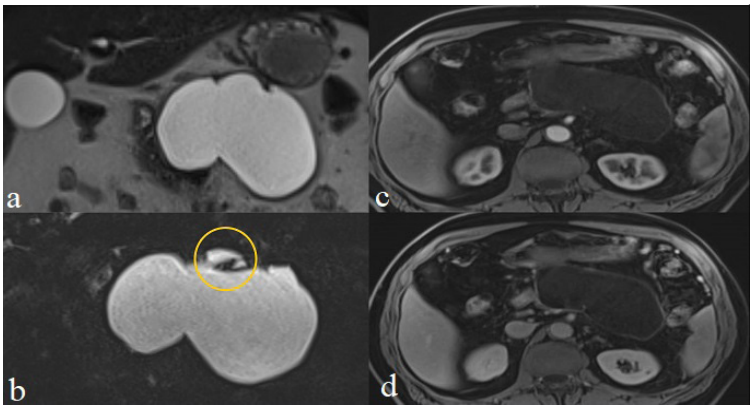


Figure 11: A female patient, age 54, with a pseudocyst. The pseudocysts of the pancreas have a thin, smooth wall, homogeneous liquid intensity on T2WI, and no solid particles in the fluid (a). On MRCP, the cystic lesion is shown to communicate with the pancreatic duct. No noticeable contrast enhancement is detected on MRI scans (c, d).

Acute necrotic collections lack capsules and exhibit mixed T1WI and T2WI signaling **(Figure 12).** Infections are a frequent complication of WON, which presents as an enclosed effusion containing non-liquid material, has banded, free-floating tissue fragments, and no increased signal on scans (35).

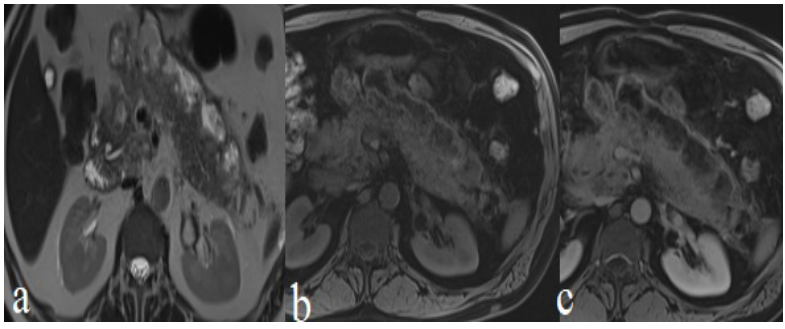


Figure 12: A man patient aged 45 with a WON. Mixed T2WI (a) and T1WI (b) signal intensity with an irregular collection. Heterogeneous contrast enhancement is seen on the MRI image (c).

3. Conclusion

Cross-sectional imaging of hepatopancreatobiliary diseases is on the rise in the emergency department due to its ability to accurately identify pathology and function as a problem-solving tool in times of diagnostic ambiguity. Even though CT is the most common imaging method, MRI is also important in hepatopancreatobiliary diseases.

Emergency evaluations of young and pregnant patients, as well as those who undergo repeated cross-sectional imaging, are aided by MRI's absence of radiation exposure. In patients with contraindications such as renal insufficiency or allergy, MRI typically eliminates the requirement for iodinated contrast exposure, and diagnostic tests can frequently be performed without any IV contrast at all. Modern MRI may be performed using rapid sequences that are tailored to the state of the patient in the clinic. This cuts down on scan time and improves diagnostic accuracy.

References

1. Kimura Y, Takada T, Kawarada Y, et al. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. J Hepatobiliary Pancreat Surg 2007;14:15-26.

2. Pinto A, Reginelli A, Cagini L, et al. Accuracy of ultrasonography in the diagnosis of acute calculous cholecystitis: review of the literature. Crit Ultrasound J 2013;5:S11.

3. Paulson EK. Acute cholecystitis: CT findings. Semin Ultrasound CT MR 2000;21:56-63.

4. Van Breda Vriesman AC, Engelbrecht MR, Smithuis RH, Puylaert JB. Diffuse gallbladder wall thickening: differential diagnosis. AJR Am J Roentgenol 2007;188:495-501.

5. Van Breda Vriesman AC, Engelbrecht MR, Smithuis RH, Puylaert JB. Diffuse gallbladder wall thickening: differential diagnosis. AJR Am J Roentgenol 2007;188:495-501.

6. Zissin R, Osadchy A, Gayer G, Kitay-Cohen Y. Extrarenal manifestations of severe acute pyelonephritis: CT findings in 21 cases. Emerg Radiol 2006;13:73-7.

7. Fagan SP, Awad SS, Rahwan K, et al. Prognostic factors for the development of gangrenous cholecystitis. Am J Surg 2003;186:481-5.

8. Bennett GL, Rusinek H, Lisi V, et al. CT findings in acute gangrenous cholecystitis. AJR Am J Roentgenol 2002;178:275-81

9. Morris BS, Balpande PR, Morani AC, et al. The CT appearances of gallbladder perforation. Br J Radiol 2007;80:898-901.

10. Sunnapwar A, Raut AA, Nagar AM, Katre R. Emphysematous cholecystitis: Imaging findings in nine patients. Indian J Radiol Imaging 2011;21:142-6.

11. Safioleas M, Stamatakos M, Safioleas P, et al. Mirizzi Syndrome: an unexpected problem of cholelithiasis. Our experience with 27 cases. Int Semin Surg Oncol 2008;5:12

12. Choi BW, Kim MJ, Chung JJ, et al. Radiologic findings of Mirizzi syndrome with emphasis on MRI. Yonsei Med J 2000;41:144-6.

13. Azizi L, Raynal M, Cazejust J, Ruiz A, Menu Y, Arrivé L. Mr imaging of sclerosing cholangitis. Clin Res Hepatol Gastroenterol 2012;36:130–8

14. O'Connor OJ, O'Neill S, Maher MM. Imaging of biliary tract disease. AJR Am J Roentgenol 2011;197:W551–8.

15. Benarroch-Gampel J, Boyd CA, Sheffield KM, Townsend CM, Riall TS. Overuse of CT in patients with complicated gallstone disease. J Am Coll Surg 2011; 213: 524–30.

16. Walas MK, Skoczylas K, Gierbliński I. Errors and mistakes in the ultrasound diagnostics of the liver, gallbladder and bile ducts. J Ultrason 2012; 12: 446–62.

17. Válek V, Kala Z, Kysela P. Biliary tree and cholecyst: post surgery imaging. Eur J Radiol 2005;53: 433–40.

18. Yeh BM, Liu PS, Soto JA, Corvera CA, Hussain HK. Mr imaging and CT of the biliary tract. Radiographics 2009; 29:1669– 88.

19. Salvolini L, Urbinati C, Valeri G, Ferrara C, Giovagnoni A. Contrast-Enhanced Mr cholangiography (MRCP) with GD-EOBDTPA in evaluating biliary complications after surgery. Radiol Med 2012;117:354–68.

20. Tamrazi A, Vasanawala SS. Functional hepatobiliary MR imaging in children. Pediatr Radiol 2011;41:1250–8.

21. Mosler P. Diagnosis and management of acute cholangitis. Curr Gastroenterol Rep 2011;13:166–72.

22. Denecke T, Degutyte E, Stelter L, et al. Minimum intensity projections of the biliary system using 16-channel multidetector computed tomography in patients with biliary obstruction: comparison with MRCP. Eur Radiol 2006;16:1719–26.

23. Kim HC, Park SJ, Park SI, et al. Multislice CT cholangiography using thin-slab minimum intensity projection and multiplanar reformation in the

evaluation of patients with suspected biliary obstruction: preliminary experience. Clin Imaging 2005;29:46–54.

24. Ahmetoglu A, Kosucu P, Kul S, et al. MDCT cholangiography with volume rendering for the assessment of patients with biliary obstruction. AJR Am J Roentgenol 2004;183:1327–32.

25. Bader TR, Braga L, Beavers KL, Semelka RC. MR imaging findings of infectious cholangitis. Magnetic Resonance Imaging 2001;19(6):781–8.

26. Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16(3):175– 184.

27. Petrov MS. Editorial: abdominal fat: a key player in metabolic acute pancreatitis. Am J Gastroenterol 2013;108(1):140–142.

28. Banks PA, Bollen TL, Dervenis C, et al. Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62(1):102–111.

29. Foster BR, Jensen KK, Bakis G, Shaaban AM, Coakley FV Revised Atlanta classification for acute pancreatitis: a pictorial essay. Radiogr Rev Publ Radiol Soc North Am, Inc 2016;36(3):675–687.

30. Türkvatan A, Erden A, Türkoğlu MA, Seçil M, Yüce G. Imaging of acute pancreatitis and its complications. Part 2: complications of acute pancreatitis. Diagn Interv Imaging 2015;96(2):161– 169.

31. Zhao K, Adam SZ, Keswani RN, Horowitz JM, Miller FH. Acute pancreatitis: revised atlanta classifcation and the role of cross-sectional imaging. AJR A J Roentgenol 2015;205(1):W32–W41.

32. Ditkofsky NG, Singh A, Avery L, Novelline RA. The role of emergency MRI in the setting of acute abdominal pain. Emerg Radiol 2014;21(6):615–624.

33. Sun H, Zuo HD, Lin Q, Yang DD, Zhou T, Tang MY, Wáng Y, Zhang XM. MR imaging for acute pancreatitis: the current status of clinical applications. Ann Transl Med 2019;7(12):269.

34. Sandrasegaran K, Tann M, Jennings SG, Maglinte DD, Peter SD, Sherman S, Howard TJ. Disconnection of the pancreatic duct: an important but overlooked complication of severe acute pancreatitis. Radiogr Rev Publ Radiol Soc North Am Inc 2007;27(5):1389–1400.

35. Dhaka N, Samanta J, Kochhar S, Kalra N, Appasani S, Manrai M, Kochhar R. Pancreatic fuid collections: what is the ideal imaging technique? World J Gastroenterol 2015;21(48):13403–13410.

CHAPTER XXVI

68GA PSMA PET CT IMAGING IN PROSTATE CANCER

Refik Bilgin

(M.D.), Institution: Department of Nuclear Medicine, Yeni Yüzyıl University Private Gaziosmanpaşa Hospital, Istanbul, TURKEY
E-mail: dr.refikbilgin@gmail.com
ORCID: 0000 – 0003 – 2322 – 2776

1. Introduction

Prostate cancer is the cancer type with the highest 5-year prevalence in men all over the world, and its incidence is the 2nd after lung cancer, and its mortality is 5th among all other cancers (1). The correct management of prostate cancer requires accurate determination of localization, metastasis and newly developed foci. Although multiparametric MRI is very successful in imaging the primary tumor and in T staging, its specificity in evaluating lymph node metastases is low, and imaging is limited to the pelvic area (2).

In recent years, new PET agents with specific molecular targets have been widely used in prostate cancer, and ^{68}Ga-PSMA is the most important of these agents. ^{68}Ga-PSMA is a radiopharmaceutical that binds to prostate-specific membrane antigen (PSMA), a membrane antigen specific to prostate cancer cells. ^{68}Ga-PSMA PET/CT has been proven to be superior to other PET agents in prostate cancer and to have a significant impact on the management of prostate cancer (3).

^{68}Ga-PSMA PET/CT is used in prostate cancer staging, treatment plan, biochemical recurrence, even at low PSA levels. It has become an increasingly preferred imaging method in determining its localization. Optimal acquisition time of ^{68}Ga-PSMA PET/CT and possible clinical contributions of additional images taken at different times has been a subject of interest (4).

Although it was stated in the ^{68}Ga-PSMA PET/CT application guide published by EANM and SNMMI in 2017 that the optimum time for PET/CT

extraction after ^{68}Ga-PSMA injection is approximately 60 minutes, ^{68}Ga-PSMA has fast blood clearance and low background activity. This suggests that images to be taken at an earlier time following the injection may also be clinically sufficient (5).

Today, Gallium-68 prostate specific membrane antigen (^{68}Ga PSMA) positron emission tomography/computerized tomography (PET/CT) imaging in prostate cancer (PC) is becoming increasingly common all over the world, and recently theranostic (therapeutic – diagnostic) has become an important component of applications. In 2017, the Ga-68 PSMA PET/CT imaging joint guide of the European Association of Nuclear Medicine and American Society of Nuclear Medicine and Molecular Imaging (EANM/SNMMI) was published for the first time. Following this published guideline, some of the ongoing prospective studies on indications were terminated and published (6).

Indications for PSMA molecular imaging in the multidisciplinary PC guideline, including EANM, updated in 2020 by the European Association of Urology (EAU) and in the American Society of Clinical Oncology (ASCO) optimal imaging strategies guideline in advanced PC in 2020 (7, 8).

