MEDICAL DIAGNOSIS
and
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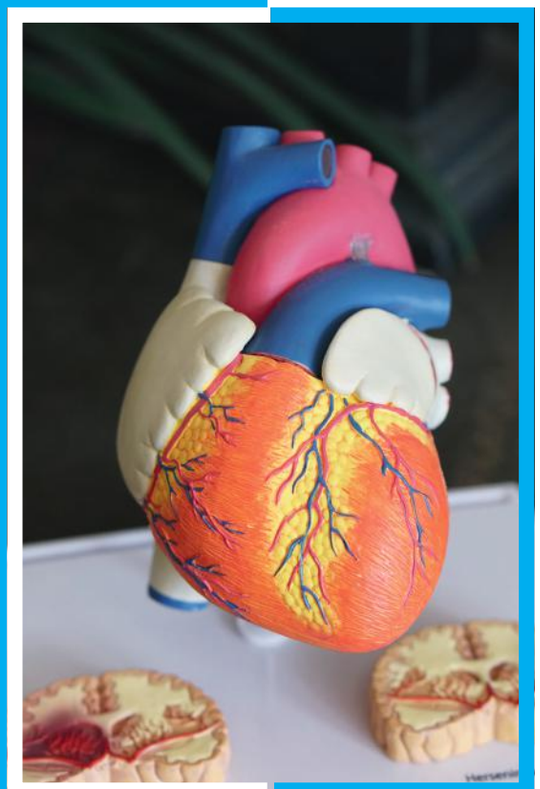
in
SURGICAL MEDICAL SCIENCES



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Assoc. Prof. Dr. Ahmet Cemil Isbir

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PREFACE

A brand new textbook is a testament to many things—an editor's vision, many authors' individual and collective expertise, the publisher's commitment, and all told hundereds of hours of hard work.

This book encapsulates all of this, and with its compendium of up-to-date information covering the full spectrum of the field of surgical medical sciences, it stands as an authoritative and highly practical reference for specialists and primary care clinicians alike. These attributes would be ample, in and of themselves, yet this important addition to the growing surgical sciences library represents a rather novel attribute.

This textbook is both timely and relevant as a resource for clinicians, educators, and researchers to ensure that the converging goals of the are realized. This book has been written; it is now all of ours to read and implement.

Assoc. Prof. Dr. Ahmet Cemil Isbir

Editor

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CHAPTER I

CURRENT APPROACHES TO REMOVE PRE-OPERATIVE ANXIETY DURING ANESTHESIA EXAMINATION

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Preoperative anxiety; It can be defined as an uneasiness or bad feeling that develops against disease, hospitalization, anesthesia and surgery (1). This anxiety negatively affects surgery, anesthesia and postoperative recovery (2). Some studies state that patients with anxiety require higher doses of anesthetic drugs in the intraoperative period (1). Patients have anxiety due to many reasons; In addition to general concerns such as health and surgery, uncertainty, leaving home, and staying away from daily work, there are also anesthesia-related concerns such as not being able to wake up after surgery, waking up during surgery, feeling postoperative pain, and staying in intensive care (3). Various studies have reported that 60-80% of patients have anxiety in the preoperative period.

A wide variety of methods are used to reduce the anxiety levels of patients. The interview made by the anesthesiologist in the preoperative period, the information provided in this interview, and the drugs used for premedication are some of these (6). It has been shown that informing patients in the preoperative period reduces anxiety and analgesic need and increases satisfaction (7). It was observed that the anxiety levels of the patients decreased when the patient was informed about the procedure and why it was performed at each stage (8). Listening to the patient's anxiety and concerns strengthens the ability to cope with anxiety.

In the recognition of patient psychology, it is important to know the degree of anxiety and the causes of anxiety, the nature of the disease, the application of anesthesia, surgical intervention, and a sufficient level of information in a way that does not increase anxiety about the postoperative period. In this context, the BATHE method, which was developed by Stuart and Lieberman and modified by Herpner et al for use in preoperative examination, can be used (9,10,11,12). This is essentially a method of psychotherapy that takes about 15 minutes with specific questions or comments that physicians can include in a standard medical interview with patients. BATHE method (BATHE; Background, Affect,

Trouble, Handling, Empathy) is the abbreviation of the initials of the words Past, Impact, Anxiety, Coping and Empathy. (Table 1).

With this method, patients can express themselves more easily and get information about their diseases more easily. In addition, this method allows physicians to empathize with their patients. There are several studies showing that the use of the BATHE method in preoperative examination decreases the anxiety of the patients and increases the patient satisfaction (13,14). Patients who are told to have surgery are now under stress due to both anesthesia and surgery. In many studies on preoperative anxiety, patients' anxiety levels were found to be high (16,17,18,19,20). There are many studies in the literature where the causes of anesthesia are investigated.

In a survey study conducted by Demir et al., The three most anxious situations related to anesthesia were found to be inability to wake up after surgery, feeling pain in the postoperative period, and waking up during surgery, respectively (21). In their study, Turhan et al. Stated the 3 thoughts that cause the most anxiety before surgery; reported that not waking up after surgery, postoperative pain and staying in intensive care unit (22) There are different results in the literature regarding the relationship between age and preoperative anxiety. While Moerman et al. Concluded that age did not affect anxiety (15), Aykent et al. Reported that anxiety was higher in the group under 30 years of age (23). Taşdemir et al. Concluded in their study that anxiety values were lower in elderly patients. (24) We think that the more fatalistic perspective prevails in our society as the age gets older and that young individuals are more aware of adverse events in the field of health, thanks to their better use of communication tools.

Considering the relationship between marital status and preoperative anxiety, Erfidan, Demir and Taşdemir could not find a significant relationship between marital status and preoperative anxiety in 3 different studies they conducted with their friends (20,21,24). In Akbulut's study, preoperative anxiety scores were found to be high in those who were married and had children (25). Studies have shown that educational status has varying degrees of influence on anxiety levels. While Taşdemir et al. Could not find a relationship between educational status and anxiety, Caumo et al. Reported in their study that preoperative anxiety levels were higher in individuals who had education for more than 12 years (26). Since the uncertainty factor will be less effective in educated patients, it may be expected that anxiety will be lower, but it may be considered that having detailed information on some issues may increase anxiety. Demir et al. Could not detect a significant relationship between income level and preoperative anxiety in their study (21).

There are studies showing that patients' previous anesthesia experience is an important variable on preoperative anxiety level. Moerman et al. Reported that anesthesia experience reduced anxiety in men and did not change it in women (15). Caumo et al. Suggested in their study that anesthesia experience did not change the level of anxiety (26). On the other hand, in two different studies of Matthias et al. And Turzakova et al., Those who had no previous anesthesia experience had higher anxiety values (16,17).

Akbulut et al. Concluded in their study that smoking or alcohol use was not associated with anxiety (25). On the other hand, in two different studies by Caumo et al. And Cuvaş et al., Anxiety was found to be high in smokers (26,27). This can be attributed to the beliefs of the patients that smoking and alcohol use will negatively affect the surgery compared to non-users. Moerman et al. Stated in their study that the type of operation did not change the anxiety level (15). In the study of Caumo et al., It was stated that while minor surgery did not change the anxiety level, moderate and major surgery increased the anxiety level (26).

Preoperative anxiety is an unpleasant psychological condition for the patient. Information is the best way to prevent patients' fears and relieve their concerns. Previous studies have shown that the anesthesiologist's meeting with the patient and establishing a good communication during the preoperative period significantly reduces anxiety (27,28). Çuvaş et al. Showed that the anesthetist's involvement greatly reduced anxiety without using medication (27). Hepner et al. Suggested in their study that the best source of information for patients about an operation is anesthesiologists. They found that if the patients were allowed to express themselves and the necessary medical explanations were made clearly, their anxiety decreased. In summary; They concluded that the BATHE interview technique, which is a special interview technique, can be included in the standard preo-operative examination (12). DeMaria et al., In their questionnaire studies including 100 patients to be operated on, found that patients who underwent BATHE interview technique in preoperative examination were more accepted and satisfied from the examination than patients who had standard interviews. In the patient satisfaction questionnaire conducted after the examination, satisfaction scores of the patients in the BATHE group were found to be significantly higher than the other group (29). There is currently only one study conducted in our country using the BATHE method in anesthesia examination. In the study conducted by Yurtlu et al. With 463 participants, a significant decrease was observed in the STAI anxiety scores of the patients interviewed using the BATHE method compared to the patients who were interviewed in the standard interview compared to the STAI anxiety scores before the examination. In addition, although the satisfaction scores of the patients in

the BATHE group were not statistically significant, they were found to be higher than the other group (30).

RESULT

Preoperative anxiety is a common health problem in our society that negatively affects surgery, anesthesia, and postoperative recovery. Therefore, the issue of preoperative anxiety should be handled more carefully and more studies should be done to reduce the anxiety of patients. We think that allowing patients to express themselves during anesthesia examination, providing explanatory information to patients, and empathy with patients can be an effective way to reduce preoperative anxiety. It can be thought that the inclusion of the BATHE interview technique, which includes all these elements, in the preoperative examination may reduce preoperative anxiety.

		ORIGINAL KEY QUESTIONS	**KEY QUESTIONS FOR PREOPERATIVE EXAMINATION**
B	BACKGROUND (Past)	How is your life going?	What is the reason that brought you here today?
A	AFFECT (Impact)	How do you feel about the course of your life?	How did you feel when you were told that you would undergo surgery?
T	TROUBLE (Concerns)	Is there anything that worries you about this trend?	What worries you the most about the surgery?
H	HANDLING (Coping)	How do you deal with it?	What have you done to deal with this anxiety?
E	EMPATHY	This must be very difficult for you.	You are right to worry, this is a very normal thing. Now I will give you some information about surgery and anesthesia.

Table 1: BATHE and Key Questions

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CHAPTER II

ABDOMINAL COMPARTMENT SYNDROME

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Compartment syndrome; can be defined as increased pressure in limited anatomical spaces. It can develop in the orbit, between the fascia of the extremity or intracranially [1,2]. Abdominal compartment syndrome (ACS) is characterized by abdominal distension, increased intraabdominal pressure (IAP) and increased airway pressure, hypoxia, insufficient ventilation with hypercarbia, impaired renal function, and is a syndrome that develops as a result of the inability to control intraabdominal hypertension furthermore, these disorders can be corrected by abdominal decompression [3,4].

The first measurements of intraabdominal pressure began to be performed after the second half of the 19th century. The first detailed study in the literature is the study conducted in 1911 and showed that animals die from respiratory failure when IAP increases to 27-46 cm H2O [5,6].

DEFINITIONS

INTRA-ABDOMINAL PRESSURE

IAP defines steady-state pressure of the abdomen [7]. As noted in a prospective study, the mean IAP of hospitalized patients enrolled in the study was 6.5 mm / Hg and correlated with body mass index [8]. Therefore, IAP may differ for each patient, and a complete range of standard values may not be mentioned.

ABDOMINAL PERFUSION PRESSURE

Abdominal perfusion pressure (APP) is set up by subtracting the IAP from the mean arterial pressure (MAP). APP has been shown to be better at predicting outcomes than resuscitation indicators such as lactate, arterial pH, hourly urine monitoring, and base deficit [9].

INTRA-ABDOMINAL HYPERTENSION

Intraabdominal hypertension is considered to be values above roughly 12mm / hg and is used as such in research studies. It is graded as: Grade 1 = IAP 12 to 15 mmHg, Grade II = IAP 16 to 20 mmHg, Grade III = IAP 21 to 25 mmHg, Grade IV = IAP> 25 mmHg [7]. IAH is classified as

hyperacute, acute, subacute, and chronic. Duration determines this classification. hyper-acute abdominal hypertension (AH) occurs within seconds (laughing, coughing, defecation), acute AH is formed within hours (trauma, hemorrhage), sub-acute AH within days (medical patients) and chronic AH (obesity, pregnancy) presents over months and years.

ABDOMINAL COMPARTMENT SYNDROME

ACS is defined as a sustained IAP >20 mmHg (with or without an APP <60 mmHg) that is associated with new organ dysfunction/failure. Patients with an intra-abdominal pressure below 10 mmHg generally do not have ACS, while patients with an intra-abdominal pressure above 25 mmHg usually have ACS [2,4]. Patients with an intra-abdominal pressure between 10 and 25 mmHg may or may not have ACS, depending upon individual variables such as blood pressure and abdominal wall compliance.