2. Importance of PSMA Screening

The rate of prostate cancer diagnosis and localized disease detection has increased, while the rate of metastatic disease has decreased due to prostate specific antigen (PSA) screening test, (7). Diagnosis is most commonly made by transrectal needle biopsy.

Histopathologically, normal epithelial-stroma relationship is impaired in PC. The histological Gleason scoring/grading (GS) of the tumor is the most important prognostic factor and is graded from the best differentiation to the worst (GS between ≤6 and 10) (9, 10). The Gleason system has been revised over the years and approved by the World Health Organization. 5 groups (Grade Group) have been defined in the Gleason grading by the current international Society of Urological Pathology (ISUP) (11, 12).

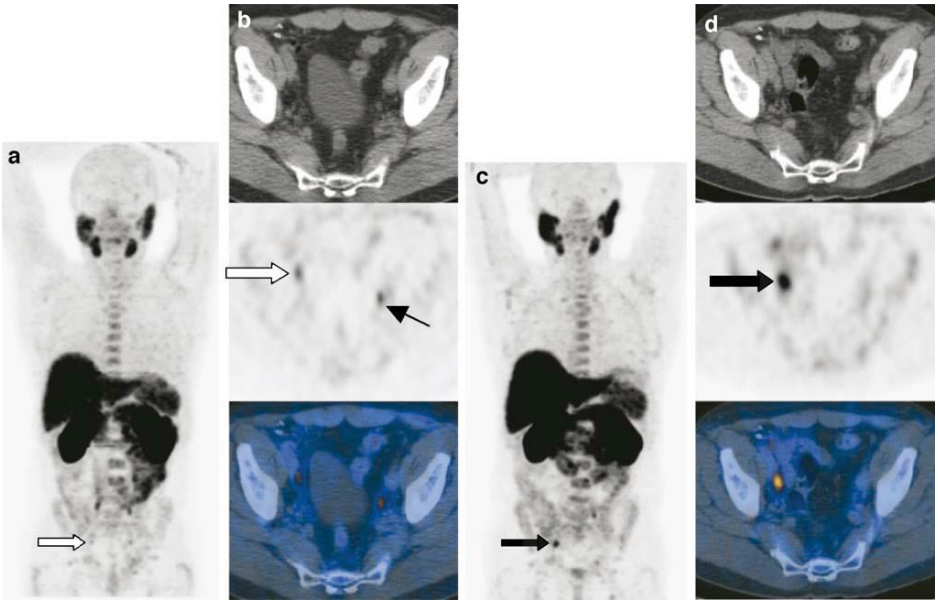


Figure 1: Pelvic lymph nodes involved in 18 – F fluorocholine PET and PET-CT

The prostate-specific membrane antigen (PSMA) glutamate carboxypeptidase II is an internal transmembrane glycoprotein that was first identified in 1987 (13). While PSMA is expressed at low levels in normal prostate tissue and benign pathologies, it is 100 to 1000 times more intense in prostate cancer, and the increase in tumor aggressiveness increases with intratumoral angiogenesis (14). While PSMA is found physiologically in extra-prostatic epithelial cells, kidney proximal tubule, nervous system cells, jejunal brush cells in small intestine, in inflammation-infection and extra-prostatic; it can also be found in solid tumors with neovascularization such as renal cell carcinoma, hepatocellular carcinoma, breast, lung, and colorectal cancers (15). Although PSMA immunohistochemistry studies are not routinely performed in pathology reports, studies are based on risk-based treatment plan and individualized treatment approach.

The importance of this is emphasized, and it is argued that its histopathological indication in pathology reports is effective in differentiating Grade 3 and 4 in terms of treatment approach (16, 17).

PSMA has been an ideal molecular target for both the diagnosis and treatment (theranostic) of prostate cancer in nuclear medicine applications. ^{68}Ga

is a $^{68}Ge/Ga^{68}$ generator product with 89% positron emission, half – life of 67.63 minutes. ^{68}Ga – labeled PSMA inhibitor radiosynthesis was first performed by Banerjee et al., in Johns Hopkins University (18). Later, the Heidelberg group developed the ^{68}Ga PSMA-11 and Eder et al. (19) showed that it was specifically internalized in human prostate cancer cells and that the radiopharmaceutical was upheld at a high level. In the process, other compounds with similar biodistribution and imaging properties such as ^{68}Ga PSMA-617, ^{68}Ga PSMA I&T were developed (20, 21).

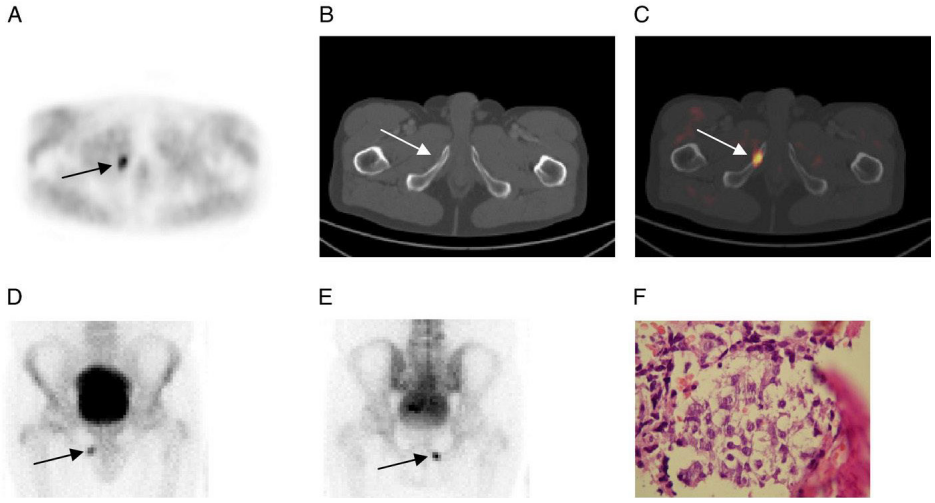


Figure 2: PET (A), CT (B), PET-CT (C), and bone scintigraphy images (D,E) before radical prostatectomy of a patient with prostate cancer (GS 7, 3+4, PSA: 6.3 ng/ml). All images show a pathological focus in the right ischium. Presence of metastases was also shown histopathologically (F)

In PET systems, the three-dimensional distribution and quantitative examination of ^{68}Ga PSMA in humans with CT or magnetic resonance imaging (MRI) components is considered non-invasive. ^{68}Ga PSMA PET/CT imaging in many centers (19).

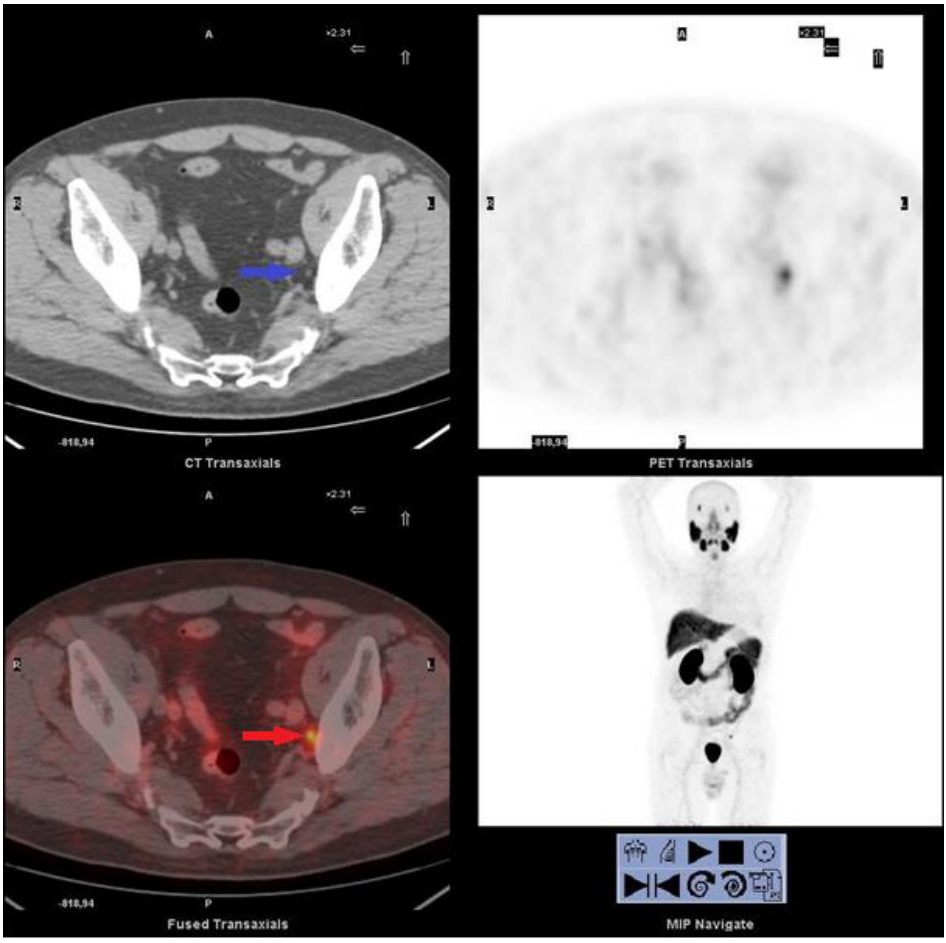


Figure 3: Prostate Cancer Case, (GS:7) PET-CT images of the patient. The patient undergoes Ga-68 PSMA PET-CT due to elevated PSA (PSA: 1.3 mg/dl, PSAv: 1 ng/ml/year, PSAdt: 6.1 months) after RT and HT. In PET-CT, pathological involvement is detected in 3 millimetric lymph nodes in the left obturator region. The patient is given targeted RT.

Data and knowledge in PET/MR systems and ^{68}Ga PSMA imaging are increasing in the world. Ga-68 PSMA is among the new agents under development, and it has not yet been approved by the US Food and Drug Administration (FDA) (19 – 21).

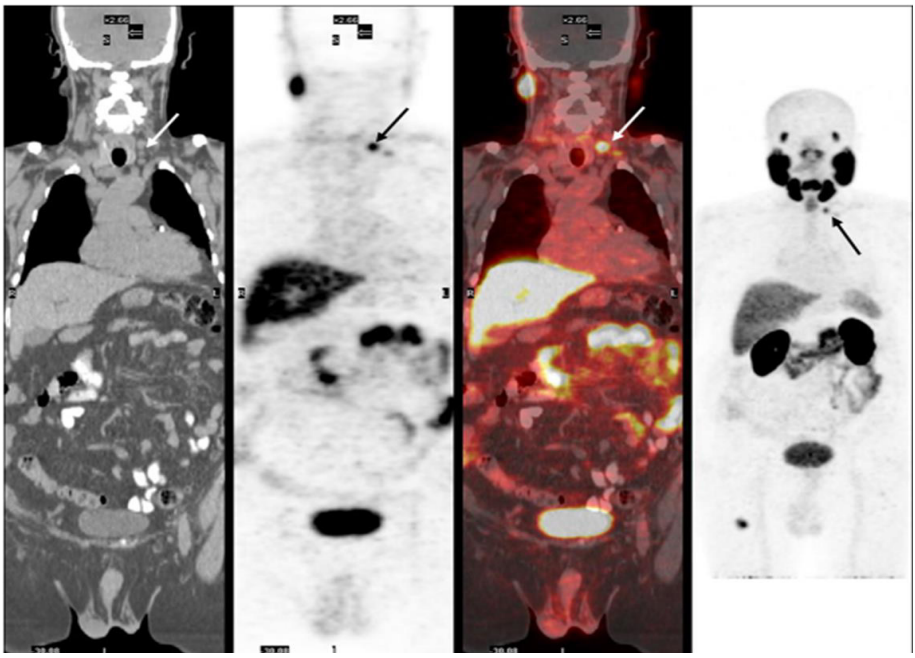


Figure 4: Pathological involvement of the left supraclavicular region lymph node on 68GaPSMA PET CT images in the patient with PSA recurrence. The patient who received RT and hormonal therapy had an increase in PSA level 2 years after the treatment (trigger PSA: 5.8 ng/ml, PSAdt: 2 months, PSAv: 12 ng/ml/year).

The most important advantage of ^{68}Ga PSMA is that it has been shown to be superior to F – 18 choline and other currently FDA-approved agents (C-11 choline, F – 18 Flucyclovin) in PET imaging at low PSA values in detecting PC recurrence (mean sensitivity 76%- 86, specificity 86-100% (22).

3. Indications

The recommendation level of ^{68}Ga PSMA PET/CT imaging for PC in the current guidelines, there is no FDA approval in the current version of the National Comprehensive Cancer Network (NCCN), but there is a positive opinion that it can be performed in clinical trials and controlled studies (22), in the EAU guideline, it is recommended in BR after radical prostatectomy, after radiotherapy (RT), multiparametric MRI (mpMR) is recommended in terms of biopsy guidance in the first place, but PSMA PET is recommended in patients suitable for curative salvage treatment. (7).”