INTRAABDOMINAL PRESSURE MEASUREMENT

IAP pressure can be measured by direct and indirect methods.

DIRECT METHODS

A metal cannula can be placed in the peritoneal cavity and connected to a saline manometer for direct measurement. In addition, surgeons using laparoscopy can monitor pressure with an insufflator.

INDIRECT METHODS

Inferior vena cava pressure: In experimental studies, it has been shown that the inferior vena cava pressure measured from the transfemorally placed catheter is equal to the IAP. It is not appropriate to measure IAP in humans through the inferior vena cava.

Gastric pressure: IAB can be measured by connecting to a water manometer through a nasogastric tube or gastrostomy tube.

Bladder pressure: Changes in intraperitoneal pressure are directly reflected in intra-bladder pressure changes. Nowadays, this simple and minimally invasive method is preferred. While the patient is lying in the supine position, the Foley catheter is closed where it meets the urinary bladder, and 50 ml sterile saline is administered into the bladder. A 3-way tap is attached from the end of the Foley catheter and connected to the water manometer. This manometer is filled with saline. The symphysis pubis level is marked as 0 cm and the saline level rising on the scale indicates IAB [10].

ETIOLOGY

ACS occurs in critically ill patients and as a result of a wide spectrum of medical and surgical conditions [11–13]. ACS, which is most

commonly recognized after abdominal trauma, may be encountered in cases of intra-abdominal hemorrhage, and these patients are generally exposed to massive fluid resuscitation [14,15]. ACS can also occur as a result of coagulopathies, abdominal aortic surgery, elective major surgery, retroperitoneal pathologies (ruptured aortic aneurysm, pancreatitis), pregnancy and delivery complications, tight abdominal closure, and hepatic transplantation. Postoperative hemorrhage is the most common cause of these conditions [14–21]. It should also be stated that ACS has been observed to develop after hypothermia, septic shock, severe burns (> 30 percent total body surface area), and cardiac arrest. Besides, retroperitoneal and visceral edema that may develop following resuscitation of patients with crystalloids is mentioned in the pathophysiology of ACS.

PATHOPHYSIOLOGY

Cardiovascular system

It has been shown in animal experiments that an increase in IAP causes a decrease in cardiac output (CO). Harman et al. [22] showed that the decrease in CO in the increase of IAP can be corrected with intravenous fluid treatment, the reason for the decrease in the preload is the increase in IAP due to the pooling of blood in the large retroperitoneal veins, and that the increase in IAP occurs due to the functional narrowing of the vena cava inferior at the diaphragm level. With the increase of IAP, CO decreases and systemic vascular resistance increases [23]. The increased pressure is reflected directly into the large retroperitoneal veins, vena cava inferior, and leads to a decrease in blood flow [24]. With the increase in IAP, functional stenosis occurs in the inferior vena cava, anatomical stenosis created by the diaphragm crus with the elevation of the diaphragm towards the chest cavity, and femoral vein pressure, central venous pressure, and right atrial pressure increase in direct proportion to the increase of IAP [24–26]. While the elevation of the diaphragm may occur at pressures as low as 10 mm/Hg, the critical IAP value with changes such as impaired venous return has been shown that 20 mm/Hg [24,27].

Pulmonary system

Respiratory failure may be the first sign of ACS [2]. The effect of IAP increase on pulmonary functions is mechanically dependent on the compression of the lung. Increased thoracic and pleural pressure depresses CO. With the increase in pulmonary vascular resistance, ventilation-perfusion balance is impaired. By pushing the diaphragm up, the lung compliance and thoracic volume decrease, and this situation cause atelectasis and pulmonary infections. The compression effect on the lung in ACS is similar to that in extra parenchymal restrictive lung disease [28]. In the increase of IAB, there is a decrease in PaO2 and an increase in PaCO2, furthermore, in parallel with the increase in pressure of ACS, there

is also an increase in pleural pressure [29]. After abdominal decompression, the airway pressure peak value becomes normal or near normal, and there is a significant improvement in static compliance and PaO2 / FiO2 ratio.

Renal effects

Numerous mechanisms affect renal functions in IAH. Compression of the renal vein increases venous resistance, which disrupts venous drainage, causing renal impairment [30,31]. With the decrease of CO, the renin-angiotensin system is activated, resulting in vasoconstriction in the renal artery [32]. Overall, glomerular perfusion and urine output decrease progressively [33]. It has been demonstrated that IAP causes oliguria at 15-20 mm/Hg and anuria above 20 mm/Hg [5].

Gastrointestinal system

With the increase in IAP, the arterial, portal, and microvascular blood flows of the liver are negatively affected [34,35]. Increased IAP decreases mesentery arterial blood flow and intestinal mucosal blood flow, as well as arterial perfusion of the stomach, duodenum, intestines, pancreas, and spleen. It has been suggested that bacterial translocation increases in regional lymph nodes due to intestinal hypoperfusion [36]. Splanchnic hypoperfusion and acidosis in the intestinal mucosa can be demonstrated with very slight increases in IAB before clinical conditions emerge. When gastric perfusion is evaluated by tonometric gastric intramucosal pH measurements, severe ischemia is observed in parallel with the pressure in the abdomen [34,36,37]. Caldwell and Ricotta [38] increased the IAB to 0-20-40 mm Hg in the study they performed in dogs and found that blood flow was significantly reduced in other abdominal organs except for the adrenal gland. When IAP reaches 10 mm/Hg, this circumstance decreases hepatic and portal blood flow, meanwhile 20 mm/Hg IAP decreases mesenteric and intestinal blood flow [34,35]. Diebel et al. showed that with an increase in IAP, blood flow decreased in the epigastric vessels and tissue hypoxia in the abdominal wall [39].

Central nervous system

Intracranial pressure (ICP) temporarily increases during the short-term rise in intra-abdominal pressure that occurs with cough, defecation, or vomiting [40]. During laparoscopic surgery, the increase in IAP has been shown to cause a significant increase in intracranial pressure [41]. An animal study conducted by Bloomfield et al. showed that without head trauma increased IAP to 25 mm Hg impaired cerebral perfusion [42]. Similarly, ICP appears to be elevated in the presence of persistent IAH. High ICP persists as long as IAH is present, which can lead to a critical reduction in cerebral perfusion and progressive cerebral ischemia [43,44].

CLINICAL FINDINGS

Communication is not feasible since most of these patients are critically ill. Therefore, IAH should be detected early and prevent it from progressing to ACS. Some of these patients may describe symptoms of abdominal pain, dyspnea, and weakness. Almost all patients have abdominal distension on physical examination. Progressive oliguria, respiratory distress are common findings in patients with ACS. Besides tachycardia, hypotension, jugular venous distension, and peripheral edema, as a sign of decreased hypoperfusion, decreased consciousness, cold skin, or lactic acidosis may be detected. Unfortunately, imaging methods are not beneficial in the diagnosis of ACS. Performing direct radiography or computed tomography may reveal abdominal and thorax findings that may cause ACS or caused by ACS.

DIAGNOSIS

Patients who have undergone abdominal or retroperitoneal surgery, requiring effective fluid resuscitation for any reason, laparotomy after abdominal trauma, coagulopathy, and hypothermia are at great risk [2,45]. An essential approach in diagnosis is the measurement of bladder pressure, which is also a minimally invasive method [46]. Due to variations in detected intravesical pressure occur with varying head position, care must be taken to ensure uniform head and body positioning from one measurement to another [47,48]. Even if there are significant physiological changes, according to the studies, there is no indication for abdominal decompression when IAP is at 10-15 cm H2O (grade I). When the IAP is 15-25 cm H2O (grade II), treatment may be required based on the clinical condition of the patient. If oliguria and hypoxia are absent or if the rise in airway pressure is not hazardous, there is no indication for abdominal decompression, but close monitoring is required. There is an indication for abdominal decompression in the majority of patients with IAB 25-35 cm H2O (grade III) and patients with 35 cm H2O (grade IV).

MANAGEMENT

Management of IAH and ACS and treatment approaches aim to keep IAH at acceptable levels with supportive treatments and abdominal decompression when necessary (IAP <12 mm/Hg). IAP should be measured every 4-6 hours, and IAP <15 should be kept medically. IAH / ACS medical management can be divided into 5 main topics. It includes removal of intraluminal contents, evacuation of intra-abdominal space-occupying lesions, improvement of abdominal wall compliance, optimization of fluid therapy, optimization of systemic and regional perfusion, respectively [46]. In addition to nasogastric decompression, rectal tube application can be performed to remove the intraluminal contents. The gastrointestinal system load is tried to be reduced by minimizing enteral

nutrition and the use of prokinetic agents [49–52]. Space-occupying formations in the abdomen are defined with the help of USG and CT, even if appropriate, initially percutaneous drainage, or if not, extraluminal relief is provided by surgical intervention [46]. Pain control and sedation is an essential step in improving abdominal wall compliance. The positioning of the patient should be in a neutral position, especially in bladder pressure measurement, and the patient should not be given a head-up position for more than 30 degrees. In cases of increased IAP, Trendelenburg position and neuromuscular blockade should be considered [47,53–57]. Fluid administration restriction in patients with IAH may reduce the risk of ACS. It is beneficial to keep the fluid administration balance at zero or negative. Hypertonic or colloids should be preferred in fluid replacement [58].

Decompressive laparotomy (DL) should be the ultimate choice in cases where medical treatment fails in severe IAH / ACS. Although the immediate decline of the IAP results in rapid recovery of organ functions, DL is associated with multiple complications despite advanced open abdominal management techniques. If the IAP is above 20 mm / Hg and is accompanied by a new organ dysfunction, besides if IAH / ACS is refractory to medical therapy, then surgical decompression is strongly recommended [46]. Surgical decompression is frequently followed by an open abdomen (OA), and OA monitoring and management is vital in terms of mortality and morbidity. The open abdomen is a life-saving method, but the longer the time, the greater the morbidity [59–61]. Through the use of negative pressure wound therapy, this technique limits visceral adherence to the anterolateral abdominal wall while supporting medial fascial traction, which may improve fascial closure rates among those with an open abdomen [62–64]. Although early closure of OA may cause recurrence of ACS, it should be closed as soon as possible to avoid morbidity.

Whether decompression is not performed or is delayed, mortality increases. Therefore, patients in the risk group should be identified, and IAP should be measured. Delay in diagnosis causes failure of organ systems. While mortality was close to 100% in high-risk cases without decompression, overall reported patient mortality is considerable (up to 50 %), even after decompression [65].

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CHAPTER III

POSTGASTRECTOMY SYNDROMES

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Postgastrectomy syndromes are cases of continuation of stomach-related signs and symptoms after gastric operations. Postgastrectomy syndromes are often caused by changes in gastrointestinal system physiology. Therefore, patients with postgastrectomy syndrome often require physiological evaluation prior to an intervention.

INCIDENCE

Changes in the need for elective gastric surgery have decreased the frequency of postgastrectomy syndromes in recent years. Due to the increased use of H2-receptor antagonists and hydrogen pump inhibitors, elective surgery for peptic ulcer disease has decreased 10-fold in the last 30 years. Gastric operations (proximal gastric vagotomy [PGV], parietal cell vagotomy) that slightly disrupt the motor functions of the stomach may also be the cause of the gradual decline in postgastrectomy syndromes. While the need for elective surgery for peptic ulcer has decreased, the need for urgent surgery has remained unchanged in the last 20 years.

Although postgastrectomy syndrome has been reported between 5-50% in patients undergoing surgery due to peptic ulcer, the incidence is approximately 20% in many publications. In a prospective study by Donahue et al., The incidence of long-term morbidity after truncal vagotomy and antrectomy was 26%, compared with only 5% after PGV (1). This difference emphasizes the physiological importance of injuring or bypassing the pylorus and distal antrum in the occurrence of postgastrectomy syndromes. Another factor affecting the incidence of postgastrectomy syndrome is the patient's gender; it is more common in women. Incidence also varies depending on the definition of syndromes used in a study and which syndromes were included in the study(2) .

PATHOGENESIS

Most postgastrectomy syndromes are due to gastric motility disorders caused by surgery. Knowing the mechanisms that control stomach motility and emptying in a healthy person helps to understand the pathogenesis.