In the ASCO guideline, there are PSMA PET imaging recommendations under the definition of new generation imaging in addition to conventional imaging under the conditions specified in advanced PC. It is thought that some application areas will be determined more clearly and will be expanded according to the results (8).

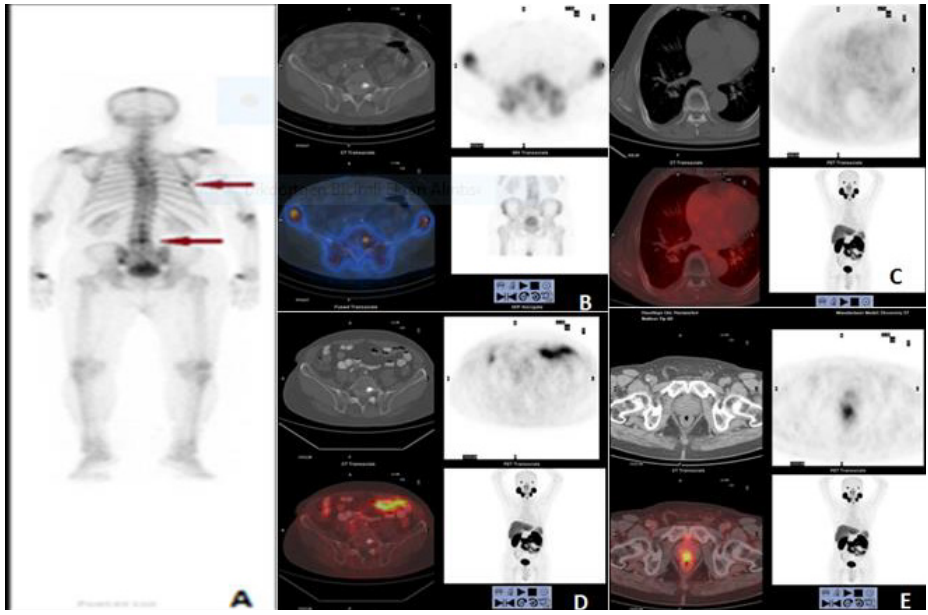


Figure 3: (GS: 7, PSA: 8.3) bone scintigraphy (A), SPECT CT (B), and PET-CT (C, D and E) images. Bone scintigraphy shows involvement in the sclerotic lesion in the left 7th rib and L5 vertebra. On PET images, only prostate involvement was detected, no involvement was observed in the areas described in bone scintigraphy, and possible bone metastases were detected. has been ruled out.

4. Clinical Applications

4.1. Recurrent-persistent Disease

Biochemical recurrence; detectable or increasing PSA level after primary radical treatments. Detection of the recurrent disease focus in the early period may allow early and effective salvage treatment. At low PSA levels (<0.4 ng/mL), multiparametric MRI, bone scintigraphy, CT, and choline-based metabolic PET/CT imaging are insufficient to detect metastatic disease. Therefore, when BR is followed after RP, although pelvic rescue RT is given empirically to the prostate bed, approximately 50% of the patients have metastatic disease (7, 8).

Therefore, when biochemical recurrence (BR) is detected after primary radical treatments, it is important to distinguish between isolated pelvic disease and/or oligometastatic disease (≤3 foci) and diffuse metastatic disease (>3 foci) in terms of local or systemic treatment decision (8).

Studies have shown that ^{68}Ga PSMA PET/CT is a more appropriate technique for detecting the focus or foci of recurrence, especially at low PSA levels (0.2 – 2.0 ng/mL) after primary treatment, compared to conventional imaging techniques (23). The sensitivity of PET/CT increases in relation to GS and PSA kinetics (PSA doubling time) (24).

In prospective and retrospective studies, it has been reported that ^{68}Ga PSMA PET/CT, with its high positive predictive value and recurrence detection rate at low PSA levels, causes up to 50% change in patient management in general (25, 26). However, according to ^{68}Ga PSMA PET/CT results, the effect or contribution of disease management-treatment plan change (RT, other local treatments, systemic treatments) on long-term disease course is not yet clear (25).

In prospective and retrospective studies, it has been reported that Ga-68 PSMA PET/CT, with its high positive predictive value and recurrence detection rate at low PSA levels, causes up to 50% change in patient management in general (25, 26). However, according to Ga-68 PSMA PET/CT results, the effect or contribution of disease management-treatment plan change (RT, other local treatments, systemic treatments) on long-term disease course is not yet clear (26).

The success rates of RT and ^{68}Ga PSMA PET/CT-guided salvage RT are compared in terms of biochemical progression-free survival. Although high-evidence data are limited, ^{68}Ga PSMA PET/CT has a potential role in demonstrating the burden of metastatic disease in hormone-sensitive PC after radical therapy or in the first PSA recurrence, identification of oligometastic disease, and treatment plan Farolfi et al. (27). There are studies showing that multimodal management of oligometastatic disease in hormone-sensitive PC, salvage treatments, direct-local treatment approaches aimed at metastasis, accurate identification and treatment of metastatic foci, can be curative and androgen deprivation therapy (ADT) can be postponed (28, 29).

4.2. Newly Diagnosed High-Risk PC Initial Staging

Lymph node metastasis or especially bone metastasis is likely to be seen in high risk group PC. Many studies have shown the superiority of ^{68}Ga

PSMA PET/CT over conventional in identifying metastatic disease in the initial staging of high-risk PC (30 – 33). In the initial staging of high and very high risk (locally advanced) PC, which is included in the indications for use in the EANM – SNMMI ^{68}Ga PSMA PET/CT application guide, in the latest ASCO 2020 guideline, scientific data are limited (32).

If the imaging is negative or there are suspicious findings, ^{68}Ga PSMA PET/CT is recommended under the name of new generation imaging, as it will provide additional information and potentially contribute to the prediction of possible changes in disease management (6, 8). In the EAU PC guideline, there is no ^{68}Ga PSMA PET/CT recommendation for initial staging in high-risk PC (7). Local, regional or systemic multimodal treatment planning is conducted according to the following: localization of disease before primary treatment (surgery or RT) in high-risk PC, or oligometastatic or widespread metastatic disease (6 – 8).

Although it is known that ^{68}Ga PSMA PET/CT may be false-negative in lymph node evaluation at low PSA levels and <5 mm lymph nodes, and it cannot replace pelvic lymph node dissection, which is the gold standard histopathologically on the basis of metastatic lymph nodes. Additionally, it can detect lymph nodes <1 cm that are not within the scope of standard primary treatments (classical lymph node dissection, RT planning), especially paraaortic, main iliac, perirectal, obturator and presacral, and can change the treatment plan (34, 35).

Studies have shown that ^{68}Ga PSMA PET/CT detects bone metastases more accurately than the standard bone scintigraphy (30). The contribution of bone scintigraphy and F – 18 Na – Fluoride (F – 18 NaF) PET/CT in dense-sclerotic bone metastases or PSMA-negative metastases is still controversial (7). PC bone metastases are mostly blastic-sclerotic, but they can also be lytic-destructive or mixed lytic-blastic. While bone metastases do not yet show reactive-blastic activity in bone tissue, in the early bone marrow period, active tumor cells can be detected molecularly at low PSA levels with ^{68}Ga PSMA (36, 37).

As a result, it has been pointed out that biochemical recurrence (BR) is seen in approximately 50% of patients despite effective treatment, especially in the high-risk PC group, and the 15-year mortality rate reaches approximately 36%, which is due to the inability to correctly staging at the beginning with conventional examinations (35, 39).

As the first-line examination before curative treatments, it is thought that with the correct staging opportunity of ^{68}Ga PSMA PET/CT, more effective

treatment will be planned and the incidence of biochemical persistent - possible residual disease will decrease and the course of the disease will improve, and current guidelines should be reviewed in the light of this information (36).

4.3. PSMA Based Radioligand Pretreatment and Treatment

During Theranostic Practice PSMA-based radionuclide therapies, especially Lutetium – 177 PSMA (Lu-177 PSMA, 2 – 6 cycles) are becoming increasingly common. Currently, PSMA-based radionuclide treatments are applied in metastatic CRPC that does not respond to standard treatments. For this treatment to be possible, PC metastases must show PSMA expression (theranostic principle). PSMA is an excellent theranostic agent and Ga-68 PSMA PET imaging is used in patient selection before treatment. Although there is no clear data for "adequate uptake" in terms of treatment, in the current Lu – 177 PSMA treatment guideline of the EANM/SNMMI, it is recommended that the metastatic lesion be higher than normal organ involvement, and in particular, the SUV_{max} value should be at least 1.5 times the SUV_{med} of the liver (40).

Metastatic lesions with low PSMA expression are not suitable for radioligand therapy. Whole body scintigraphic imaging is routinely performed after Lu – 177 PSMA treatments. SPECT and/or additional information is obtained with SPECT/CT. In the current EANM/SNMMI Lu – 177 PSMA treatment guideline, in addition to PSA and post-treatment imaging in evaluating radionuclide treatment response, ^{68}Ga PSMA PET is preferred for the possibility of growth of PSMA negative lesions. It is recommended to perform cross-sectional imaging after every 2 cycles (40).

Considering the ^{68}Ga PSMA and F – 18 FDG uptake patterns of metastatic lesions before treatment (for example, heterogeneous involvements), serial PSA levels, and the addition of cross-sectional imaging such as SPECT/CT to whole body imaging after Lu – 177 PSMA treatment may provide sufficient information for the evaluation of intermediate treatment follow-up (37, 38).

5. Uptake of Radiopharmaceutical

The average uptake time of ^{68}Ga PSMA is 60 minutes (50 – 100 minutes), which is the time to wait after injection for imaging. In some studies, an increase in lesion detection was reported 3 - 4 hours after ^{68}Ga PSMA injection. If there are suspicious findings that overlap with urinary activity or have low PSMA uptake, decreased background activity and increased tumor/background activity ratio in late imaging may help to solve the problem (41).

6. Standard Uptake Value (SUV)

Along with visual assessment, SUV measurements are widely used in routine and clinical studies. The SUV measurement is a numerical value that can be normalized to body mass (most common), lean body mass, or body surface area. It is the SUV_{max} value that shows the highest uptake in a single voxel in the PET image. It is important to have PET/CT device quality controls performed for minimal error and reliability in SUV value. In addition, it should be ensured that patient data (such as dose, injection time, age, kg) are entered correctly (41).

The use of SUV values and volumetric parameters such in ^{68}Ga PSMA PET/CT in the detection of primary prostate tumor, its relation to GS and treatment response, its place in treatment planning, clinical its contribution to prognosis and disease management is among the research topics (42).

7. Conclusion

In PC, computerized tomography (CT) imaging is performed according to the Response Evaluation Criteria in Solid Tumors (RECIST) criteria to determine the treatment response in routine practice (43). The use of RECIST in PC is limited as the target lesion is bone lesions. It can only be used in the presence of a soft tissue lesion >1 cm and lymph node with a short axis >1.5 cm. Since 75% of advanced stage patients have bone metastases and sclerotic lesions are a problem in CT in evaluating response with RECIST (43).

Bone scintigraphy is widely used in the detection of bone metastases due to its low cost and easy accessibility. Despite the high sensitivity in the detection of osteoblastic bone metastases, the specificity is low and increased uptake can be observed in many non-tumor pathologies. F – 18 NaF positron emission tomography (PET/CT) shows increased sensitivity in detecting skeletal metastases, but is not informative about soft tissue metastases. In addition, it is difficult to use in response assessment because of the flare phenomenon after treatment. Since methods such as CT and bone scintigraphy are based on tumor-matrix interaction, they do not show tumoral cell viability (44).

Another problem is that it is slow as micrometastatic lymph node/hyperplastic abundant. PSA level is the most widely used test as a clinical parameter to evaluate treatment response. However; it has been shown that serum PSA levels can incorrectly predict treatment response and course. Serum PSA levels are within normal reference values in 20% - 30% of PC patients. In addition, PSA can be seen at high values in benign prostatic hyperplasia and inflammation. On the other hand, PSA is a blood test, it does not provide

information about the extent and localization of the disease, and cannot show the success of treatment in a particular lesion (45). In the light of these findings, it is clear that other methods are required for disease monitoring and evaluation of treatment response in patients with metastatic PC. Functional imaging modalities such as PET offer an innovative approach to treatment response assessment. PET/CT, which can perform both metabolic changes and anatomical imaging in a single session, can evaluate the treatment response in many tumors earlier and more precisely than conventional imaging methods (44, 45).