GASTRIC EMPTYING IN A HEALTHY PERSON

Motor functions of a healthy stomach; The reservoir function in which food is accepted and stored in the form of loading, the mechanical-digestion function that breaks down large pieces of food into small pieces and the transport function that allows food to pass into the small intestine for further digestion and absorption. The decrease in the tone of the proximal part of the stomach with swallowing (receptive relaxation) or overeating (accommodation, compliance) are vagal managed responses and are related to the reservoir function of the stomach. Subsequently, tonic contractions of the proximal stomach allow the proximal gastric contents to be transported to the distal stomach and duodenum. The peristaltic contractions of the distal stomach and pylorus assist in the mechanical grinding and transport of large food particles. Vagal stimulation of the distal stomach increases these contractions. A healthy pylorus region has a separate function that prevents the passage of large particles to the small intestine while controlling the reflux of the duodenal contents to the stomach. The small intestines also play a role in gastric emptying by resisting the flow of stomach contents and by activating neural and hormonal mechanisms that slow down gastric emptying with feedback.

POST-OPERATIONAL CHANGES

Gastric surgery can affect some or all of the motor functions of the stomach. PGV disrupts the compliance of the proximal stomach and reduces reservoir function. Distal gastric vagotomy or distal gastric resection, including pyloric resection or ablation, reduces mechanical-digestive function. Pyloric operations allow intestinal contents to return to the stomach. The type of gastroenterostomy can affect the transport function of the stomach mechanically or functionally by decreasing or increasing the resistance to flow.

The functions of the gastric mucosa that can be changed by gastric surgery: acid and enzymatic secretion, protection of the stomach from corrosive digestive fluids, hormonal secretion that prolongs the gastric phase of digestion, and secretion of the intrinsic factor that facilitates vitamin B12 absorption and the gastric factor that provides iron absorption. Changes in these functions may contribute to the occurrence of postgastrectomy syndrome.

GENERAL APPROACH

Advances in understanding the control of gastric emptying have enabled surgeons to classify postgastrectomy syndromes more specifically. Anatomical factors associated with the syndrome should be considered and, if possible, the previous procedure should be fully defined. Usually, endoscopy and barium radiography are required. Liquid- and solid-phase gastric emptying scintigraphs are useful in documenting gastric emptying patterns. In addition, measurement of gastrointestinal motility is an excellent research modality useful in patient management. Considering the long-term complaints and economic losses of the patients, all possible tests should be performed if the operation planned or performed is desired to be the last operation (Congo red test, Sham feeding test, solid phase discharge radionuclide imaging, bile reflux radionuclide imaging, alkaline infusion studies, esophageal pH / pressure / telemetry studies, psychiatric evaluation).

Postgastrectomy syndromes usually improve over time. Medical treatment should be extended to 1 year, except in severe cases. Medical treatment mainly consists of changing diet and habits, so this component should be treated before surgical treatment is recommended. Operation can be considered if medical, diet and psychological treatments are not successful (3).

VAGOTOMY COMPLICATIONS

Since vagotomy is an important part in operations performed on the stomach and duodenum, complications of vagal denervation are also discussed. Vagotomy types that have a place in practical use:

Truncal vagotomy (TV); total abdominal vagotomy causes denervation of the whole stomach, biliary system, pancreas, small intestine and proximal colon.

Selective gastric vagotomy (SV); Although there is denervation in the whole stomach, hepatic and celiac branches are preserved.

Highly selective (Proximal gastric or parietal cell) vagotomy (HSV); only acid-secreting parietal cells (corpus, fundus) are denervated. Since the anterior and posterior Laterjet nerves are protected, the innervation of the antrum of the stomach continues. Therefore, although gastric emptying changes slightly, there is no need for drainage as in others (4).

OPERATIVE COMPLICATIONS OF VAGOTOMY

Complications during the operation are usually the result of technical errors. If these complications are noticed intraoperatively, the first steps to be taken are summarized in the table 1.

Table 1: Intraoperative Complications Of Vagotomy

Complication	Management
Spleen injury	Aviten / gelfoam, splenorrhaphy, splenectomy
Distal esophagus injury	Repair, fundoplication (Nissen)
Esophagogastric rupture	Resection of fragmented tissues, possible indication for esophagogastrectomy
The rupturing of crus	Repair
Pneumothorax	If asymptomatic or <15% follow-up and repeat X-ray; if not tube thoracostomy
Liver trauma	
Hematoma	Follow-up
Laceration	Omental patch in the application of pressure, deep injury or parenchymal laceration
Pancreatic trauma	Drainage (somatostatin)
Colon injury (splenic flexure)	Repair if contamination is minimal or <50% of the injury environment; resection and reanastomosis if the injury is larger but contamination is less; diverting colostomy in other cases
Vascular injuries	
Phrenic vein	Stitched lacing

Left hepatic vein	Repair if possible, otherwise stitched lacing
Ductus thoracicus	Stitched binding and drainage
Left gastric artery	Stitched lacing

If the complication is not detected at the time of operation, the patient will have severe upper abdominal and chest pain; There will also be complaints of mediastinal air or left-sided atelectasis and pleural effusion. Water-soluble contrast radiographs are useful to assess leakage. When the diagnosis is considered, antibiotics should be started and continued until the postoperative sepsis findings disappear (5).

EARLY POSTOPERATIVE COMPLICATIONS OF VAGOTOMY

Recognized early complications of vagotomy include (1) gastric atony and delayed empthying (TV or SV) despite proper drainage, (2) dysphagia and even achalasia, (3) functional gastric outlet obstruction due to excessive denervation of the antral-pyloric region with HSV, and (4) It is the small curvature necrosis of the stomach due to devascularization during HSV.

Gastric atony with delayed gastric emptying, the distal stomach and pacing-maker potential regulating the peristalsis of the pylorus is in the greater curvature of the stomach. The loss of coordinated peristalsis can be attributed to the loss of this single dominant pace-maker and ultimately multiple pace-maker activity begins in the myenteric plexus. This condition impairs gastric dilatation and the advancement of stomach contents. The dominant symptoms are nausea, bloating, and abdominal distention. Serious atony is reported in 1%, although it has been reported between 2 and 20% in various series. In most of the cases, nasogastric decompression, use of prokinetic agents and giving time solves the problem in 3-4 weeks. In rare cases where the problem cannot be solved, drainage procedures should be considered (6).

Dysphagia is rare following vagotomy and is observed in 2% of patients. It is more common after HSV. It occurs about 4 weeks after leaving the hospital. Although the cause is not fully clarified, it is thought that manipulation and surgical trauma on the esophagus caused this. If no other etiological reason to explain can be found, the picture will recover spontaneously over time (7).

Post-Extended HSV Antral-Pyloric Stasis, the important point in HSV operation is the determination of the distal border of denervation. If

the denervation is done too wide, damage to the antrum motor fibers causes gastric stasis and insufficient discharge from the pylorus. Major symptoms are bloating, nausea and vomiting. Permanent stasis may occur if the pylorus and duodenal bulbus are deformed as a result of the scatrization of the pyloric region. If there is a significant stenosis in the pyloroduodenal region and endoscopic interventions are inconclusive, a drainage operation is required, with Finney pyloroplasty being preferred (8).

Necrosis OF stomach lesser curvature after HSV is usually observed within 24-72 hours. In these patients, sudden and severe pain in the lower abdomen, sensitivity and defense together with a shock condition are seen. In reefloration, a limited or wide area of necrosis is detected in the small curvature. The small curvature arteries of the stomach are of the terminal type, and although their devascularization plays a role during HSV, gastric distension, underlying atherosclerosis, or inattentive damage to surgical instruments play a more important role. The management of this frightening complication is resection, primary closure and omental patch placement if the necrotic area is limited, whereas near total or total gastrectomy may be required in large necrosis (8).

LATE COMPLICATIONS OF VAGOTOMY

Among the complications of vagotomy, diarrhea and changes in bowel habits have been the most striking since the beginning. Intestinal function changes ranging from constipation to severe diarrhea have been reported in 0-70% of patients who underwent truncal vagotomy.

Postvagotomic diarrhea, although all types of gastric surgery may cause postoperative diarrhea, the incidence of diarrhea is higher in patients who undergo vagotomy. While the highest incidence is truncal vagotomy with 20%, this rate is 6% and 4% in PGV with selective vagotomy and pyloroplasty, respectively. Diarrhea is usually episodic. Explosive diarrhea attacks can last for days and then not recur for months. Although symptoms of dumping syndrome may be present, postvagotomic diarrhea can generally be distinguished from dumping-related diarrhea. Symptoms usually resolve in the first year following the operation and rarely remain a serious and persistent problem.

The mechanism of postvagotomic diarrhea has not been explained. The decrease in the incidence with the application of more selective vagotomy suggests that vagal denervation of the small intestine and biliary tract plays a role in the pathogenesis. There are also changes in the rate of gastric emptying. Decreased receptive relaxation and rapid emptying of gastric juices are associated with the presence of postvagotomic diarrhea. Changing the enteric flow path and velocity of the chyme causes malabsorption of nutrients normally digested by mucosal cells. In this way eg. Subclinical lactase insufficiency is revealed by gastric surgery and

postoperative diarrhea may develop against the intake of previously asymptomatic foods.

Mechanisms suggested in etiopathogenesis:

1- Growth of coliforms and other bacteria as a result of fermentation due to gastric alkalinization and gastric stasis.

2- Motility change; receptive relaxation and gastric emptying variations from the pylorus lead to a timing disorder in the discharge of gas, fluid and chyme into the intestine.

3- Decreased intestinal villi and enzyme content and enzyme activity in epithelial cells

4- Splanchnic blood flow decreased

5- Disturbance in bile discharge into the duodenum

There are no specific tests for diagnosis. The diagnosis is made by clinical findings and attention should be paid to distinguish it from other postgastrectomy syndromes that often coexist. Other causes of diarrhea should also be considered. Stool culture and stool fat measurement should be done routinely. Gluten-sensitive enteropathy may occur after gastrectomy, which can cause diarrhea and malabsorption. Endoscopy and small bowel biopsy should be performed in patients with weight loss and malabsorption.

Reducing the intake of liquid and lactose-containing foods are effective dietary practices in treatment. Postvagatomic diarrhea usually resolves spontaneously within 6 months to 1 year. Antidiarrheal agents such as diphenoxylate or loperamide and bile salt resin such as cholestyramine are useful in combination with atropine. Surgical treatment is rarely recommended, but if necessary, success has been reported in creating the 10- or 15-cm antiperistaltic jejunal segment 100 cm distal to the gastroenterostomy or Trietz ligament (3).

Postvagotomic reflux esephagitis is extremely rare. An inexperienced surgeon can cause distal esophagus dysfunction with trauma such as disrupting the right crus fibers while mobilizing the vagus.

Postvagotomic cholelithiasis is a general belief that vagotomy causes gallstone formation, although the debate continues. It has been reported that especially truncal vagotomy increases the incidence of gallstones and this increase is seen especially in patients with hypotonic gall bladder (9).

POSTGASTRECTOMY COMPLICATIONS

Complications seen after gastric and duodenal operations are divided into two categories; The first is complications seen in the early

period, and generally depends on operational errors and pathological anatomy. The second group is the physiology-related complications that occur during long-term follow-up and are changed by operation. At the same time, chronic obstructive problems of the upper gastrointestinal system, which are involved in the reconstruction procedure performed in case of removal of the stomach, are also included in the second group.

EARLY POSTGASTRECTOMY COMPLICATIONS

BLEEDING

Although intragastric bleeding is frequently observed after gastric resection, the aspiration fluid acquires a serohemorrhagic character after a short time and no blood is seen after 24-48 hours. If the bleeding originates from the veins in the anastomosis line or the ulcer area and the bleeding that starts 2-3 days after the operation continues 5-6 days after the operation, endoscopic interventions may be beneficial. However, operative approaches are safer in most cases. The timing of the reoperation is the real decision. If the amount of bleeding exceeds three units, a reoperation decision should be taken. Existing reconstruction can be changed when using various bleeding control techniques (Rosoff method).

Intraperitoneal hemorrhage is usually the result of intraoperative injuries of various organs and often results from inadequate control of omental vascular bleeding. Reoperation decision is based on clinical signs such as increased heart rate, decreased blood pressure and abdominal distension. Systematic control of the operated area is required (10).