In general, PET/CT imaging using F – 18 fluorodeoxyglucose (FDG), F – 18 fluorothymidine (FLT), and C – 11 choline is used to evaluate treatment response in many cancers, but there are many published reports with these agents for evaluation of treatment response in patients with metastatic PC. there is little data. Androgen ablation is the mainstay of treatment in patients whose PCs are mostly androgen-dependent and who would not receive curative radical therapy. Experimental studies simulating androgen ablation showed that F – 18 FDG uptake in tumor tissue decreased within 3 weeks after androgen cessation (46). Again, the effect of androgen ablation in PC was investigated in 10 patients with FDG uptake in their primary tumor and bone metastases. After the initiation of hormone therapy, it was observed that FDG uptake decreased and PSA level decreased in both prostate and metastatic lesions in all patients (47). Although these studies show that F – 18 FDG PET can show early changes in glucose metabolism with androgen deprivation therapy or chemotherapy in PC, it can be used in metabolic monitoring of changes that develop after treatment. Due to the low glucose use in PC, F – 18 FDG PET has relatively low sensitivity and specificity in detecting primary tumors and distant metastases (75% sensitivity for staging, 26% sensitivity for restaging). Therefore, it should be kept in mind that there may be incompatibility with serum PSA or the number of circulating tumor cells and, more importantly, with the current RECIST response criteria (46, 47).

F – 18 FLT is a Thymidin analog and a marker of tumor proliferation. Its increased uptake has been shown to be proportional to DNA synthesis rate and proliferative indices. Although being less affected by inflammatory changes after treatment is an advantage in evaluating response, its use in PC has been generally in the form of preclinical studies so far. Since FLT PET has extensive activity in normal bone marrow and extensive bone metastasis in many advanced prostate cancers, its potential to assess treatment response seems difficult (48).

Despite the success of C – 11 or F – 18 labeled PET – CT in the literature, the need for cyclotron for radiopharmaceutical synthesis limited the use of these agents. For this reason, ^{68}Ga-labeled compounds synthesized in accordance with GMP rules in hospitals with the help of generators and synthesis modules with a lifespan of approximately 1 year have gained popularity. Among these compounds, ^{68}Ga labeled PSMA PET, which is used for prostate cancer imaging, is increasingly used instead of choline PET-CT (44 – 48).

PSMA, labeled with ^{68}Ga, is a type 2 cell membrane glycoprotein and its synthesis is increased in prostate cancer. In the past, ligands developed against this glycoprotein have been used to bind different radionuclides to screen for prostate cancer (49, 50).

However, the radiopharmaceuticals used in these studies were only suitable for shooting with gamma cameras and their limited availability limited their widespread use. ^{68}Ga PSMA, on the other hand, has found use in the last 5 years and is about to become a standard in prostate cancer imaging. In a limited number of studies comparing choline PET, ^{68}Ga PSMA was found to be superior to 18 F – choline PET – CT in metastatic lesion detection and lesion contrast. The radionuclide being ^{68}Ga allowed imaging of the patient with PET – CT, providing superior sensitivity, resolution and quantification (49, 50).

Abbreviations:

ADT	:	androgen deprivation therapy
ASCO	:	American Society of Clinical Oncology
BR	:	biochemical recurrence
CRPC	:	castration-resistant prostate cancer
CT	:	computerized tomography
EANM	:	European Association of Nuclear Medicine
EAU	:	European Association of Urology
FDG	:	fluorodeoxyglucose
FLT	:	fluorothymidine
^{68}Ga PSMA	:	Gallium-68 prostate specific membrane antigen
GS	:	Gleason scoring
ISUP	:	International Society of Urological Pathology
MRI	:	magnetic resonance imaging
mpMR	:	multiparametric MRI
NCCN	:	National Comprehensive Cancer Network

PC	:	prostate cancer
PET	:	positron emission tomography
PSA	:	prostate specific antigen
PSMA	:	prostate-specific membrane antigen
RECIST	:	Response Evaluation Criteria in Solid Tumors
RT	:	radiotherapy
SNMMI	:	Society of Nuclear Medicine and Molecular Imaging
SUV	:	Standard Uptake Value
Theranostic	:	therapeutic – diagnostic

References

1. Mottet N, van den Bergh RCN, Briers E, Bourke L. EAU-ESUR-ESTRO-SIOG guidelines on prostate cancer. 2018. https://uroweb.org/wp-content/uploads/EAUESUR-ESTRO-SIOG-Guidelines-on-Prostate-Cancer-large-text-V2.pdf. Accessed June 5, 2019.

2. Budiharto T, Joniau S, Lerut E, et al. Prospective evaluation of 11C-Choline positron emission tomography/computed tomography and diffusion-weighted magnetic resonance imaging for the nodal staging of prostate cancer with a high risk of lymph node metastases. European Urology. 2011;60(1):125-130.

3. Briganti A, Abdollah F, Nini A, et al. Performance characteristics of computed tomography in detecting lymph node metastases in contemporary patients with prostate cancer treated with extended pelvic lymph node dissection. European Urology. 2012;61(6):1132-1138.

4. Fütterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. European Urology. 2015;68(6):1045-1053.

5. Castelluci P, Nanni C, Ambrosini V. 68Ga-Based Imaging Techniques. In: Lin EC, Alavi A, eds. PET and PET/CT: A Clinical Guide. 3. basım. New York: Thieme; 2019:311-313.

6. Fendler WP, Eiber M, Beheshti M, et al. 68Ga-PSMA PET/CT: Joint EANM and SNMMI procedure guideline for prostate cancer imaging: version 1.0. Eur J Nucl Med Mol Imaging 2017;44:1014-1024.

7. Mottet N, Bellmunt J, Briers E. et al. Members of the EAUESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. EAUESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Edn. presented at the EAU Annual Congress Amsterdam 2020. 978-94-92671-07-3. Arnhem: EAU Guidelines Office; 2020.

8. Trabulsi EJ, Rumble RB, Jadvar H, et al. Optimum Imaging Strategies for Advanced Prostate Cancer: ASCO Guideline. J Clin Oncol 2020;38:1963-1996.

9. Gleason DF. Classification of prostate carcinoma. Cancer Chemother Rep 1966;50:125-128.

10. Gleason DF. Veterans Adminstration Cooperative Urological Research Group. 1977. Histologica grading and clinical staging of prostatic carcinoma. In: Urologic pathology: The prostate. editors Tannenbaum M: Lea & Febinger; Philadelphia. pp. 171-197.

11. Epstein JI, Egevad L, Amin MB, Delahunt B, Srigley JR, Humphrey PA. The 2014 International Society of Urological Pathology (ISUP) Consensus Conference on Gleason Grading of Prostatic Carcinoma: Definition of grading paterns and proposal for a new grading system. Am J Surg Pathol 2016;40:244-252.

12. Moch H, Humphrey PA, Ulbright TM, Reuter V. WHO classification of tumours of the urinary system and male genital organs. Lyon, France: International Agency for Research on Cancer; 2016.

13. Horoszewicz JS, Kawinski E, Murphy GP. Monoclonal antibodies to a new antigenic marker in epithelial prostatic cells and serum of prostatic cancer patients. Anticancer Res 1987;7:927-935.

14. Heston WD. Characterization and glutamyl preferring carboxypeptidase function of prostate specific membrane antigen: a novel folate hydrolase. Urology 1997;49(Suppl 3A):104-112.

15. Silver DA, Pellicer I, Fair WR, Heston WD, Cordon-Cardo C. Prostate-specific membrane antigen expression in normal and malignant human tissues. Clin Cancer Res 1997;3:81-85.

16. Hupe MC, Philippi C, Roth D. Expression of prostatespecific membrane antigen (psma) on biopsies ıs an ındependent risk stratifier of prostate cancer patients at time of ınitial diagnosis. Front Oncol 2018;8:623.

17. Bravaccini S. Puccetti M, Bocchini M, PSMA expression: a potential ally for the pathologist in prostate cancer diagnosis. Sci Rep 2018;8:4254.

18. Banerjee SR, Pullambhatla M, Byun Y, 68Ga-labeled inhibitors of prostate-specific membrane antigen (PSMA) for imaging prostate cancer. J Med Chem 2010;53:5333-5341.

19. Eder M, Schafer M, Bauder-Wust U, 68Ga -complex lipophilicity and the targeting property of a urea-based PSMA inhibitor for PET imaging. Bioconjug Chem 2012;23:688-697.

20. Afshar-Oromieh A, Hetzheim H, Kratochwil C, The Theranostic PSMA ligand PSMA-617 in the diagnosis of prostate cancer by PET/CT: biodistribution in humans, radiation dosimetry, and first evaluation of tumor lesions. J Nucl Med 2015;56:1697-1705.

21. Herrmann K, Bluemel C, Weineisen M, et al. Biodistribution and radiation dosimetry for a probe targeting prostatespecific membrane antigen for imaging and therapy. J Nucl Med 2015;56:855-861.

22. National Comprehensive Cancer Network. NCCN Clinical Guidelines in Oncology. Prostate Cancer. Version 2.2020. 2020; https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf

23. Eiber M, Maurer T, Souvatzoglou M, Evaluation of hybrid (68) Ga-PSMA ligand PET/CT in 248 patients with biochemical recurrence after radical prostatectomy. J Nucl Med. 2015;56:668-674.

24. Verburg FA, Pfister D, Heidenreich A, et al. Extent of disease in recurrent prostate cancer determined by [(68)Ga]PSMAHBED-CC PET/CT in relationto PSA levels, PSA doubling time and Gleason score. Eur J Nucl Med Mol Imaging 2016;43:397-403.

25. Calais J, Fendler WP, Eiber M, Impact of 68Ga-PSMA-11PET/CT on the management of prostate cancer patients with biochemical recurrence. J Nucl Med 2018;59:434-441.

26. Sonni I, Eiber M, Fendler WP, Impact of 68Ga-PSMA-11 PET/CT on staging and management of prostate cancer patients in various clinical settings: a prospective single center study. J Nucl Med 2020;61:1153-1160.

27. Farolfi A, Gafita A, Calais J, 68Ga-PSMA-11 Positron Emission Tomography Detects Residual Prostate Cancer after Prostatectomy in a Multicenter Retrospective Study. J Urol 2019;202:1174-1181.

28. Deandreis D, Guarneri A, Ceci F, 68Ga-PSMA-11 PET/CT in recurrent hormone-sensitive prostate cancer (HSPC): a prospective single-centre study in patients eligible for salvage therapy. [published online ahead of print, 2020 Apr 20]. Eur J Nucl Med Mol Imaging 2020;10.1007/s00259-020-04809-8.

29. Ost P, Reynders D, Decaestecker K, Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: aprospective, randomized, multicenter phase II trial. J Clin Oncol 2018;36:446-453.

30. Pyka T, Okamoto S, Dahlbender M, Comparison of bone scintigraphy and 68Ga-PSMA PET for skeletal staging in prostate cancer. Eur J Nucl Med Mol Imaging 2016;43:2114- 21121.

31. Maurer T, Gschwend JE, Rauscher I, Diagnostic efficacy of (68) gallium-PSMA positron emission tomography compared to conventional

imaging for lymph node staging of 130 consecutive patients with intermediate to high risk prostate cancer. J Urol 2016;195:1436-1443.

32. Hijazi S, Meller B, Leitsmann C, Pelvic lymph node dissection for nodal oligometastatic prostate cancer detected by 68Ga-PSMA-positron emission tomography/ computerized tomography. Prostate 2015;75:1934-1940.

33. Ferraro DA, Muehlematter UJ, Garcia Schüler HI, (68)Ga- PSMA-11 PET has the potential to improve patient selection for extended pelvic lymph node dissection in intermediate to high-risk prostate cancer. Eur J Nucl Med Mol Imaging 2020;47:147-159.

34. Öbek C, Doğanca T, Demirci E, Members of Urooncology Association, Turkey. The accuracy of 68Ga-PSMA PET/CT in primary lymph node staging in high-risk prostate cancer. Eur J Nucl Med Mol Imaging 2017;44:1806-1812.

35. Dorff TB, Fanti S, Farolfi A, Reiter RE, Sadun TY, Sartor O. The evolving role of prostate-specific membrane antigen-based diagnostics and therapeutics in prostate cancer. Am Soc Clin Oncol Educ Book 2019;39:321-330.

36. Hofman MS, Lawrentschuk N, Francis RJ, Prostatespecific membrane antigen PET-CT in patients with highrisk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet 2020;395:1208-1216.

37. Weilbaecher KN, Guise TA, McCauley LK. Cancer to bone: a fatal attraction. Nat Rev Cancer 2011;11:411-425.

38. Høilund-Carlsen PF, Hess S, Werner TJ, Alavi A. Cancer metastasizes to the bone marrow and not to the bone: time for a paradigm shift! Eur J Nucl Med Mol Imaging 2018;45:893-897.