SUTURE LINE LEAKS

DUODENAL STUMP

Duodenal stump leaks following gastrectomy and Billroth II reconstruction are serious, life-threatening complications if not recognized and managed appropriately. It may not always be possible to avoid complications, as certain patients are at higher risk. These patients were cases with intense inflammation surrounding the pylorus and duodenal bulb, where the anastomotic margins could not be brought together without creating tension, and a large (2.5 cm) ulcer penetrated deeply in the posterior duodenum. Other factors that increase the occurrence of this type of leakage; Devascularization of the stump due to unnecessary overuse of sutures, localized infection due to hematoma or fluid accumulation, bleeding from the pancreatic bed, postoperative pancreatitis and afferent loop obstruction. Leakage is often seen between 2nd and 5th days postoperatively. The symptoms of the patient are sudden severe abdominal pain, fever and shock-like clinical condition. In some cases, the clinical picture may be subtle. Jaundice, which occurs as a result of absorption of bile spreading into the peritoneal cavity, is a late-stage finding. Duodenal

leakage is diagnosed with bile aspirated from the right upper quadrant fluid meeting seen on computed tomography or ultrasound. Treatment is adequate and adequate closed-suction drainage of the upper right quadrant. Small localized fluid collections can be drained using interventional radiological techniques. If the fluid collection is large and not well localized, operative drainage is the most reliable approach. Nasogastric drainage and feeding jejunostomy to the efferent leg should be performed in addition to the gum-drainage. The aim is to create a controlled fistula to the skin and to reduce biliary and pancreatic secretions by preventing food entry into the stomach. In this sense, it is also appropriate to use octreotide (there is no condition such as non-responsiveness of high flow [> 500cc / day] fistulas). Intensive supportive care is very important in the postoperative period. Broad-spectrum antibiotics and total parenteral nutrition may be required. Failure of fistula closure is often due to tract infection, insufficient drainage, presence of foreign bodies, and distal obstruction(10).

BILLROTH I GASTRODUODENOSTOMY

The occurrence of this type of anastomotic leak is more common in cases of severe scarring and inflammation of the duodenum. Leakage is rare in appropriately selected patients and if it occurs, the picture is mild. Rarely, mild pain and tenderness may be detected with bilious fluid. Usually, drainage is interrupted within 24-48 hours and reoperation is rarely required. Administration; It includes the investigation and control of enhancing factors such as distal obstruction, serial evaluation of the fluid cavity with CT sectioning, complete drainage and antibiotic administration until the symptoms of sepsis, followed by enteral alimentation of the initiated intravenous hyperalimentation from feeding catheters that will be placed beyond the anastomosis, and the use of octreotide.

The main indications for surgery are peritonitis, sepsis, or failure to control intraabdominal fluid collection. Small leaks can be managed with repair and omental patch, while reconstruction is indicated for large separations.

BILLROTH II GASTROJEJUNOSTOMY

This complication is extremely rare. If there are signs of peritoneal irritation, diagnosis can be made by gastrograph examination or endoscopy. Although small leaks can close spontaneously, operation is indicated for uncontrolled leaks. Omental patch and external drainage should be preferred for small leaks in the operation; If there is a wide opening, gastric stump resection and a new Billroth II anastomosis can be performed, or preferably Roux-en-Y operation is applied (11).

OBSTRUCTION SYNDROMES

STOMA OBSTRUCTION

They are uncommon complications following Billroth I, Billroth II or Roux-en-Y operations. Generally, the patient can take it orally for 3-6 days. If nausea, bloating and vomiting occur with oral intake, there is a congestion.

Although loss of vagal innervation plays a role, the cause is often edema. The blockage causes fluid accumulation in the gastric stump, causing distension and plenty of fluid comes out; intravenous fluid support and drainage solve the problem in a few days. Prolonged obstruction, inability to pass through the endoscope, or the absence of passage in barium radiography indicate inadequate or incorrect surgical technique. Choosing Billroth I is a wrong decision when there is excessive intraoperative scarring in the duodenum. If there is persistent stomal stenosis after Billroth II operation, inflammatory adhesions should be considered in the sections just below the anastomosis line of the effent loop. In some cases, both loops can be affected by inflammation. Causes such as excessive fat necrosis, omentum inflammation or anastomotic leak may also play a role in stoma obstruction. Herniation of the loops can also be caused by a defect in the mesocolon. Barium radiography can be made as early as the 7th postoperative day. If the feeding tube cannot be placed in the efferent loopa under fluoroscopy, there is an indication for parenteral nutrition.

If prolonged obstruction lasts more than two weeks, reoperation is required. Endoscopic or surgical dilatation often does not improve in these types of anastomosis. If Billroth I is done, side-to-side gastrojejunostomy should be done before the anastomosis is handled.

If the first operation is Billroth II, the decision is made based on intraoperative findings. If there is kink due to adhesion, it is sufficient to remove it and a feeding jejunostomy is recommended. If there is a herniation of the efferent or afferent loop, reduction is performed and the defect is closed. In the presence of necrosis, resection is performed and gastrojejunostomy is renewed or Roux-en-Y reconstruction is performed according to the situation. In such cases, removal of the omentum majus is recommended.

In some cases, discharge is difficult, although an obstruction cannot be demonstrated with radiological and endoscopic examinations. It can recover spontaneously after weeks. Most surgeons attribute this to vagotomy. This situation is more common after Roux-en-Y anastomosis (3).

ACUTE AFFERENT LOOP OBSTRUCTION

Afferent loop syndrome is caused by obstruction of the afferent loop of loop gastrojejunostomy. This can occur in both acute and chronic forms. Although its acute form is usually seen in the first 1-2 weeks after surgery, it can also be seen 30 years after gastrectomy. This situation occurs with the bending of the afferent loop, its adhesions, rotation around itself, herniation or complete obstruction due to its volvulus. Acute obstruction of the leg predisposes to duodenal stump leakage, in which case acute obstruction should be investigated. It has become a rare syndrome with better recognition of anatomical factors, including the use of the long afferent loop that cause this syndrome.

Afferent loop obstruction is a closed-loop obstruction. Bile and pancreatic secretions accumulate, the pressure increases and as the ductus pressure increases, serum amylase and alkaline phosphatase increase, mimicking pancreatitis. Patients may complain of severe abdominal pain, nausea, and biliary vomiting. A fluid-filled mass can be observed in physical or radiological evaluation or by ultrasound studies. With increasing pressure in the afferent period, serum amylase concentration may increase, leakage from the duodenal stump and pressure necrosis may occur in the intestine. Immediate surgical treatment is required as soon as the diagnosis is confirmed. In surgery, as long as pressure necrosis of the afferent loop does not occur, jejunojejunostomy is performed, or the necrotic segment can be removed and a duodenojejunostomy can be performed on the Roux leg. If severe ischemic damage has occurred that cannot be done, larger resection, including pancreaticoduodenectomy, may be required (11).

HEPATOBILIARY-PANCREATIC COMPLICATIONS

POSTOPERATIVE PANCREATITIS

Although it is a rare complication (<5% after gastric resections), its mortality and morbidity are quite evident. Generally, the reason is the trauma of the pancreatic head during the dissection of the large ulcer crater during the operation or the closed dissection of the pancreatic head distant from the duodenum. In extreme dissection, the Santorini canal can be injured and in 5-8% of cases this duct is the main channel of the pancreas.

Pancreatitis attacks develop in the first 3 days after the operation. The patient complains of generalized abdominal pain and fever when there is restlessness, agitation; there is tenderness in the abdomen and bowel sounds have decreased or disappeared. There is an increase in leukocytosis, serum amylase and lipase in blood tests. If there is pancreatitis due to trauma in cases with Billroth II, the treatment is medical and morbidity can

be increased with early operation. Conversely, it requires urgent surgery if there is acute afferent loop syndrome. Therefore, emergency ultrasound and preferably CT, if possible, should be performed for differential diagnosis. Standard medical pancreatitis treatment will be sufficient (12).

POSTOPERATIVE JAUNDICE

Mild jaundice is likely to be observed in the early postoperative period of gastrectomy operations, especially if there is extensive dissection of the duodenum. Postoperative edema in this area can lead to partial obstruction of the compound bile duct. There is mild hyperbilirubinemia, it regresses in a few days. Other causes of jaundice; Re-absorption of bile discharged into the peritoneum after anastomotic leaks, overlooked common bile duct stones, acute pancreatitis, ascending cholangitis, transfusion reactions, pulmonary embolism, sepsis, hemoperitoneum, anesthetic toxicity, liver failure, and iatrogenic injuries of the common chole (12).

BILE DUCT OR PANCREATIC DUCT INJURIES

It is not seen very often, but this complication exists as a dangerous possibility in duodenum showing excessive scarring and shortening. In distal gastric resections, if there is excessive scarring, the hepatoduodenal ligament should be opened and the duodenum should be cocherized to determine the place where the common bile duct was fully explored and opened to the duodenum. In cases where the anatomy is seriously impaired, a T-tube or catheter is placed. If severe bile duct injury occurs, appropriate management should be done (12).

UNCLASSIFIABLE COMPLICATIONS

NECROSIS OF THE GASTRIC STUMP

It is a rare complication of gastric resections. In cases where the gastric artery is ligated from its root, the possibility of developing this complication increases if splenectomy is also performed. In cases where the gastric artery is ligated from its root, the stump can only be fed by the branches of the phrenic artery, rarely, the left lower phrenic artery emerges from the left gastric artery, and if it is tied in this case, the stump is fed to the splenic artery. In this last case, if splenectomy is added, stump necrosis will be inevitable, so there is a near total gastrectomy indication.

Symptoms of such necrosis are severe pain in the upper abdomen. A condition similar to shock develops within 24-72 hours following the operation. Dark brown colored fluid may come from the upper quadrant drain or leak is observed in contrast radiographs given from the nasogastric. As soon as the diagnosis is made, the operation is inevitable. If there is a viable gastric remnant, an end-to-side gastrojejunostomy is performed on the jejunum leg of the Roux-en-Y. Otherwise, gastrectomy

and Roux-en-Y esophagojejunostomy should be performed. If there is necrosis in the esophagus, then esophagostomy and nutritional jejunostmi come to the fore. In this case, mortality is high(13).

GASTROSTOMY COMPLICATIONS

This procedure, which was performed less frequently than in previous years, is limited to patients with severe pulmonary dysfunction, esophageal reflux or motility disorder who cannot tolerate nasogastric decompression. No matter how much attention is paid to the surgical technique, 5-15% of complications are seen. Intra-gastric or peritoneal bleeding, peritoneal leakage and peritonitis, intestinal obstruction, failure of gastrostomy opening to close, and separation of the stomach from the abdominal wall are complications.

FAULTY GASTROILEOSTOMY

This complication is not as rare as it might seem. It is caused by a combination of reasons such as inadequate exposure, an inexperienced surgeon, and poor anesthesia, as the ileum is presumed to be the proximal jejunum. Symptoms are sometimes mild and disappear in the second week after the operation. In most of the cases, malodorous belching is manifested by intense diarrhea and electrolyte disturbances when the patient starts eating. In the following weeks, the patient rapidly loses weight, develops malnutrition and cachexia. The diagnosis is made with barium upper GIS radiographs. Its management consists of reoperation, disruption of anastomosis, and gastrojejunostomy (Billroth II, Roux-en-y).

OMENTAL INFARCT

It is a rare complication caused by strangulation and incarceration of the omentum in the retroanastomotic space or other internal spaces. Symptoms are sudden pain, local tenderness, fever and leukocytosis within 1-3 days. The table resembles appendicitis. Abdominal exploration is often to rule out possible more serious complications.

INTRAABDOMINAL ABSCESS

This complication is not uncommon and is often more prone to development in patients with gastric cancer and long-term obstruction of the gastric outlet. It depends on the spread of the colonized lumen content. Symptoms include gradually worsening upper abdominal pain, anorexia, fever, and leukocytosis. Although CT-guided percutaneous evacuation of intra-abdominal abscesses has been popular lately, its use is limited to single lumen abscesses; Multiple abscesses and abscesses adjacent to the intestinal wall should be treated surgically(13).