39. Ceci F, Fanti S. PSMA PET/CT imaging in prostate cancer: why and when. Clin Transl Imaging 2019:377-379.

40. Kratochwil C, Fendler WP, Eiber M, EANM procedure guidelines for radionuclide therapy with 177Lu-labelled PSMA-ligands (177Lu-PSMA-RLT). Eur J Nucl Med Mol Imaging 2019;46:2536-2544.

41. Afshar-Oromieh A, Malcher A, Eder M, et al. PET imaging with a [68Ga]gallium-labelled PSMA ligand for the diagnosis of prostate cancer: biodistribution in humans and first evaluation of tumour lesions. Eur J Nucl Med Mol Imaging 2013;40:486-495.

42. Grubmüller B, Rasul S, Baltzer P, et al. Ressponse assessment using [68Ga]Ga-PSMA ligand PET in patients undergoing systemic therapy for metastatic castration-resistant prostate cancer. Prostate 2020;80:74-82.

43. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009;45:228-247.

44. Van den Wyngaert T, Strobel K, Kampen WU et al. The EANM practice guidelines for bone scintigraphy. Eur J Nucl Med Mol Image 2016;43:1723-1738.

45. Cook GJ, Azad G, Padhani AR. Bone imaging in prostate cancer: the evolving roles of nuclear medicine and radiology. Clin Transl Imaging 2016;4:439-447.

46. Agus DB, Golde DW, Sgouros G, Ballangrud A, Cordon-Cardo C, Scher HI. Positron emission tomography of a human prostate cancer xenograft: association of changes in deoxyglucose accumulation with other measures of outcome following androgen withdrawal. Cancer Res 1998;15;58:3009-3014.

47. Oyama N, Akino H, Suzuki Y, et al. Prognostic value of 2-deoxy-2-[F-18]fluoro-D-glucose positron emission tomography imaging for patients with prostate cancer. Mol Imaging Biol 2002;4:99-104.

48. Kairemo K, Ravizzini GC, Macapinlac HA, Subbiah V. An Assessment of Early Response to Targeted Therapy via Molecular Imaging: A Pilot Study of 3'-deoxy-3'[(18)F]-Fluorothymidine Positron Emission Tomography (18) F-FLT PET/CT in Prostate Adenocarcinoma. Diagnostics (Basel) 2017:7.

49. De Bono JS, Oudard S, Ozguroglu M, et al. Cabazitaxel or mitoxantrone with prednisone in patients with metastatic castration-resistant prostate cancer (mCRPC) previously İlknur Ak Sivrikoz, Porstat Kanseri'nde Tedavi Yanıtı Değerlendirmede Ga-68 PSMA PET/BT treated with docetaxel: final results of a multinational phase III trial (TROPIC). J Clin Oncol 2010;28:4508.

50. West TA, Kiely BE, Stockler MR. Estimating scenarios for survival time in men starting systemic therapies for castration-resistant prostate cancer: a systematic review of randomised trials. Eur J Cancer 2014;50:1916-1924.

CHAPTER XXVII

INTESTINAL MICROBIOTA

Esin Doğantekin

(MD, Assoc. Prof.), 25 Aralık State Hospital,
Medical Microbiology Laboratory,
E-mail: esindogantekin23@gmail.com
ORCID: 0000-0002-3989-0421

1. Introduction

Human microbiota; major bacteria, viruses, fungi and lots of eukaryotic consists of microorganisms. He moved away from the view that it is harmful to cells. Our human microbiota is healthy inside of us. The idea that it creates a microbial environment is advocated as a new paradigm (1). When we look at the types of microbiota in our body; temporary microbiota that stay in our body for hours or days, can cause physical changes and not consent other microorganisms to stay in the area. In the intestinal flora of healthy personals; Proteobacteria (includes gram-negative genera such as Enterobacteria), Firmicutes (includes gram-positive genera such as Clostridium, Eubacterium, Ruminococcus, Butyrivibrio, Anaerostipes, Roseburia, Faecalibacterium etc.), Bacteroidetes (includes gram-negative genera such as Bacteroides, Porphyromonas, Prevotella, etc.), Actinobacteria (includes gram-negative genera) There are 6 types of bacterial microbiota expressed as Fusobacteria (including gram positive Bifidobacterium) and Verrucomicrobia (including Akkermansia etc.) (2). The microbiota has important tasks in our body in regulating the development of diseases and health conditions, creating the necessary signals to promote the maintenance of immune system functions, and absorbing undigested carbohydrates. The largest part of the human microbiota is located in our digestive system (3). The gut microbiota has been the leading subject of scientific research in recent years. The reason for this is that the intestinal microbiota occupies a very important place in the human body. If you look at the numbers, about 1-2 kg of a 70 kg person consists of bacteria. About 90% of these bacteria are located in the intestines. Interestingly, 80% of

our immune system cells are located in our intestines. Therefore, the intestinal microbiota and the immune system are located side by side by forming an interface. From this point of view, it has an important place in terms of its effects on the immune system. Again, in terms of the number of living cells in the human body, only 10% of these cells are human cells, while the others are bacterial cells. In terms of the number of genomes, the genome of bacteria is many times greater than the number of human genomes. In terms of surface area, the bacteria are the size of two tennis courts. Considering all these figures, the microbiota is actually a virtual organ and its functions, genetic structure and metabolism are larger than many organs. Another issue is that when we look at the neurons that our intestines contain, it is seen that they contain as many neurons as our brains, and that's why our intestines are called the second brain (4). The ecosystem that occurs of microorganisms such as bacteria, viruses, fungi and protozoa colonized in the gastrointestinal tract and functions like an organ is called the "intestinal microbiota" (5). The intestinal tract microbiota in humans is a combined and high pressure ecosystem formed by a lots of and variety of microorganisms. It is very difficult to reach clear information about the number and diversity of bacteria in this ecosystem. The inability of existing culture methods to culture all bacteria in the intestinal tract is a fact accepted by all researchers., it is estimated that there are more than 35,000 bacterial species in total in the gastrointestinal tract (6). In the gastrointestinal tract microbiota; There are anaerobic, facultative anaerobic and aerobic bacteria. However, important part of the intestinal microbiota is mainly anaerobic bacteria, including Bacteroides and Firmicutes. Apart from Bacteroides and Furmicutes, other important anareobic bacteria include Proteobacteria Verrucomicrobia, Actinobacteria, Fusobacteria, Lentisphaerae, Spirochaet and Cyanobacteria (7). In physiological conditions, there is an extremely high pressure balance in the digestive system microbiota. While short-term changes can be observed in the microbiota with daily diet , long-term and constant changes may occur with aging. Nutritional habits are one of the most important factors affecting the gastrointestinal tract microbiota. While feeding with plenty of carbohydrates causes significant changes in the microbiota; Consumption of prebiotics containing inulin causes F. Prausnitzii and Bifidobacterium to be seen more in the flora. (8).

2. Factors Affecting Intestinal Microbiota

The gastrointestinal microbiota is closely associated with many diseases, and some animal studies link causality.. Therefore, modulation of our gut

microbiota becomes important. Some factors affect the development or deterioration of the microbiota. These factors can be divided into two as intrinsic and extrinsic. The most important of the intrinsic factors is gastric acidity. Gastric acid is divided into basal and stimulated acid secretion. When hungry, there is a basal secretion. Therefore, our stomach has a constantly acidic environment. Bacteria are eliminated in this acidic environment. This mechanism prevents harmful bacteria that we take from outside from reaching our intestines.

When gastric acidity decreases, this protection mechanism is disrupted and dysbiosis occurs. Atrophic gastric and hypoacidity, which develops especially with advancing age, is the main reason for the change of intestinal microbiota in advanced ages. Other factors are oxygen content, motility, mucus, gastrointestinal secretions, antimicrobial peptides, immunity (9). Diet is one of the environmental factors. In studies, the microbiota changes very rapidly (within 48-72 hours) in humans with diet. Probiotics (useful microorganisms) and prebiotics (foods that increase beneficial bacteria in the gut) are effective when taken as nutritional supplements or supplements. Again, among drugs, proton pump inhibitors (PPI) and antibiotics can cause serious harm. Apart from these, prokinetic agents, laxatives, opioids, non-steroidal anti-inflammatory drugs (NSAIDs) are effective. As a result, the gut microbiota can be considered as a virtual organ. Its effects on the metabolic and immune system are quite high and sometimes have deeper effects than other organs. Research in the field of gut microbiota has the potential to offer new diagnostic and therapeutic possibilities (10).

3. Formation and Development of Intestinal Microbiota

Microbiota is the general definition given to all microorganisms, including bacteria, viruses and fungi, that live together in all anatomical regions, and the system that includes the genetic loads of all these microorganisms is called the "microbiome"(11). In the period following the Human Microbiome Project, studies on microbiota composition have accelerated all over the world. In recent years, the basis of studies in the field of microbiota is the determination of the factors affecting the microbiota in adulthood in health or disease. The period defined as the first 1000 days covers the period from the first day of pregnancy to the first 2 years of age of the baby. This period affects many systems from infancy to adulthood, and it has been shown that factors affecting the microbiota in the first 1000-day period have decisive effects from childhood to adulthood (12). It has been shown that most of the factors affecting the microbiota over the

first 1000 days, therefore, are related to the MOTHER. Changes in the mother's microbiota; It is closely related to the mode of delivery, age at which she was conceived, breastfeeding and diet. It is known that the factors that the baby is exposed to in the womb, pregnancy-related conditions, and the amniotic fluid microbiota are effective in the development of the baby's microbiota (13). Mode of birth is thought to be one of the most influential factors on the microbiota. The first study in this area was done by Dominguez-Bello et al.4 in 2010. This study included 9 pregnant women and 10 newborn babies between the ages of 21-33 at Purto Ayacucho Hospital in Venezuela. The mode of delivery was normal spontaneous vaginal delivery in 4 pregnants and cesarean section in 5 pregnant women. As a result of this study, it has been shown for the first time in the literature that there is a difference between spontaneous vaginal delivery and cesarean section in terms of microbiota profile. It has been shown that Lactobacilli in the mother's vaginal microbiota are dominant in many anatomical positions of the baby after birth in infants born by spontaneous vaginal delivery, while the other dominant bacteria of the microbiota in these infants are Atopobium, Sneathia and Prevotella. The researchers showed that Lactobacilli are not dominant among the microbiota content in babies born by cesarean section, and Staphylococcus is a dominant microbiota composition. There are also limitations such as the different geography of the study and the fact that it was performed in very few pregnant women (14). In the study conducted by Azad et al.5 in Canada, which followed this study, it was shown that there is a difference between spontaneous vaginal delivery and cesarean section, as well as between elective cesarean section and emergency conditions. In addition, in this study, researchers showed that besides the mode of delivery, postpartum breast milk intake was also a determinant (15).

4. Content of Microbiota

Microorganisms along the intestinal tract; They play an important role in the formation and development of both gastrointestinal tract mucosal immunity and systemic immunity. The combination of microorganisms colonizing the oral cavity in humans is similar to the general microbiota of the intestinal tract. These microorganisms; Firmicute (70%), Bacteroidetes (10%), Actinobacteria (10%), Fusobacteria (5%), Proteobacteria (4%) and Spirochaet, TM7, SR1, Tenericute (1%). Interestingly, in a recent study, it was reported that changes in the oral cavity microbiota in humans are associated with atherosclerosis, which is the most common cause of mortality today (16). It has been reported that

there are 10 bacteria per gram of stomach content and these bacteria are mainly composed of Lactobacillus, Veillonella and Helicobacter. It was determined that there were 10^3 /gram bacteria in the duodenum, 10^4 /gram in the jejunum and 10^7/gram in the ileum. Bacteria isolated from the small intestine are respectively; It can be summarized as Bacillus, Streptococcus, Actinobacteria, Actinomycinea and Corynebacteria. When the colon is passed, the number of bacteria increases to 10^{12} per gram. These bacteria are mainly composed of Bacteroidetes, Lachnospiraceae and Firmicutes. Along the intestinal tract, there is a thick and chemically complex mucus layer on the epithelial cells of the gastrointestinal tract. In the intestines, Bacteroides, Bifidobacterium, Streptococcus, Enterobacteri, Enterococcus, Lactobacillus and Ruminococcus are found on the mucus layer and participate in the structure of the feces. On the other hand, Clostridium, Lactobacil and Enterococcus can colonize deeper. It is possible to encounter these bacteria in the mucus layer and on the intestinal epithelial cells (17).

5. Diseases and Intestinal Microbiota

Considering the effects of the intestinal microbiota on the maturation of the gastrointestinal system epithelium and the development of intestinal peristalsis, it is thought to play a role in the pathogenesis of diseases such as inflammatory bowel disease and motility-related diseases such as irritable bowel disease. However, intestinal microbiota; Because of its close relationship with inflammation, immune system, nutrition and even endocrine system, gastrointestinal it is also effective in the pathogenesis of a surprising number of diseases outside the system (18).