LATE POSTGASTRECTOMY COMPLICATIONS

RECURRENT ULCER SYNDROMES

STOMAL ULCERATION / RECURRENT ULCER (MARGINAL ULCER)

Marginal ulcer is also called anastomotic ulcer, stoma ulcer, these ulcers usually form on the side of the efferent jejunal loops in the immediate vicinity of the anastomosis. Although the average incidence is 1-5%, this rate varies according to the type of surgery performed. It is only 15-20% after gastroenterostomy, 10% after vagatomy and pyloroplasty or PGV surgery, 5% after only subtotal gastrectomy, 0.5-3% after vagotomy and antrectomy (14).

Predisposing factors leading to marginal ulcer formation include:

1. Incomplete vagotomy (the most common cause)
2. Insufficient antrum resection
3. Gastric stasis
4. Zollinger Ellison syndrome
5. Long afferent loop
6. G-cell hyperplasia
7. Gastrinoma (with / without MEN syndromes)
8. Ulcerogenic drugs (eg: NSAIDs)
9. Non-absorbable suture material
10. Parathyroid adenoma

All these factors lead to the continuation of the acid-peptic activity and the development of marginal ulcer due to the continuation of direct parietal cell stimulation, the release of gastrin, and the inability of sufficient alkaline fluid to reach the anastomosis line.

Symptoms in patients are the same as symptoms of peptic ulcus. The pain is usually to the left of the midline in the epigastrium. It rarely spreads to the back. Complications such as bleeding, perforation, penetration and obstruction can be seen. Major gastrointestinal bleeding may occur in 1/3 of patients with marginal ulcers. Perforation is seen at a rate of 5%. If the ulcer penetrates the colon, a gastrojejunocolic fistula may develop.

Barium radiography and endoscopy are required to differentiate marginal ulcer from other postgastrectomy syndromes. 50% of marginal

ulcers are seen with barium X-ray. Today, endoscopy is usually performed as the first step and ulcers that cannot be seen on barium radiography are detected. Occasionally, non-absorbable sutures also cause marginal ulcers. If this suture is removed endoscopically, the ulcer will heal. In patients with marginal ulcers, performing gastric acid analysis and measuring serum gastrin levels as a second step may rule out gastrinoma, insufficient antrum resection, G-cell hyperplasia and incomplete vagotomy. The differentiation of insufficient antrum resection from gastrinoma is made with the secretin test. While secretin stimulation (2 U / kg) raises the gastrin level in gastrinoma (increase> 100pg / ml), in healthy individuals, G-cell hyperplasia and insufficient antrum resection does not respond (increase <40pg / ml). In terms of hyperparathyroidism, serum calcium levels of patients with gastrinoma should also be checked.

If the aforementioned reasons are ruled out, the focus should be on incomplete vagotomy first. If there is no response to medical treatment and reoperation is considered, the cornerstone of the evaluation is acid secretion studies.

Medical therapy is often sufficient to control symptoms in cases where endoscopy confirms the presence of recurrent ulcers. In this way, 80% success is achieved, and other recurrences that may occur are prevented by 70% by continuing the treatment. Omeprazole is the drug of choice, but its long-term effects are not yet clear.

Surgical treatment is indicated for patients who do not respond to medical therapy. Endoscopy performed before surgery provides information about the localization while confirming the ulcer. In addition, solid-phase radionuclide gastric emptying studies are required to distinguish concomitant gastric outlet disorders. Surgical treatment depends entirely on the type of first surgery. Recurrent peptic ulcer development following a definitive operation necessitates a more definitive operation. There is no consensus on the generally accepted optimal approach for the management of recurrent duodenal ulcers. Truncal vagatomy and antrectomy are performed in the surgical treatment of ulcers that develop after PGV. Vagotomy and antrectomy are applied only for ulcers that develop after gastroenterostomy. In the surgical treatment of ulcers that develop after vagotomy and drainage, if the vagotomy is incomplete, revagatomy is performed. If the vagatomy is complete, antrectomy is added. The reason for recurrence after vagotomy and antrectomy is usually incomplete vagatomy, in which case the vagatomy is completed. If recurrence cannot be prevented, total gasrectomy and Roux-en-Y reconstruction are preferred. If medical treatment is unsuccessful in ulcers due to Zollinger-Ellison Syndrome, total gastrectomy is performed. If hyperparathyroidism is detected, this condition is treated first.

The role of Roux-en-Y reconstruction in recurrent ulcer management is controversial. Although Roux-en-Y operation prevents bile reflux, the risk of developing marginal ulcers on the jejunal side of the reconstruction is high. In all cases, extreme care should be taken to ensure complete re-vagotomy.

GASTROJEJOCOLIC FISTULA

This complication is almost non-existent these days. The observation of this complication following a definitive operation requires questioning the presence of Crohn's Disease or carcinoma. The long-term high-dose use of NSAIDs and abuse by patients is the etiological cause of reported anecdotal cases.

Symptoms are excessive weight loss, diarrhea, phechaloid-smelling belching and phecaloid vomiting. Diagnosis is made by barium contrast studies and CT. While endoscopy is useful in differential diagnosis, it is often surprisingly insufficient for observing fistulae.

Although the bowel is rested, parenteral nutrition, IV antibiotics and antisecretory agents (H2 blockers) are started in the treatment, most of the cases require surgery. The crucial point in necessary resection and reconstruction operations is to complete the vagotomy. The specimen removed should be evaluated pathologically for cancer investigation (12).

MECHANICAL DISORDERS.

CHRONIC AFFERENT LOOP OBSTRUCTIONS

The chronic form of afferent loop syndrome is caused by partial occlusion of the afferent loop, often following Billroth II. With the accumulation of bile and duodenal secretions in the lumen of the afferent loop, the pressure inside the lumen begins to increase. The patient feels pain with distension due to pressure increase; when the pressure reaches a certain level, the obstruction is overcome and the lumen contents rapidly flow into the gastric cavity, causing projectile vomiting; however, food left the stomach through the efferent loop until the pressure parallel to the increased secretions with food intake reaches a sufficient level. Therefore, the fact that the used material does not contain the eaten foods surprises the patient and guides the clinician in terms of diagnosis. Symptoms include eating pain, nausea, and vomiting in the right upper quadrant. Following vomiting, abdominal pain subsides.

The patient reduces food intake to relieve symptoms. Weight loss occurs. Blind loop syndrome occurs with bacterial growth, bile salt deconjugation, steatorrhea, vitamin B12 and iron deficiency in the obstructed bowel loop.

Many mechanisms can cause chronic afferent loop syndrome. As in the acute form, bending or herniation, folding and volvulus of a long afferent loop causes partial occlusion. Anastomotic stricture, adhesion formation, stoma ulcer, jejunogastric intussusception and carcinoma may also cause the chronic form.

The main problem in diagnosis is to differentiate alkaline reflux gastritis from this disease. If the foods are mixed with bile and the pain continues after vomiting, this situation is mostly in favor of alkaline reflux gastritis. With endoscopy, the anastomosis area can be examined directly, pathological areas can be distinguished and biopsy can be taken. CT and ultrasound are other treatment modalities that can be used.

After the diagnosis has been made, surgical correction is required. Billroth II anastomosis can be converted to Billroth I. Performing a Roux-en-Y anastomosis may be simpler and good clinical results are seen (15).

CHRONIC EFFERENT LOOP OBSTRUCTIONS

Efferent loop syndrome is the result of partial or complete mechanical obstruction of the efferent loop at or near the gastrojejunostomy line. Symptoms may appear months or years after surgery and consist of diffuse abdominal pain, nausea, and bilious vomiting. After Billroth II reconstruction, two traps can be prepared in the posterior; Above and below the anastomosis, these potential areas may predispose to internal herniations, particularly in antecholic anastomosis. If the symptoms appear in chronic and mild forms, obstruction is partial and mostly intermittent. The diagnosis is confirmed by observing a slowing or stopping of gastric emptying above the obstructed point of the efferent loop in radiological examination with contrast material. Surgical treatment is required. In laparotomy, it is often found that the cause of obstruction is the adhesion of the efferent loop close to the gastric anastomosis. Other causes are uncovered mesocolon defects of the efferent loop or retroanastomotic herniation between abdominal structures, jejunogastric intussusception, stoma ulcer and stomach cancer. The operative process is usually just the dissolving of adhesions. Operative signs may require revision of the anastomosis or conversion to Billroth I or Roux-en-Y gastrojejunostomy (16).

JEJUNOGASTRIC INTUSSUSCEPTION

Intussusception of the jejunal loop into the gastric stump is a rare late complication (17). Intussusception of the efferent loop to the stomach (retrograde) is more frequent than the anterior intussusception of the afferent loop. When intussusception occurs, symptoms are sudden and severe. The patient complains of upper abdominal pain, nausea and vomiting. A firm mass is palpable in the epigastrium. The appearance of a

folded arc within the gastric stump on radiographs with water-soluble contrast materials is pathognomonic. If it resolves and recurrence becomes chronic, the operation indication is placed and the efferent loop is reduced and hanged on the parietal peritoneum or anatomical structures or the gastrojejunustomi (especially in necrotic cases) is renewed, and Roux-en-Y reconstruction is often preferred .

LATE GASTRODUODENAL OBSTRUCTIONS

Inflammation of the duodenum and postbulbar area following Billroth I operations for duodenal ulcer causes scarring and distortion of the anatomy in the gastroduodenal anastomosis. The epigastric fullness that the patient feels at the beginning turns into nausea and vomiting over time. Post-operative anastomotic leak, hematoma, and fibrosis that develops over time after acute pancreatitis can cause obstruction. These types of strictures often do not respond to endoscopic dilatation, but there is no harm in trying it. In persistent or worsening cases, gastrojejunostomy of the greater curvature proximal to the anastomosis is the most effective treatment (18).

PHYSIOPATHOLOGICAL DISORDERS

GENERAL PHYSIOLOGICAL DISORDERS

Chronic sequelae of gastrectomies result from gastric motility and mucosal function changes. It stores intense food intake with food, shrinks large pieces, the gate function that controls the passage of small food pieces into the duodenum. Also, mostly vagal controlled receptive relaxation and accommodation properties are mostly observed in the proximal stomach. Motor functions are affected negatively by gastric surgery and neural functions by vagotomy.

ALKALINE REFLUX GASTRITIS

Alkaline reflux gastritis is the most common complication of postgastrectomy that requires correction operation. In 5% -15% of patients who undergo gastric surgery, symptoms of alkaline reflux gastritis develop in flammable epigastric pain, nausea, and bilious vomiting that cannot relieve abdominal pain. While eating can increase the pain, the onset of pain is not usually related to eating. Vomit often contains foods mixed with bile. These symptoms cause reduced calorie intake, weight loss, and anemia. Alkaline reflux gastritis requires surgical treatment more often than other postgastrectomy syndromes.

Reflux gastritis occurs when the pylorus is resected, deactivated, or destroyed, when the intestinal contents pass back into the stomach. For this syndrome to occur, the anastomosis must allow the bile intestinal contents to come into contact with the gastric mucosa. The surgery with the highest incidence of this disease is Billroth II gastrojejunostomy; The

incidence is lower in loop gastrojejunostomy, Billroth I, and pyloroplasty. It has not been explained which component of the intestinal ingredient is harmful, but bile salts, especially dehydroxylated and deconjugated salts, lysolecithin, pancreatic enzymes and bicarbonate, or combinations of these agents, are suggested to play a role in the pathogenesis. Mucosal destruction leads to disruption of the gastric mucosal barrier and ultimately to back diffusion of the hydrogen ion. A decrease in gastric mucosa pH stimulates histamine release and consequently, capillary permeability and gastric mucosal bleeding increase. The severity of reflux does not correlate with the presence of symptoms. The delay in cleaning bile is thought to be important in the pathogenesis of this syndrome (19).

Endoscopic examination, biopsy of gastric mucosa and examination of gastric anastomosis should be performed to make the diagnosis and to rule out afferent loop syndrome, which is the first differential diagnosis in the patient with biliary vomiting. The endoscopist sees the reflux of bile to the stomach as an acute inflamed or even ulcerated, restricted mucosa in the gastric mucosa. Although mucosal biopsy shows intestinalisation of the gastrointestinal glands, inflammation, ulceration and bleeding, the severity of symptoms does not parallel the histological changes. Some surgeons recommend evaluating gastric emptying with scintigraphic images before a corrective surgery because delayed biliary clearance can be found and delayed gastric emptying is the most common complication of treatment.

Medical treatment is generally ineffective. Cholestyramine, which binds bile salts, antacids, mucosal protective drugs, prokinetic agents and H2 receptor antagonists can be administered. Surgical treatment is applied to patients who do not respond to medical treatment. The aim of surgical treatment is to remove pancreatic and biliary secretions from the stomach. The most common treatment is Roux-en-Y gastrojejunostomy. In a study of 92 patients with enterogastric reflux, 75% of the patients treated with the Roux procedure had very good and good results. If vagotomy was not performed in the first surgery, vagotomy should be added during the Roux procedure to prevent the development of stoma ulcer in the proximal Roux loop. Because of the high postoperative Roux stasis syndrome and its unpredictability, some surgeons suggested adding subtotal gastrectomy to the Roux procedure to accelerate gastric emptying in the post-operative period. Henley jejunal interposition has also been used in the treatment of alkaline reflux. After the Henley procedure, as immediately after the Roux procedure, bile reflux measured less than 1% of scintigraphically secreted isotopes, while the presence of reflux was reported to be 2.5% and 32%, respectively, in patients with unoperated ulcer and Billroth II anastomosis.

The recently described "duodenal switch" procedure can be applied in rare patients with alkaline reflux gastritis in an intact pylorus. In

this procedure, the duodenum is cut 5-7 cm distal to the pylorus, the distal end is closed, and the proximal duodenal cut end and jejunal Roux loop end-to-end anastomosis. Initial experiences have shown symptomatic and endoscopic improvement in 9 out of 10 patients.

DUMPING SYNDROME

Dumping is one of the most common postgastrectomy syndromes (20). It can be divided into early and late types according to the time between food intake and the onset of symptoms. Both types are seen with hyperosmolar, carbohydrate-rich food intake. Early dumping begins within 10-30 minutes after a meal and includes both gastrointestinal and vasomotor symptoms. Gastrointestinal symptoms are a feeling of fullness, cramping abdominal pain, nausea, vomiting and explosive diarrhea. Vasomotor symptoms are sweating, weakness, dizziness, facial redness, and palpitations. Late dumping occurs 2-4 hours after a meal, and vasomotor symptoms are similar to early dumping, but gastrointestinal symptoms are absent. Dumped patients often reduce their food intake because of severe food-related discomfort. As a result, they lose weight and develop malnutrition.

The term "dumping" describes patients who were acquired by Mix in 1922 and showed rapid emptying of gastric contents on barium radiography. The main mechanism causing dumping syndrome is the loss of the stomach's reservoir function and the rapid discharge of hyperosmolar carbohydrates into the small intestine. 4 surgical factors that decrease reservoir function and accelerate gastric emptying;

-Proximal gastric receptive relaxation and loss of compliance with vagotomy,

-Loss of stomach capacity with gastric resection,

-Loss of emptying control by ablation or bypass of the pilor,

-Gastrojejunostomy and duodenum bypass prevents duodenal feedback inhibition of gastric emptying.

Experiments by Machella and Roberts et al have shown that the rapid introduction of large amounts of carbohydrate-rich fluid into the small intestine causes fluid flow from the intravascular space into the intestine (21,22). This appears to be the main factor leading to the development of vasomotor and gastrointestinal symptoms of early dumping syndrome. With the loss of intravascular volume, many enteric hormones (serotonin, gastric inhibitory polypeptide (GIP), vasoactive inhibitory peptide (VIP) and neurotensin) are secreted during dumping and may be responsible for some vasomotor manifestations of early dumping. Late dumping develops as a result of enteroglucagon release in response to high carbohydrate concentration in the small intestine. Enteroglucagon

causes β-cell stimulation and insulin hypersecretion. After complete absorption of carbohydrates, hyperinsulinemia causes hypoglycemia. Hypovolemia in early dumping and hypoglycemia in late dumping are accompanied by epinephrine secretion, which is associated with the symptoms that occur. Early dumping symptoms worsen with carbohydrate intake, while late dumping symptoms alleviate with carbohydrate intake.

The occurrence of dumping syndrome is proportional to the rate of gastric emptying after truncal vagotomy and drainage or truncal vagotomy and antrectomy. The incidence of dumping is high after operative procedures that cause rapid gastric emptying. Since Billroth II gastrojegenostomy bypasses both pyloric and duodenal control mechanisms, it may cause very rapid gastric emptying and the incidence of dumping in the early postoperative period may exceed 50%. Billroth I gastroduodenostomy preserves duodenal resistance and the incidence of dumping syndrome is reduced. In a series of 455 patients who had undergone truncal vagotomy and drainage, postoperative dumping syndrome developed in 14%. Due to the motility characteristic of the Roux loop of the Roux-en-Y gastrojegenostomy, gastric emptying that causes dumping rarely occurs in this type of anastomosis. Proximal gastric vagotomy can also accelerate gastric emptying. Vagal denervation of the proximal stomach decreases receptive relaxation and compliance, resulting in rapid emptying. However, dumping is seen in only 1-6% of patients after proximal gastric vagotomy.

Dumping syndrome is diagnosed mainly by clinical symptoms; however, specific tests can be helpful in diagnosis. Scintigraphic studies using solid and liquid phase markers can show rapid gastric emptying. Endoscopy and barium radiography can help define anatomy and diagnose other postgastrectomy syndromes that may be.

Dumping is usually treated medically. Reducing the amount of meals, increasing the frequency of meals, taking liquids 30 minutes after meals, avoiding concentrated carbohydrate meals constitute the basis of treatment. This diet modification reduces the osmotic load of jejunum and minimizes symptoms without disturbing nutrition. Rest and antispasmics may be recommended after a meal. Successful treatment of dumping syndrome with somatostatin or its synthetic analogue octreotide has recently been reported. This substrate has an inhibitory effect on enteric hormone secretion. Side effects are diarrhea and paradoxical hypoglycemia. In about 1% of patients, symptoms of dumping syndrome persist despite medical treatment and surgery is required.

The aim of surgical treatment is to slow down gastric emptying. Many different surgeries have been proposed for dumping treatment.

Converting gastroduodenostomy to gastroduodenostomy restores normal gastroduodenal flow and duodenal receptors slow down gastric emptying.

Antiperistaltic jejunal loop interposition is another surgical method. In the antiperistaltic jejunum interposition, a 10-15 cm jejunum segment is inverted and anastomosed between the gastric remnant and the duodenum. This operation may bring along problems such as bezoar formation due to prolonged retention and development of alkaline reflux gastritis.

Roux-en-Y gastrojejunostomy is an excellent operation for the treatment of dumping syndrome. This operation has been used successfully by many surgical groups. Investigating the motor function of the Roux louse in animal and human studies has elucidated the mechanism by which this surgery slows gastric emptying. Interruption of the jejunum during construction causes a decrease in the frequency of contraction in this segment. These retrograde contractions increase the resistance of the chyme to the passage of the segment and slow the gastric emptying. Functional obstruction and Roux-en-Y syndrome can be seen in this method. This syndrome is characterized by painful distention relieved by chronic abdominal pain, postprandial fullness, gas sensation, nausea, and vomiting. It is suggested that this syndrome is due to vagal denervation in the gastric remnant. Betanekol has been shown to be useful in the medical treatment of this delay in gastric emptying.

If Roux-en-Y diversion is to be performed, care should be taken to ensure complete vagotomy and antrectomy, otherwise the development of marginal ulcer will be inevitable. Pyloric reconstruction has recently gained popularity in the treatment of dumping syndrome caused by vagotomy pyloroplasty (20).

CHRONIC GASTRIC ATONIA

The decrease in the motor tone of the stomach may be the result of gastric surgery and may cause a delay in gastric emptying. These patients complain of epigastric fullness and pain, nausea after eating, and vomiting of partially digested meals eaten hours or even days earlier (10). Many patients cannot tolerate solid foods, but can maintain adequate nutrition with fluids. Symptoms can be aggravated enough to cause malnutrition and weight loss even with liquid diet. The clinical picture may be aggravated by the formation of bezoars occurring in 12% of the patients with this condition.

Stomach atony mainly occurs with the loss of the vagal innervation of the stomach. Proximal gastric tonic contractions in the late phase of gastric emptying are under vagal control. However, it may cause gastric atony in 0.7% to 3% of the patients who undergo denervation of the

proximal stomach with PGV. Strong peristaltic antral contractions in the postprandial period are also under vagal control. The loss of these contractions inhibits the mechanical digestive function of the stomach. Less selective vagotomies have a higher incidence of delayed gastric emptying. Conditions that increase the risk of developing gastric atony are: preoperative gastric outlet obstruction, diabetes mellitus, hypothyroidism and autonomic neurological diseases.

The most important topic in the differential diagnosis of this syndrome is to decide whether resistance to gastric flow is mechanical or functional. Contrast radiography will often show a distended, flaccid gastric stump without mechanical obstruction. Endoscopy confirms that there is no obstructed gastroenterostomy. The diagnosis is confirmed by scintigraphy, which shows delayed gastric emptying, especially against solid foods.

Medical treatment with prokinetic agents such as metoclopramide and erythromycin has limited success and many patients require surgical treatment. Since vagal innervation cannot be repaired, operative treatment aims to reduce the reservoir capacity of the stomach. Antrectomy can be applied in cases who have previously undergone vagotomy and pyloroplasty. Most of the time, the gastric stump is very dilated, atonic and relaxed, so a nearly total gastrectomy is required. Roux-en-Y gastrojejunostomy should be used with near total gastrectomy to prevent bile reflux esophagitis.

ROUX STASIS SYNDROME

Patients with Roux-en-Y gastroenterostomy have an increased risk of delayed gastric emptying and symptoms such as epigastric fullness, abdominal pain, nausea and food vomiting. Serious symptoms can lead to malnutrition and weight loss. Bezoars may develop in the stomach. The prevalence of the syndrome is between 10-50%.

Although their relative role in stasis is not fully explained, both the vagotomy treated gastric stump and the Roux loop play a role in the development of Roux stasis syndrome. As with gastric atony, vagotomy reduces the tone of the gastric stump, and removal of the atonic stomach often improves symptoms. This cannot fully explain the syndrome because Roux stasis syndrome can occur after total gastrectomy and oesophagojejunostomy.

Recent studies on the motor properties of the Roux loop have explained the mechanism of slowed transit through this intestinal segment. Normally, the mechanical contractions of the jejunum are controlled by electrical depolarisation of smooth muscles, also called pacemeters, that radiate distally from the duodenum to the jejunum. Cutting the jejunum in

the construction of the Roux loop prevents this propagation and causes an electric potential in the intestine at a lower frequency. Truncal vagotomy causes loss of vagal innervation of the jejunum. In this case, contractions caused by ectopic pacemakers go towards the stomach. This slows down the moment of transition.

As with gastric atony, it is important to rule out the causes of mechanical obstruction in patients with Roux stasis. Barium radiography and endoscopy are useful here. Scintigraphic imaging is the best method to measure the slowed discharge of solid and liquid foods from the gastric stump and Roux ance. Although emptying studies are useful, treatment is planned according to the severity of symptoms, not the specific results of emptying studies.

Medical treatment is rarely successful in Roux stasis syndrome and surgical revision is often required. Surgical treatment usually includes near total gastrectomy and correction of the length of the Roux loop to 40cm.

SPECIFIC MALABSORPTION AND NUTRITIONAL DISORDERS

Nutritional follow-up events following gastric surgery result from food digestion or nutrient absorption irregularities as well as a reduction in nutrient intake (10). The decrease in food intake is due to the patients anxiety to prevent nausea or dumping symptoms. However, specific digestive and malabsorption disorders may develop due to the removal of part or all of the stomach and non-physiological rearrangement of the upper GI system. These disorders are digestive disorders of complex protein, fat and carbohydrates, steatorrhea and rarely azotore, abnormal feeling of satiety, iron, vitamin B12 and folate deficiency, osteomalacia.

DIGESTIVE DISORDERS

Normal value of 24-hour fecal fat excretion is <6% of dietary fat intake and fecal nitrogen excretion <2g. Serious problems are more common in patients with total gastrectomy; mean fecal fat excretion is 16% and nitrogen excretion is 2 g. It is less common in other gastric resections with or without vagotomy. It is seen more frequently in Billroth II.