5.1. Microbiota and Hypertension

17.5 million (one third) of deaths in the world are due to cardiovascular diseases is taking place. Bacteria and bacterial products have been associated with cardiovascular diseases for many years, and bacterial DNA and cells have been detected in atherosclerotic plaques. The observation that many of the bacterial products in atherosclerotic plaque are identical to human oral and intestinal bacteria has led to the belief that bacteria in this region play a role in the atherosclerotic process. Considering the etiopathogenesis of atherosclerosis, it is seen that high-fat and protein nutrition is effective in this process. As a result of deterioration in mucosal integrity as a result of high-fat diet, wall permeability

and plasma LPS levels in intestinal cells increase. The increase in plasma LPS level is effective in the increase of basal inflammation and the formation of environments that are factors in the formation of metabolic diseases (19).

5.2. Microbiota and Obesity

Dysbiosis occurs with the deterioration of the intestinal microbiota and the decrease in functional diversity (20). When dysbiosis occurs in the intestinal microbiota, it has been shown that there is an increase in intestinal permeability and a change in short-chain fatty acid production. These changes cause changes in glucose and lipid metabolism, inflammation and metabolic endotoxemia, and eventually lead to obesity (21). Data obtained in studies on obesity show that the intestinal microbiota content of obese individuals varies compared to healthy individuals. It was found that there was an increase in the microbiota of obese individuals in Bacteriodetes and Prevotella species, and a decrease in the amount of Firmicutes and Bifidobacterium. The results obtained in animal studies on obesity also show that the microbiota content has changed. When obese mice were given a typical Western diet, the intestinal microbiota of the mice was increased in Firmicutes species and decreased in Bacteroidetes species. In the study of Ley et al. comparing the microbiota contents of obese and normal weight individuals; It was determined that the rate of Firmicutes in the microbiota of obese individuals is higher and the rate of Bacteroidetes is lower (22). In the study of Turnbaugh et al., it was found that there was a decrease in the rate of Bacteroidetes in obese individuals compared to healthy individuals, an increase in the rate of Actinobacteria, but no significant difference in the rate of Firmicutes (23). Armougom et al., on the other hand, obtained similar results and found that there was an increase in Lactobacillus from Firmicutes species and a decrease in Bacteroidetes species in obese individuals compared to healthy individuals. The genus Bifidobacterium from the Actinobacteria species found in the microbiota has been associated with obesity in many studies (24). Million et al., in obese individuals compared to healthy individuals; It was determined that the rate of Bacteroidetes was similar, the rate of Firmicutes increased, and the rate of Bifidobacterium decreased (25).

5.3. Microbiota and Cardiovascular Diseases

The gastrointestinal tract is thought to be a large ecosystem that hosts trillions of microbial communities and produces metabolites, along with bacteria,

viruses, fungi, and protozoa (26). Intestinal microbiota; It has many functions such as stimulating the immune system in the body, supporting innate immunity against pathogens, digestion of indigestible foods, regulation of mucosal barriers, production of vitamins and hormones (27). The main bacterial groups in the human gut are Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Verrucomicrobia and Fusobacteria species. There is a mutualistic relationship between homeostatic balance and gut microbiota in humans. This relationship can be disrupted in pathological conditions and this process, which is defined as dysbiosis, can be harmful to the host. The gut microbiota produces many biologically active molecules that can contribute to the regulation of the circulatory system and energy balance (28). The gut microbiota is the largest endocrine organ capable of influencing signaling molecules within the host. Therefore, an abnormal change in the intestinal flora may be associated with obesity, diabetes, and cardiovascular diseases (29). Although there are many epidemiological studies supporting the relationship between cardiovascular disease and gut microbiota, the underlying pathogenetic causes are unclear. When the studies are evaluated, some mechanisms such as inflammation caused by endotoxemia and lipopolysaccharide load, impaired cholesterol metabolism, foam cell formation from macrophages and atherogenic lipid/plaque formation are suggested.

5.4. Microbiota and Inflammatory Bowel Diseases

There are three main components in the pathogenesis of inflammatory bowel disease: genes, immunity and microbiota.. By revealing the molecular mechanisms between these three, valuable information has been revealed in terms of disease pathogenesis. Is there an abnormal immune response to the normal gut microbiota or an abnormal, the issue of whether there is a specific response to the intestinal microbiota has been studied for years, and current animal studies on this subject have shown that both conditions may develop and overlap (30). In other words, changes in the intestinal microbiota due to certain diseases in the genetically innate immune system can cause colitis. Depending on the use of antibiotics in the first years of life, the immune system may lead to frequent illness in the early period and inflammatory diseases in the future. This situation can also prepare the ground for intestinal diseases. Factors such as stress, unnecessary drug use and air pollution greatly affect the formation and functional activity of the intestinal microbiota. As a result, damage to the mucosal barrier causes uncontrolled proliferation of T cells, which paves the

way for inflammation and therefore inflammatory bowel diseases. Intestinal microbiota may also have effects on the clinical course in various stages of inflammatory bowel diseases. Many studies have shown that bacteria and their metabolites contribute to the development of complications with high morbidity such as fibrosis, adhesions, stenosis or abscess.

Intestinal microbiota may also have effects on the clinical course in various stages of inflammatory bowel diseases. The development of complications and clinical conditions with high morbidity such as fibrosis, adhesions, stenosis or abscess It has been shown in several studies that bacteria and their metabolites contribute (31). No specific microbial sign or persistent pattern of change has been identified to date in people with inflammatory bowel disease. Although studies have shown changes in the total number of bacteria in the mucosa and decreased bacterial diversity, a definite relationship has not been demonstrated yet. The best significant changes were shown in mucosal specimens, with an increase in Enterobacter, Fusobacter, Pasteurella and Bifidobacter species. These changes were thought to have predictive significance, especially in terms of the activity index in pediatric patients, and negative correlations were shown especially for Enterobacter and positive relationships for Fusobacter and Haemophilus (32). Again, it has been shown that the number of Faecalibacterium prausnitizi, which has the ability to produce short-chain fatty acids as an energy source for the colon epithelium by using anti-inflammatory protein and dietary fiber, is reduced in ileal Crohn's disease and this condition is associated with the recurrence of postoperative ileal Crohn's disease (33). Although most of the studies focus on the bacterial component of the intestinal microbiota, opinions have been expressed about the active effects on the immune system, especially regarding viruses. virus can replace the beneficial function of commensal bacteria (34).

5.5. Microbiota and Type 2 Diabetes Mellitus

The role of inflammatory pathways in the formation of insulin resistance is emphasized. Significant endotoxemia has been demonstrated in patients with metabolic syndrome and Type 2 Diabetes Mellitus (T2DM). In one study, it was reported that mice with diabetes induced on a high-fat diet had increased intestinal permeability and endotoxemia (35). Another study found high levels of certain bacterial DNAs (more than 85% Proteobacteria) in the blood of prediabetic individuals. Therefore, it has been suggested that microbial endotoxin may play a role in T2DM-related insulin resistance. In addition, in T2DM studies, it has been revealed that there is a defect in the

production of SCFAs (especially butyrate), and it has been hypothesized that this may contribute to the inflammation seen in T2DM (36). Moderate dysbiosis, characterized by a reduction in butyrate-producing bacteria, was seen in stool samples from patients with T2DM in a cohort study. In addition, opportunistic pathogen colonies such as Bacteroides caccae, Clostridiales, Escherichia coli and Desulfovibrio have been detected in the intestinal microbiota of individuals with T2DM. T2DM has been associated with intestinal microbiota oxidative stress response, increased glucose and branched chain amino acid transport, and decreased butyrate biosynthesis. It has been determined that there is more than 3% difference in intestinal microbial genes between healthy individuals and patients with T2DM. Thus, it has been shown that specific bacterial genes and metabolic pathways are correlated in T2DM patients. Karlsson et al. (2012), in a complementary cohort study of postmenopausal women, it was found that the levels of butyrate-producing bacteria Roseburia intestinalis and Faecalibacterium prausnitzii were low in women with T2DM (37). In both cohort studies, the increase in Lactobacillus species was shown to be associated with T2 DM. Zhang et al. (2013) reported that the levels of Verrucomicrobiaceae and Akkermansia muciniphila (A. Muciniphila) were significantly decreased in prediabetic individuals (38). Shin et al. (2014) showed that administration of metformin to mice fed a high-fat diet for 6 weeks changed the microbial profile (29 strains) and increased the amount of A. muciniphila. Oral administration of A. muciniphila alone to mice fed a high-fat diet improved metabolic function, glucose tolerance, and systemic inflammation (39). In a study of 784 human genomes from the MetaHIT (Metagenomics of the Human Intestinal Tract) project, it was determined that there was a significant decrease in butyrate-producing taxa in the intestinal microbiota of T2DM patients, and increased butyrate and propionate production in the intestinal microbiota of the patients receiving metformin treatment. It has been found that intestinal microbiota function changes and intestinal lipid absorption and inflammation decrease after metformin treatment. Thus, evidence is presented that metformin treatment makes significant functional and regulatory changes in the human gut microbiota. In a study in which data from 42 human studies were compiled, it was suggested that T2DM and Bifidobacterium, Bacteroides, Faecalibacterium, Akkermansia and Roseburia genera were negatively correlated, while Ruminococcus, Fusobacterium, and Blautia genera were positively correlated (40). Although the genus Lactobacillus has been detected in many studies, it has been found that there is inconsistency between the results of these studies.

References

1- Altındiş S, Adıgül MP. Ethics in Microbiota Studies. SDU J of Health Sciences 2017:8(3);62-68.

2- Varım P, Vatan MB, Varım C. Cardiovascular Diseases and Microbiota. Journal of Biotechnology and Strategic Health Research 2017:1;141-147.

3- Yılmaz K, Altındiş M. Digestive microbiota and fecal transplantation. Nobel Medicus 2017:13(1);9-15.

4- Human Microbiome Project C. Structure, function and diversity of the healthy human microbiome. Nature 2012;486:207–14.

5- Ficara M, Pietrella E, Spada C, et al. Changes of intestinal microbiota in early life. The Journal of Maternal-Fetal & Neonatal Medicine, 2020:33(6);1036-1043.

6- Frank DN, St Amand AL, Feldman RA, et al. Molecular-phylogenetic characterization of microbial community imbalances in human inflammatory bowel diseases. Proc Natl Acad Sci USA 2007;104:13780-5.

7- Eckburg PB, Bik EM, et al. Diversity of the human intestinal microbial flora. Science 2005;308:1635-8.

8- Ramirez-Farias C, Slezak K, Fuller Z, et al. Effect of inulin on the human gut microbiota: stimulation of Bifidobacterium adolescentis and Faecalibacterium prausnitzii. Br J Nutr 2009;101:541 50.

9- LynchSV, PedersenO.The humanintestinal microbiome in health and disease. N Engl J Med 2016;375:2369–79.

10- Li J, Jia H, Cai X, et al. An integrated catalog of reference genes in the human gut microbiome. Nat Biotechnol 2014;32:834-41.

11- Filyk HA, Osborne LC. The Multibiome: The Intestinal Ecosystem's Influence on Immune Homeostasis, Health, and Disease. EBioMedicine. 2016 Nov;13:46-54.

12- Cunha AJ, Leite ÁJ, Almeida IS. The pediatrician's role in the first thousand days of the child: the pursuit of healthy nutrition and development. J Pediatric (Rio J). 2015 Nov-Dec;91(6 Suppl 1):S44-51.

13- Amenyogbe N, Kollmann TR, Ben-Othman R. Early-Life Host-Microbiome Interphase: The Key Frontier for Immune Development. Front Pediatr. 2017 May 24;5:111.

14- Dominguez-Bello MG, Costello EK, Contreras M, Magris M, Hidalgo G, Fierer N, Knight R. Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proc Natl Acad Sci U S A. 2010 Jun 29;107(26):11971-5.

15- Azad MB, Konya T, Maughan H, Guttman DS, Field CJ, Chari RS, Sears MR, Becker AB, Scott JA, Kozyrskyj AL; CHILD Study Investigators. Gut microbiota of healthy Canadian infants: profiles by mode of delivery and infant diet at 4 months. CMAJ. 2013; 185(5): 385-94.

16- Koren O, Spor A, Felin J, et al. Human oral, gut, and plaque microbiota in patients with atherosclerosis. Proc Natl Acad Sci USA 2011;15;108(Suppl 1):4592-8.

17- Swidsinski A, Loening-Baucke V, Lochs H, Hale LP. Spatial organization of bacterial flora in normal and inflamed intestine: a fluorescence in situ hybridization study in mice. World J Gastroenterol 2005;11:1131-40.