Gastric resections also impair the digestion and absorption of carbohydrates. Gas in the intestines is a common complaint, gastrectomy reveals latent or mild lactose intolerance before the operation. Gas, cramp and expansive diarrhea following milk and dairy intake is dependent on rapid lactose entry into the colon. Digestive disorders are caused by the inadequate mixing of the foods taken with bile and pancreatic fluids in accordance with normal physiology. If efferents are cut into the pancreas and biliary tract by vagotomy, the amount of secretion to be produced will

also decrease. For these reasons, nutrition is impaired although there is no mucosal damage.

Despite all these explanations, the digestive capacity and absorption capacity are kept at a sufficient level in most of the cases and digestive disorders are not followed up clinically.

IMPAIRED FEELING OF SATURATION

Although the feeling of early satiety after gastrectomy is attributed to the small volume of the gastric stump, deactivating more than 90% of the stomach in morbid obese patients can only provide early saturation. Saturation receptors have been identified in the gastric mucosa in animal experiments. Similar receptors are also present in the distal ileum with their more intense triggering potential and may cause satiety to reach them early with the rapid passage of food. Lack of early saturation in patients who have undergone vagotomy also supports this.

ANEMIA AND IRON DEFICIENCY

Hypochromic and microcytic anemia is common after gastric resection and is attributed to iron deficiency. Diet iron is in ferric (Fe + 3) form and its absorption is more difficult than ferrous (Fe + 2). Decrease in acid secretion alone cannot provide the deterioration of iron reduction. Iron is mostly absorbed from the duodenum and absorption through the GI tract gradually decreases. In general, iron absorption adapts over time, even following Billroth II operations.

Vitamin B12 deficiency is the cause of macrocytic anemia, neurological symptoms and pernicious anemia. After total gastrectomy, if no vitamins are given, it occurs after 2-5 years. Even if 75% of the stomach is resected, the incidence of pernicious anemia is <1%. Folate levels also drop due to the loss of B12. Even if vitamin B12 levels do not drop too low, lowering the intake of high-fiber vegetables rich in follate by the patient due to postcibal symptoms leads to folate deficiency.

Routine monitoring of these vitamins and iron is not required, except for total and near-total gastrectomy. Following the follow-up, the controls are carried out at three-month intervals in the first 2-3 years, and the control is continued at six-month intervals after reaching the fixed levels.

BONE DISEASES

Bone demineralization is normal with old age, but clearly increases with gastric resection. Although it is said more after total gastrectomy, it is not related to the type of resection. Osteoporosis and osteomalacia may occur, but osteomalacia is common. High alkaline phosphatase levels, low calcium levels, low serum 25-hydroxy vitamin D and high 1,25 dihydroxy

vitamin D levels support the diagnosis, although confirmation is made according to serum albumin. Pathological fractures are three times normal.

Although the mechanism is not known exactly, the scarcity of its intake is blamed. The best treatment is to prevent its occurrence and balance it with diet.

UNCLASSIFIABLE

SMALL GASTRIC STUMP

As mentioned in the previous section, early satiety is not only due to small gastric stump. If more than 80% of the stomach is removed, early satiety, postcibal pain and vomiting are largely due to excessive reduction of the gastric reservoir. Small gastric stump syndrome; weight loss is characterized by malnutrition and mixed anemia. Medical treatment is successful and it will be sufficient to reduce the amount of meals and increase their frequency.

BEZOAR FORMATION

Bezoars are a mixture of hair (tricobezoars), fruit, and undigested vegetables (phytobezoars). Occurrence is more common in Billroth I and small reconstructed gastric outlets. The accumulation of such substances indicates motility disorders. Bezoars develop in 10-15% of patients with motility disorder (Roux stasis, gastric stasis). They rarely cause congestion, premature saturation or malabsorption.

It is dissected and removed with endoscopic interventions and repeated sessions. It repeats frequently. While surgery is rarely required in the stomach, the passage of bezoars into the intestine and obstruction requires urgent surgery. The patient undergoing surgery should be considered as having gastric atony and appropriate operation; preferably, complementary gastrectomy and Roux-en-Y reconstruction will be appropriate.

GASTRIC STUMP CARCINOMA

The overall incidence of gastric carcinoma following gastric resection is 1-5%. Although it is controversial that it is predisposing to gastric carcinoma, Billroth II reconstruction, gastric ulcer operations and more than 20 years after surgery require careful follow-up of the cancer. The results of the various series raise the need for annual endoscopic control 12-15 years after the operation. Gastrectomy is completed in such lesions.

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CHAPTER IV

PROGNOSTIC FACTORS IN GASTRIC CANCER

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Gastric cancer occupies an important place among the health problems all over the world in terms of prognosis and incidence despite the increasing developments in treatment modalities in recent years. It is ranked 5th among the most common cancers worldwide and 3rd in cancer-related mortalities.[1,2] Its asymptomatic course until advanced stages and frequent lymph node involvement and distant metastases when diagnosed are undoubtedly among the most important causes for this. As it is usually diagnosed at advanced stages in Western countries, its prognosis is poor. However, an increase in early diagnosis rates in countries such as Japan and South Korea, where endoscopic scans are widely used, contributed to the improvement of prognosis.[3,4] Nonetheless, the 5-year overall survival is 25%, with the potential between 24% and 57% in patients with curative resection.[5] This poor prognosis has been the subject of many researches and has been demonstrated by studies with a wide range of multifactor in the literature.

Tumor invasion depth and lymph node involvement have been determined to be the most important factors in prognosis[6-9], and in recent years, researchers suggesting the use of metastatic lymph node ratio instead of the number of lymph nodes in staging have revealed that N-Ratio is a stage-independent prognostic factor.[11-16] In the TNM staging system, which was evaluated to be an important prognostic factor in previous studies and was prepared by the American Joint Committee on Cancer (AJCC), unlike the Japanese Gastric Cancer Association (JGCA) staging system, the number of lymph node involvement was used instead of the location of lymph node involvement. Furthermore, the recently published clinical staging (cStage) of TNM classification (8th Edition) has also been confirmed to be a useful indicator in predicting prognosis and determining treatment options in the study conducted by Bando et al.[17].

More than 95% of gastric cancers are adenocarcinomas that are histologically (Lauren classification) divided into intestinal and diffuse types. The poorly differentiated diffuse type is often associated with

genetic abnormalities and includes a signet ring cell component. [10,18] In the retrospective analysis of 769 patients by Kwon et al.,[19] it was found that the signet ring cell type was associated with poor prognosis in advanced stage tumors, although there was no significant prognostic difference between signet ring cell histology and other subtypes for early gastric carcinoma. In another cohort study analyzing 2199 patients,[20] it was determined that the signet ring cell histology was a poor prognostic factor associated with a decrease in survival and its cause was explained with the infiltrative growth pattern, lymph node metastasis and peritoneal spread and a higher potential for distant metastasis.

Lymphovascular invasion was found to be a prognostic factor associated with recurrence and reduced survival in both node-negative gastric carcinoma and metastatic lymph node patients in studies conducted in the literature.[21-24] There are many studies regarding tumor size with different cutoff values.[25-27] In the retrospective analysis of 2405 patients with gastric cancer who underwent R0 curative gastrectomy and lymphadenectomy by Zhao et al., the 5-year overall survival of the 5 subgroups (Ts1: <2.5 cm, Ts2: 2.5-4.5 cm, Ts3: 4.5-7.5 cm, Ts4: 7.5-10 cm and Ts5> 10 cm) found to be 80.5%, 68.2%, 57.4%, 49.3% and 31.8%, respectively, and the tumor size found to be increasing and statistically significant was stated to be correlated with the poor prognosis.[26]

Although the effect of age on survival is the matter in question, generally being older at the time of diagnosis is associated with poor prognosis. In a study [28] in which 1473 gastric cancer patients undergoing curative resection were analyzed and the age range was divided into ten-year groups, the ten-year survival rate was found to be 83.8% in patients <50 years old, whereas it was found to be 70.2% in patients aged 70 years and above, and this statistically significant difference was associated with worse survival. In another study conducted by Park et al.[29] evaluating the clinicopathological characteristics and prognosis according to age, 3362 gastric cancer patients were analyzed sequentially and the patients were divided into three groups (group1: <45 years, group2: 46-70 years and group3:> 71 years). The proximal location, linitis plastica and the 5-year survival of group 1 patients histologically associated with the signet ring cell type were found to be significantly higher as compared to the elderly groups. This situation may be explained with the avoidance of aggressive lymph node dissection, limitations in chemotherapy administration and comorbidity in elderly patients, and better tolerance of surgery and less postoperative complications in younger patients.

Inadequate and unbalanced diet is another factor that adversely affects the quality of life, treatment process and survival in cancer patients. In this context, many scoring systems have been developed in order to define malnutrition and in a meta-analysis of 14 studies evaluating one of

the scoring systems called the prognostic nutritional index (PNI)[30], it was predicted that it may be an important indicator of prognosis in cancer-related survival, especially gastrointestinal carcinomas. In another study conducted by Liu et al.,[31] a new scoring system was developed by including serum albumin, body mass index and preoperative weight loss in addition to PNI, and by evaluating 1320 patients with curatively resected gastric cancer, Liu et al. concluded that the scoring called preoperative nutritional status (PNS) was independently related to the overall survival of patients with stage I-III gastric cancer.

Human epidermal growth factor receptor 2 (HER2) is a proto-oncogene encoded by ERBB2 on chromosome 17, and molecular studies have shown that it is associated not only with breast cancer but also with stomach and many other types of cancer. While HER2 overexpression/amplification is clearly associated with poor prognosis in breast cancer, the same may not be claimed for gastric cancer. Although there are studies in the literature reporting that HER2 positivity is a significantly worse prognostic indicator, there are some studies reporting the opposite.[32-36] The important point here is that, as a result of the studies, trastuzumab and other anti-HER2 monoclonal antibodies targeting HER2 are among the treatment regimens.

Microsatellites are repetitive short motif nucleotide sequences, and the damage to the DNA mismatch repair mechanism (MMR) manifests as microsatellite instability. Microsatellite instability, which is an expression of genomic instability, is known to be a good prognostic indicator especially for colorectal carcinomas, and this issue has been the subject of many studies for gastric cancer. In a meta-analysis of 24 studies, microsatellite instability was reported to be associated with good prognosis.[38] In the meta-analysis investigating the value of MSI, Pietrantonio et al. evaluated individual data of patients with resectable gastric cancer registered in the MAGIC, CLASSIC, ARTIST and ITACA-S trials and explained that MSI-low or microsatellite stable (MSS) patients develop a better response to chemotherapy (neoadjuvant/adjuvant), while MSI-high patients can achieve good results even with surgery alone, without additional chemotherapy.[39]

As a result, it is important to know the clinicopathological, demographic and molecular factors related to both the patient and the tumor and to increase the number of such studies, to obtain better survival results in the near future and to determine individualized targeted treatment strategies.

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CHAPTER V

PARATHYROID CANCER

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1. INTRODUCTION

Parathyroid cancer (PC) is a rare slowly progressing malignant neoplasm originating from the parathyroid gland[1]. It is the rarest endocrine cancer among all cancers with a prevalence of 0.005%, and it accounts for 0.5-5% of all primary hyperparathyroidism cases[2,3]. Most PCs secrete parathyroid hormone (PTH), and usually occur in patients with severe hypercalcemia symptoms. Although clinically similar to parathyroid adenomas, these patients have higher serum calcium and PTH levels than parathyroid adenoma[4]. PC has its own characteristics. As with all malignancies, PC is the result of uncontrolled or unregulated growth of parathyroid cells, and most PCs are functional i.e. they secrete parathyroid hormone. Approximately 10% of those with poor prognosis are not functional, so the diagnosis is made with local invasion and distant metastases[5-7]. Parathyroid adenomas are more common in women, but the incidence of parathyroid cancers in men and women is equal[8]. They are diagnosed about 1 decade before Adenoma patients and in 4th-5th decades in their lives[9]. The disease usually has a slow and painless course, and most patients succumb to the complications of persistent hypercalcemia rather than tumor invasion and spread. However, none of these are strict rules. Indeed, the first documented case of PC was a nonfunctional carcinoma reported by Swiss surgeon Fritz De Quervain in 1904[10]. De Quervain did not mention any signs or symptoms of hypercalcemia in his case. However, it is not always easy to distinguish between PC and adenoma at an early stage, and metastasis may be the only sign of malignancy. These features can mislead physicians and have a negative impact on treatment strategies and approaches. As a result, an inappropriate approach to patients may deprive patients of a chance for treatment. Although there has been no progress in treatment options, many studies have been conducted in recent

years to understand the molecular pathogenesis of parathyroid carcinoma[11-13]. New indicators can help make diagnosis more precise in uncertain situations. In addition, more drugs have become available to manage difficult-to-treat patients[12].