18- Saulnier DM, Riehle K, Mistretta TA, et al. Gastrointestinal microbiome signatures of pediatric patients with irritable bowel syndrome. Gastroenterology 2011;141:1782-91.

19- Clarke, S. F., Murphy, E. F., O'Sullivan, O., Lucey, A. J., Humphreys, M., Hogan, A., Hayes, P., O'Reilly, M., Jeffery, I.B., Wood-Martin, R. ., Kerins, D. M. (2014). Exercise and associated dietary extremes impact on gut microbial diversity. Gut, 63(12), 1913-1920.

20- Blandino G, Inturri R, Lazzara F, et al. Impact of gut microbiota on diabetes mellitus. Diabetes & metabolism 2016;42:303-315.

21- Nadal I, Santacruz A, Marcos A, et al. Shifts in clostridia, bacteroides and immunoglobulin-coating fecal bacteria associated with weight loss in obese adolescents. Int J Obes 2009; 33:758-767.

22- Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbialecology: human gut microbes associated withobesity. Nature 2006; 444:1009-1010.

23- Turnbaugh PJ, Hamady M, Yatsunenko T, et al. A core gut microbiome in obese and lean twins. Nature 2009; 457:480-484.

24- Armougom F, Henry M, Vialettes B, et al. Monitoring bacterial community of human gut microbiota reveals an increase in Lactobacillus in obese patients and methanogens in anorexic patients. PLoS One 2009; 4:e7125.

25- Million M, Maraninchi M, Henry M, et al. Obesity-associated gut microbiota is enriched in Lactobacillus reuteri and depleted in Bifidobacterium animalis and Methanobrevibacter smithii. Int J Obes 2012; 36:817-825.

26- Peng J, Xiao X, Hu M, Zhang X. Interaction between gut microbiome and cardiovascular disease. Life Sci 2018;214:153–7.

27- Wang Z, Zhao Y. Gut microbiota derived metabolites in cardiovascular health and disease. Protein & Cell 2018;9(5):416–31.

28- Nowinski A, Ufnal M. Trimethylamine N -oxide: A harmful, protective or diagnostic marker in lifestyle diseases? Nutrition 2018;46:7–12.

29- Ahmadmehrabi S, Tang WHW. Gut microbiome and its role in cardiovascular diseases. Curr Opin Cardiol 2017;32(6):761-6.

30- Buttó LF, Haller D. Dysbiosis in intestinal inflammation: Cause or consequence. Int J Med Microbiol. 2016 Aug;306(5):302-9.

31- Shanahan F, Quigley EM. Manipulation of the microbiota for treatment of IBS and IBD-challenges and controversies. Gastroenterology 2014;146:1554–63.

32- Gevers D, Kugathasan S, Denson LA, et al. The treatment-naive microbiome in new-onset Crohn's disease. Cell Host Microbe 2014;15:382–92.

33- Sokol H, Pigneur B, Watterlot L, et al. Faecalibacterium prausnitzii is an antiinfl ammatory commensal bacterium identifi ed by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci USA 2008;105:16731–6.

34- Kernbauer E, Ding Y, Cadwell K. An enteric virus can replace the beneficial function of commensal bacteria. Nature 2014;516:94–8.

35- Serino M, Luche E, Grease S, Baylac A, Berge M, Cenac C, Waget A, Klopp P, Iacovoni J, Klopp C, Mariette J, Bouchez O, Lluch J, Ouarne F, Monsan P, Valet P, Roques C , Amar J, Bouloumie A, Theodorou V, Burcelin R. Metabolic adaptation to a high-fat diet is associated with a change in the gut microbiota. Gout. 2012;61:543-553.

36- Tilg H, Moschen AR. Microbiota and diabetes: An evolvingrelationship. Gout. 2014;63:1513-1521.

37- Karlsson CL, Onnerfalt J, Xu J, Molin G, Ahrne S, Thorngren-Jerneck K. The microbiota of the gut in preschool children with normal and excessive body weight. Obesity 2012;20:2257-2261.

38- Zhang X, Shen D, Fang Z, Jie Z, Qiu X, Zhang C, Chen Y, JiL. Human gut microbiota changes reveal the progression of glucose intolerance. PLoS One. 2013;8:e71108.

39- Shin NR, Lee JC, Lee HY, Kim MS, Whon TW, Lee MS, Bae JW. An increase in the Akkermansia spp. population induced by metformin treatment improves glucose homeostasis in diet-induced obese mice. Gout. 2014;63:727-735.

40- Gurung M, Li Z, You H, Rodrigues R, Jump DB, Morgun A, Shulzhenko N. Role of gut microbiota in type 2 diabetes pathophysiology. EBioMedicine. 2020;51:102590.

CHAPTER XXVIII

PELVIC VENOUS CONGESTION SYNDROME

Zihni Mert Duman

(MD.), Cizre State Hospital, Department of Cardiovascular Surgery
E-mail: dumanzihnimert@gmail.com
ORCID: 0000-0002-3628-8080

1. Introduction

Pelvic varicose veins are a common public health problem, especially in women. Pelvic venous congestion syndrome (PVCS) was systematically described by Taylor in 1949 (1). PVCS occurs due to reflux or obstruction in the pelvic veins. Mainly, PVCS is characterized by pain, discomfort and varicose veins in the pelvic region, but PVCS may present with different clinical manifestations depending on the hemodynamically affected vein. Although PVCS is mostly known as ovarian vein diseases by clinicians, renal vein diseases, iliac vein diseases are also included (2).

PVCS is most common in premenopausal women (20-45 years), with a prevalence of approximately 6-15% (3, 4). The risk of PVCS in women increases with multiparity. Compensatory ovarian venous dilatation during pregnancy may not return to its pre-pregnancy state and may contribute to venous reflux (5). PVCS should be suspected in chronic pelvic pain lasting longer than 3-6 months even so the absence of pelvic or vulvar varices.

2. Pathophysiology

The mechanism of PVCS is similar to the development of lower extremity varicose veins. Blood stasis is essential. For the development of PVCS, there must be hemodynamic impairment in the pelvic venous structure. The most common cause of hemodynamic abnormalities in the pelvic veins is reflux, and the second cause is obstruction (6).

Pelvic venous reflux is caused by valvular insufficiency. Venous dilatation, previous venous thrombosis, valvular agenesis, hormonal imbalances, such as an increase of estrogen are risk factors for valvular insufficiency (7, 8).

Venous obstruction occurs through external compression or thrombosis of veins. Venous obstruction due to external compression that leading to PVCS include May–Thurner syndrome (compression of the left iliac vein by the right iliac artery.), anterior nutcracker syndrome (left renal vein trapped between the abdominal aorta and the superior mesenteric artery), and posterior nutcracker syndrome (compression of the retroaortic left renal vein by the abdominal aorta) (9, 10).

Evidence of pelvic venous insufficiency or obstruction by ultrasound or other imaging modalities alone should not be considered PVCS. It has been reported that 40% of patients with pelvic vein dilatation do not have symptoms related to PVCS (11).

3. Clinical Features

Patients with PVCS present with different complaints such as pelvic pain, dyspareunia, dysuria, hematuria, tenderness in the perineum and atypically located varicose veins. Because PVCS is not fully understood, it may not be considered among the differential diagnoses of pelvic pain by most clinicians. Therefore, diagnosis of PVCS may be delayed in some patients. Patients with suspected PVCS are referred to gynecologists and vascular specialists.

Pelvic pain, dyspareunia and dysmenorrhea caused by PVCS can be confused with gynecological diseases that cause chronic pelvic pain, such as endometriosis, pelvic inflammatory disease (12, 13).

Pelvic pain due to PVCS increases during menstruation and pregnancy in women. In addition, the pain is affected by the intra-abdominal pressure, the pelvic pain decreases in the lying position and increases standing position.

More than half of patients with pelvic venous congestion have lower extremity venous insufficiency (14, 15). On the other hand, the presence of atypical located varicose veins that can be seen on the vulvar, suprapubic, gluteal and posterior thigh is pathognomonic for PVCS (8). Atypical venous connections may be found between the pelvic veins and varicose veins in the lower extremities. These atypical venous connections may cause non-saphenofemoral reflux in the superficial veins of the inguinal region (16, 17). Correspondingly, after lower extremity varicose vein surgery, 17% of recurrent varicose vein are due to pelvic venous insufficiency (18).

4. Imaging

4.1. Ultrasound

The first-line imaging technique is transabdominal duplex ultrasound for patients with suspected PVCS. Dilatation and twist of pelvic venous structures can be detected in ultrasound (19). Pelvic venous reflux can be detected by performing the Valsalva maneuver. Pelvic veins with a diameter greater than 4 mm and a slowed blood flow (3 cm/sec) support the diagnosis (20). Moreover, duplex ultrasound is useful in the differential diagnosis of other causes of chronic pelvic pain, such as endometriosis and pelvic mass. Although ultrasound is relatively cheap and easily available, it has some disadvantages. Visualization of pelvic vessels can be difficult in obese patients. The patient should be starving to obtain the appropriate images. In addition, ultrasound is an operator-dependent technique, the radiologist's experience with PVCS is also important. Transvaginal duplex ultrasound can be used in the diagnosis of PVCS in patients in whom transabdominal duplex ultrasound is insufficient. Obesity and starving do not affect the evaluation of pelvic vein by transvaginal ultrasound (21).

4.2. Computed Tomography Venography and Magnetic Resonance Venography

Computed tomography venography and magnetic resonance venography can be used to evaluate the pelvic veins (22). Computed tomography venography is useful in planning conventional venography by evaluating the three-dimensional reconstruction of pelvic venous structures. Further, computed tomography venography is also used to examine showing external compression of the vein, such as pelvic masses, May-Thurner syndrome, and nutcracker syndrome (23). Magnetic resonance venography provides dynamic and morphological evaluation of pelvic vessels.

4.3. Conventional Venography

The gold standard imaging method of PVCS is conventional digital subtraction venography. In conventional venography, vein lumen occlusion, duration of venous reflux and the condition of the collateral vessels can be evaluated with selective catheterization of the renal vein, gonadal and iliac veins. In conventional venography, the diagnosis of PVCS is confirmed and concomitant endovascular treatment can be performed (24). On the other hand, conventional venography has some disadvantages such as radiation and the fact

that it is invasive (22). The diagnostic criteria for PVCS on venography are similar to the Doppler ultrasound.

4.4. Diagnostic Laparoscopy

There are studies suggesting laparoscopy for the diagnosis of PVCS (25). Laparoscopy is used up to 40% for the diagnosis of chronic pelvic pain that cannot be diagnosed by non-invasive methods (26). However, the CO2 pressure used for ideal exploration in diagnostic laparoscopy may press on the veins and the dilated veins may appear less aneurysmatic than they are (27). Moreover, laparoscopy is also a much more invasive technique than endovenous methods.

5. Classification

Although the importance of venous disorders of the pelvis has increased in recent years, it has not been adequately studied by clinicians before. Therefore, a systematic classification of pelvic venous disorders has not been developed until recently. Inadequacies in the classification of pelvic venous disorders have been resolved with the Symptoms- Varices- Pathophysiology (SVP) classification published in 2021 by the American Venous & Lymphatic Society International Pelvic Venous Disorders Working Group (2). The SVP classification was developed similarly to the Clinical-Etiologic-Anatomic-Physiologic (CEAP) classification used for venous disorders of the lower extremities. The pathophysiology (P) domain of SVP classification was divided into 3 sub-domains: Anatomic (A), hemodynamic (H) and etiologic (E). Details of the $SVP_{A,H,E}$ classification are given in Table 1. The CEAP classification should be used in addition to the SVP classification in lower extremity varices of pelvic origin.

Table 1: Details of the $SVP_{A,H,E}$ classification

Symptoms (S)	Varices (V)	Pathophysiology (P)		
		Anatomic (A)	Hemodynamics (H)	Etiology (E)
S0: No symptoms	V0: No varices on clinical or imaging examination	Inferior vena cava	Obstruction (O): Thrombotic or nonthrombotic	Thrombotic (T): Reflux or obstruction arising from a previous episode of DVT
S1: Renal symptoms	V1: Renal hilar varices	L renal vein	Reflux (R): Thrombotic or nonthrombotic	Nonthrombotic (NT): Reflux arising from a degenerative process of the vein wall or proximal obstruction; Obstruction arising from extrinsic compression
S2: Chronic pelvic pain	V2: Pelvic varices	L & R & B gonadal vein		Congenital (C): Congenital venous malformations
S3: Extrapelvic symptoms S3a: Localized symptoms with veins of the external genitalia S3b: Localized symptoms associated with pelvic origin nonsaphenous veins of the leg. S3c: Venous claudication	V3: Pelvic origin extrapelvic varices V3a: Genital varices V3b: Pelvic origin lower extremity varicose veins (typically over the posteromedial thigh)	L & R & B common iliac veins		
		L & R & B external iliac vein		
		L & R & B Internal iliac veins		
		Pelvic escape veins (inguinal, obturator, pudendal, and/or gluteal)		

DVT: Deep vein thrombosis, L: left, R: right, B: Bilateral

6. Treatment

6.1. Compression Therapy

Compression therapy is widely used in the treatment of varicose veins of the lower extremities. It has been shown that compression stockings have no symptoms effect in PVCS. On the contrary, compression shorts reduce symptoms such as chronic pelvic pain and dyspareunia due to PVCS (28).

6.2. Medical Treatment

There are several medical treatment options that effect through different mechanism for PVCS. On the other hand, standard medical treatment protocol has not been defined for PVCS. Medical treatment should be arranged according to the underlying pathophysiology of the congestion.

Micronized purified flavonoid fraction, one of the venotonics commonly used in the treatment of lower extremity varicose veins, is effective in PVCS (29). Venotonics agents have anti-inflammatory and analgesic effects as well as improving blood microcirculation. Nonsteroidal anti-inflammatory drugs (NSAIDS) can be used to relieve the pain for a short time. Long-term NSAID use is not recommended in PVCS because NSAID has no effect on the pathophysiology of the disorders. Further, NSAIDs are known to have long-term risks such as gastrointestinal bleeding and renal failure (30). Ovarian suppression drugs can also be used in the treatment of PVCS to reduce the vasodilation effect of progesterone. Disadvantages of ovarian suppression drugs include predisposing to thrombosis and reproductive suppression (31, 32). Other drugs used in the medical treatment of PVCS are psychotropic agents, gonadotropin-releasing hormone (GnRH) agonists and vasoconstrictor drugs such as ergod alkaloids (19, 33).

6.3. Endovascular Treatment

The mostly recommended treatment for PVCS is endovascular treatment, which provides 68.3% to 100% improvement in symptoms, is less painful and requires a shorter hospital stay than surgical treatment (34). Due to the wide spectrum of PVCS, there is no definitive endovascular protocol. Depending on the underlying pathology of disorders, embolization for reflux or stent insertion for obstruction is preferred.

Embolization has been shown to be a safe procedure and significantly improves quality of life, particularly in reflux-induced PVCS (24). Embolization

of the pelvic veins can be performed using different materials that are sclerosants, coils and plugs (35). One of the controversial issues is which veins to embolize, especially in the insufficiency of the ovarian veins. There are studies suggesting that embolization of only the left ovarian vein is satisfactory and there are also studies that argue that bilateral ovarian vein should be embolized (36, 37). Embolization complications may develop in 3.4-9% of patients. Some of these complications are coil migration to the pulmonary system, thrombophlebitis and paradoxical embolism (38). Although the effect of embolization on fertility is not fully known, Santos et al. published a case series of 8 patients suggesting that pregnancy following embolization of the pelvic veins is safe (39). Moreover, Liu and colleagues showed that embolization of the pelvic veins can treat infertility caused by pelvic venous congestion (40).

6.4. Surgical Treatment

Patients whom endovascular therapy has failed can be treated with transperitoneal approach or retroperitoneal approach. As in medical and endovenous treatment, surgery is planned according to the underlying pathology. Left renal vein transposition, ligations of the ovarian veins are among the various surgical strategies of PVCS (41,42).

7. References

1) Taylor HC Jr. Vascular congestion and hyperemia; their effect on structure and function in the female reproductive system. Am J Obstet Gynecol. 1949;57(2):211-230.

2) Meissner MH, Khilnani NM, Labropoulos N, Gasparis AP, Gibson K, Greiner M, et al. The Symptoms-Varices-Pathophysiology classification of pelvic venous disorders: A report of the American Vein & Lymphatic Society International Working Group on Pelvic Venous Disorders. J Vasc Surg Venous Lymphat Disord. 2021;9(3):568-584.

3) O'Brien MT, Gillespie DL. Diagnosis and treatment of the pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord. 2015;3(1):96-106.

4) Howard FM. Chronic pelvic pain. Obstet Gynecol. 2003;101(3):594-611.

5) Perry CP. Current concepts of pelvic congestion and chronic pelvic pain. JSLS. 2001;5(2):105-110.

6) Champaneria R, Shah L, Moss J, Gupta JK, Birch J, Middleton LJ, et al. The relationship between pelvic vein incompetence and chronic pelvic pain

in women: systematic reviews of diagnosis and treatment effectiveness. Health Technol Assess. 2016;20(5):1-108. doi:10.3310/hta20050

7) Phillips D, Deipolyi AR, Hesketh RL, Midia M, Oklu R. Pelvic congestion syndrome: etiology of pain, diagnosis, and clinical management. J Vasc Interv Radiol. 2014;25(5):725-733.

8) Mahmoud O, Vikatmaa P, Aho P, Halmesmäki K, Albäck A, Rahkola-Soisalo P, et al. Efficacy of endovascular treatment for pelvic congestion syndrome. J Vasc Surg Venous Lymphat Disord. 2016;4(3):355-370.

9) Possover M, Khazali S, Fazel A. Pelvic congestion syndrome and May-Thurner syndrome as causes for chronic pelvic pain syndrome: neuropelveological diagnosis and corresponding therapeutic options. Facts Views Vis Obgyn. 2021;13(2):141-148.

10) Kurklinsky AK, Rooke TW. Nutcracker phenomenon and nutcracker syndrome. Mayo Clin Proc. 2010;85(6):552-559.

11) Borghi C, Dell'Atti L. Pelvic congestion syndrome: the current state of the literature. Arch Gynecol Obstet. 2016;293(2):291-301.

12) Ganeshan A, Upponi S, Hon LQ, Uthappa MC, Warakaulle DR, Uberoi R. Chronic pelvic pain due to pelvic congestion syndrome: the role of diagnostic and interventional radiology. Cardiovasc Intervent Radiol. 2007;30(6):1105-1111.

13) Scultetus AH, Villavicencio JL, Gillespie DL, Kao TC, Rich NM. The pelvic venous syndromes: analysis of our experience with 57 patients. J Vasc Surg. 2002;36(5):881-888.

14) Bora A, Avcu S, Arslan H, Adali E, Bulut MD. The relation between pelvic varicose veins and lower extremity venous insufficiency in women with chronic pelvic pain. JBR-BTR. 2012;95(4):215-221.

15) Gavrilov SG, Moskalenko YP. Does pelvic congestion syndrome influence symptoms of chronic venous disease of the lower extremities?. Eur J Obstet Gynecol Reprod Biol. 2019;243:83-86.

16) Villavicencio JL. Recurrent leg varices and intrapelvic and extrapelvic venous connections: it's anatomy, my dear Watson!. Vascular. 2007;15(2):61-62.

17) Jiang P, van Rij AM, Christie RA, Hill GB, Thomson IA. Non-saphenofemoral venous reflux in the groin in patients with varicose veins. Eur J Vasc Endovasc Surg. 2001;21(6):550-557.

18) Perrin MR, Labropoulos N, Leon LR Jr. Presentation of the patient with recurrent varices after surgery (REVAS). J Vasc Surg. 2006;43(2):327-334.

19) Antignani PL, Lazarashvili Z, Monedero JL, Ezpeleta SZ, Whiteley MS, Khilnani NM, et al. Diagnosis and treatment of pelvic congestion syndrome: UIP consensus document. Int Angiol. 2019;38(4):265-283.

20) Patel MD, Young SW, Dahiya N. Ultrasound of Pelvic Pain in the Nonpregnant Woman. Radiol Clin North Am. 2019;57(3):601-616.

21) Valero I, Garcia-Jimenez R, Valdevieso P, Garcia-Mejido JA, Gonzalez-Herráez JV, Pelayo-Delgado I, et al. Identification of Pelvic Congestion Syndrome Using Transvaginal Ultrasonography. A Useful Tool. Tomography. 2022;8(1):89-99

22) Bookwalter CA, VanBuren WM, Neisen MJ, Bjarnason H. Imaging Appearance and Nonsurgical Management of Pelvic Venous Congestion Syndrome. Radiographics. 2019;39(2):596-608.

23) Kim KW, Cho JY, Kim SH, Yoon JH, Kim DS, Chung JW, et al. Diagnostic value of computed tomographic findings of nutcracker syndrome: correlation with renal venography and renocaval pressure gradients. Eur J Radiol. 2011;80(3):648-654.

24) Senechal Q, Echegut P, Bravetti M, et al. Endovascular Treatment of Pelvic Congestion Syndrome: Visual Analog Scale Follow-Up. Front Cardiovasc Med. 2021;8:751178.

25) Arnaoutoglou C, Variawa RS, Zarogoulidis P, Ioannidis A, Machairiotis N. Advances of Laparoscopy for the Diagnosis of Pelvic Congestion Syndrome. Medicina (Kaunas). 2021;57(10):1041.

26) Howard FM. The role of laparoscopy as a diagnostic tool in chronic pelvic pain. Baillieres Best Pract Res Clin Obstet Gynaecol. 2000;14(3):467-494.

27) Wagner E, Chandler JN, Mihalov LS.. Minimizing trendelenburg position for laparoscopic gynecologic surgery [6L]. Obstet. Gynecol. 2019;133(1):130S–130S.

28) Gavrilov SG, Karalkin AV, Turischeva OO. Compression treatment of pelvic congestion syndrome. Phlebology. 2018;33(6):418-424.

29) Akhmetzianov RV, Bredikhin RA. Clinical Efficacy of Conservative Treatment with Micronized Purified Flavonoid Fraction in Female Patients with Pelvic Congestion Syndrome. Pain Ther. 2021;10(2):1567-1578.

30) Marcum ZA, Hanlon JT. Recognizing the Risks of Chronic Nonsteroidal Anti-Inflammatory Drug Use in Older Adults. Ann Longterm Care. 2010;18(9):24-27.

31) Soysal ME, Soysal S, Vicdan K, Ozer S. A randomized controlled trial of goserelin and medroxyprogesterone acetate in the treatment of pelvic congestion. Hum Reprod. 2001;16(5):931-939.

32) Shokeir T, Amr M, Abdelshaheed M. The efficacy of Implanon for the treatment of chronic pelvic pain associated with pelvic congestion: 1-year randomized controlled pilot study. Arch Gynecol Obstet. 2009;280(3):437-443.

33) Schuller-Petrovic S, Wolzt M, Böhler K, Jilma B, Eichler HG. Studies on the effect of short-term oral dihydroergotamine and troxerutin in patients with varicose veins. Clin Pharmacol Ther. 1994;56(4):452-459.

34) Brown CL, Rizer M, Alexander R, Sharpe EE 3rd, Rochon PJ. Pelvic Congestion Syndrome: Systematic Review of Treatment Success. Semin Intervent Radiol. 2018;35(1):35-40.

35) Tiralongo F, Distefano G, Palermo M, Granata A, Giurazza F, Vacirca F, et al. Liquid and Solid Embolic Agents in Gonadal Veins. J Clin Med. 2021;10(8):1596.

36) Gloviczki P, Comerota AJ, Dalsing MC, Eklof BG, Gillespie DL, Gloviczki ML, et al. The care of patients with varicose veins and associated chronic venous diseases: clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. J Vasc Surg. 2011;53(5 Suppl):2S-48S.

37) Venbrux AC, Chang AH, Kim HS, Montague BJ, Hebert JB, Arepally A, et al. Pelvic congestion syndrome (pelvic venous incompetence): impact of ovarian and internal iliac vein embolotherapy on menstrual cycle and chronic pelvic pain. J Vasc Interv Radiol. 2002;13(2 Pt 1):171-178.

38) Borghi C, Dell'Atti L. Pelvic congestion syndrome: the current state of the literature. Arch Gynecol Obstet. 2016;293(2):291-301.

39) Dos Santos SJ, Holdstock JM, Harrison CC, Whiteley MS. The effect of a subsequent pregnancy after transjugular coil embolisation for pelvic vein reflux. Phlebology. 2017;32(1):27-33.

40) Liu J, Han L, Han X. The Effect of a Subsequent Pregnancy After Ovarian Vein Embolization in Patients with Infertility Caused by Pelvic Congestion Syndrome. Acad Radiol. 2019;26(10):1373-1377.

41) Reed NR, Kalra M, Bower TC, Vrtiska TJ, Ricotta JJ 2nd, Gloviczki P. Left renal vein transposition for nutcracker syndrome. J Vasc Surg. 2009;49(2):386-394.

42) Gargiulo T, Mais V, Brokaj L, Cossu E, Melis GB. Bilateral laparoscopic transperitoneal ligation of ovarian veins for treatment of pelvic congestion syndrome. J Am Assoc Gynecol Laparosc. 2003;10(4):501-504.