2. EPIDEMIOLOGY

PC is a rare cause of primary HPT. Some case series suggest that it accounts for 2–5% of all cases[14,15]. However, data from a broader literature review show that it accounts for less than 1% of all cases in many parts of the world[16]. It is an extraordinarily rare malignancy with an incidence of approximately 3.5-5.7 years per 10 million population. Men make up about 50% of all cases. The average age of diagnosis in the range of 12-90 years compiled in the studies is 44-48 years[1,9].

3. PATHOGENESIS AND MOLECULAR BIOLOGY

As with other malignancies, the etiology of PC includes the interaction of many environmental and genetic factors. Especially in childhood, exposure to radiation increases the risk of benign parathyroid disease as well as concomitant thyroid and parathyroid neoplasia, but it remains unclear whether such exposure is an etiological factor in PC[17]. Most PCs are idiopathic and sporadic, however, they are associated with Multiple Endocrine Neoplasia (MEN) syndrome type I and IIa as well as hyperparathyroidism-jaw tumor syndrome (HPT-JT). An increased risk is also seen in familial hyperparathyroidism, a rare autosomal dominant disorder. The recent understanding of PC's genetics has mainly stemmed from the clinical and molecular genetic characterization of HPT-JT. In this syndrome, patients develop primary hyperparathyroidism, mandibular and maxillary fibro-osseous lesions, cysts and neoplasms in the kidneys. The mutation of HRPT2 (CDC73), a tumor suppressor gene, has been described in the molecular pathogenesis of parathyroid carcinoma. HRPT2 found in 1q31 encodes a nuclear protein called "parafibromin "[18-20]. This mutation is much more common in sporadic PC cases than benign adenomas. This is an indication that this mutation points to an important role in the pathogenesis of PC. Parafibromin mainly acts as a nuclear protein and a transcription regulator. Overexpression of this protein causes inhibition of cell proliferation and arrest of the G1 phase. PC is present in about 15% of those with primary hyperparathyroidism due to HPT-JT. Hereditary hyperparathyroidism dysfunctional isoforms such as mutations in HPT-JT syndrome have anti-apoptotic effects. An inactivating mutation of the HRPT2 (CDC73) gene found in most people with classic HPT-JT symptoms can be demonstrated. Approximately 10% of gene carriers have no clinical symptoms[20-22].

4. PATHOLOGY

PC is often difficult to diagnose. It is often solitary and originates from a single gland; however, there are publications on multiglandular involvement. Both the right and left lower glands were counted as the most common location. Ectopic tumors usually arise from glands in the mediastinum, but ectopic placement does not increase the chance of a gland becoming malignant. Synchronous PC and adenoma cases have been reported. PC often occurs with a palpable neck mass and laboratory values associated with hyperparathyroidism. The presence of this palpable mass is an important finding that should warn a careful clinician that there may be malignancy[22-24]. Typically, they are hard, firm and adhered to surrounding tissues. Since they are generally asymptomatic, their average size at the time of diagnosis is around 3 cm and their weight can be between 2 and 10 g. They are generally irregular, hard and grayish white in color. Carcinomas are strongly adhered to surrounding tissues. Tumor cells may invade the ipsilateral lobe of the thyroid, strep muscles, recurrent laryngeal nerve, trachea or esophagus. Local metastases are rare, but distant metastases are even more common. If distant metastases are present, they may occur in the lungs, bone, mediastinal lymph nodes, liver, and kidney. Patients with PC tend to have very high PTH levels compared to patients with benign primary hyperparathyroidism and almost always have refractory, high serum calcium[25]. Microscopic diagnosis of PC can be difficult, as its histologically very similar to a parathyroid adenoma. Mitotic activity is the primary factor in the diagnosis of PC, but they are also present in adenoma and hyperplasia. Therefore, their absence does not exclude cancer. Parathyroid adenomas may show increased mitotic activity as well as capsular invasion. Cells with minimal atypia can be difficult to distinguish from parathyroid adenoma. Extra glandular spread is a hallmark but is not required for diagnosis. Microscopically, the tumor is surrounded by a capsule and the fibrous septa extends into the tumor creating a lobular appearance[26,27]. Cells may show clear, oxyphilic, uniform, or metaplasia. Cells with minimal atypia can be difficult to distinguish from parathyroid adenoma. Mitotic figures are usually present and are the primary factor in the diagnosis of PC, but they are also found in adenoma and hyperplasia. Therefore, their absence does not exclude cancer. Extra glandular spread is a hallmark but is not required for diagnosis. Focal calcification, cystic changes and coagulative necrosis may be seen. Vascular invasion occurs but less common than capsular invasion[26-28].

5. CLINICAL FEATURES

The vast majority of PCs are functional tumors. Therefore, patients often present with symptoms and signs of hypercalcemia such as fatigue, weakness, fatigue, weight loss, and anorexia. More pronounced are

symptoms of kidney and skeletal involvement. These include kidney stones, arrhythmias, and osteoporosis. A palpable neck mass or hypercalcemia with hyperparathyroidism suggests parathyroid carcinoma. Up to 70% of patients present with a palpable neck mass; This is extremely rare in benign disease. A comprehensive head and neck assessment is essential in these patients[22,29]. Symptoms of hyperparathyroidism occur long before the local invasion of the tumor produces any symptoms. There are renal and skeletal involvement, including osteopenia, osteoporosis, osteofibrosis, osteitis fibrosa cystica, subperiosteal resorption, pathognomonic "salt and pepper" appearance on direct cranial radiography and pathological fractures. Bone pain and pathological fractures are also reported. Kidney disease often occurs as nephrolithiasis and kidney failure. Renal colic is a common complaint in patients with parathyroid carcinoma. In a study including 43 cases, the prevalence of nephrolithiasis was reported as 56%, and the prevalence of renal failure as 84%[26,30]. Psychiatric symptoms such as depression and symptoms of the digestive tract (e.g. nausea, vomiting, abdominal pain, peptic ulcer, pancreatitis and constipation) have also been described. It is important to question a very detailed endocrine and family history of patients. Although the development of PC after radiation is rarely reported, a history of ionizing radiation to the head and neck should be taken. The physical examination should include a comprehensive mouth, chin, and neck examination. A careful physical examination is important in terms of masses and lymphadenopathy, paying particular attention to lateral and central neck examination, thyroid palpation at rest and during swallowing [6,11]. In a subset of patients with PC, a different PTH fragment is produced. The significance of this form is not yet clear. Serum levels of alkaline phosphatase and human chorionic gonadotropin alpha and beta subunits also increased. Bone involvement can be seen in imaging studies[31,32]. Nonfunctional PCs are extremely rare and only 19 cases have been reported since 1929. It usually occurs at an advanced stage with signs and symptoms of local growth, invasion (neck mass, hoarseness, dysphagia)[33]. These tumors tend to metastasize to many locations including the cervical lymph nodes, lungs, liver, and bone. In contrast to hypercalcemia, abnormal tumor burden is the more common cause of death in these patients (Table 1).

Table 1: Effects of PTH level in PC

Normocalcemic **Serum Ca < 10.5 mg/dL**	**Hipercalcemic**	**Hipercalcemic Crisis** **Serum Ca > 14 mg/dL**
May be asymptomatic or have a palpable mass	Generally symptomatic, gastrointestinal complaints, kidney stones or fatigue, neurocognitive problems	May occur in extreme situations, with various levels of sensorium or stupor findings
Diagnosed in more advanced stages	calcium and PTH levels may be an important marker	requires rapid intervention with hydration, bisphosphonates, calcitonin or denosumab
Higher propensity for metastasis		Emergency surgery should be planned

6. DIFFERENTIAL DIAGNOSIS AND DIAGNOSIS

The main purpose is to distinguish between malignant and benign diseases before any surgical intervention. This is difficult because PC does not have a specific distinguishing feature. Generally, the effects of hypercalcemia are more pronounced in cancer than in adenoma, and some effects are more common in patients with carcinoma (Table 2). Some clinical features can help distinguish PC from parathyroid adenoma. The following diagnostic features should clinically suspect parathyroid carcinoma.

Table 2: Clinical features of benign and malignant parathyroid tumors

	Benign Tumor	**Malign Tumor**
Female-Male Ratio	3 : 4,1	1 : 1
Average Age	55	48
Kidney Involvement	<%20	% 56-84
Serum Calcium	<11.2 mg/dl	>14 mg/dl
Serum Parathyroid Hormones	Little high	3-10 times high (up to 75 times)
Palpable Cervical Mass	Rare	% 50-70
Radiological Skeletal Features (Osteitis Fibrosa Cystica Vb.)	< %5	% 44-91
Hypercalcemic Crisis	Very rare	More common
Unilateral vocal cord paralysis	None	Later

Fine needle aspiration biopsy is generally not recommended in patients presenting with a palpable neck mass. The reason for this is the extreme difficulty in distinguishing between benign and malignant disease in cytology. Another concern with preoperative parathyroid biopsies is the formation of hematoma or abscess, as well as inflammation in this area after the biopsy, which can increase the difficulty of surgery in the future. The only definitive evidence of malignancy is the presence of metastases. However, this feature is not common. Many pathological criteria have been proposed to distinguish between benign and malignant lesions and many molecular studies have been conducted. However, no clear scientific

distinguishing feature has been identified. Pathological diagnosis of PC remains challenging. The absence of a gold standard test, a multidisciplinary approach that considers the clinical, biochemical, and structural aspects of the disease still offers the best chance for an accurate diagnosis [34-37] (Table 3).

Table 3: Symptoms and signs of PC-associated hyperparathyroidism

Subcortical bone resorption	Renal colic	Anorexia
Bone ache	Ulcer	Polyuria
Pathological fractures	Recurrent pancreatitis	Polydipsis
Palpable neck mass	Tiredness	Dehydration
Kidney stone	Muscle weakness	Nausea and vomiting
Kidney disease	Weight loss	

There is no defined clinical and pathological staging system for PC, as there is no correlation between tumor size or lymph node status and survival, the disease is rarely diagnosed preoperatively and intraoperatively, and limited data on its prognosis. [7,25].

7. PREOPERATIVE IMAGING METHODS

Neck ultrasound and sestamibi scintigraphy are the preferred imaging methods in benign parathyroid disease and can be used for similar purposes in malignancy. Because of its non-invasiveness and ease of use, ultrasound is often the first diagnostic tool. Usually PC is distinguished from benign parathyroid adenomas due to a larger sized mass and a decrease in echogenicity and tendency to be homogeneous. Sestemabi scintigraphy is another commonly used imaging method in preoperative localization determination studies. Although they have a relatively high level of sensitivity, to identify parathyroid lesions, they are not sensitive to differentiate between parathyroid adenomas and PC. Another important point to be considered is that PC with cystic degeneration may appear as false negatives in sestamibi scintigraphy. At the same time, there may be involvement of the thyroid gland, leading to false positive results. Magnetic Resonance Imaging and 18-FDG PET (fluoro-deoxy-glucose positron emission tomography) are useful methods for detecting tumors, especially malignancies [38].

8. TREATMENT

Treatment and management of PC can be divided into two categories: interventions aimed at potential therapeutic and therapeutic interventions to control advanced cases. En bloc surgical excision is the only method that can offer potential therapy. No evidence has been shown that the tumor was eradicated with radiotherapy and chemotherapy. Surgical excision and removal of hormone-producing tissues provide significant symptom relief. In cases of diffuse metastatic disease or situations that cannot be surgically removed, different types of drugs are attempted to lower serum calcium levels and alleviate the effects of diffuse hypercalcemia. Almost 96% of patients with PC are treated surgically, and surgery is the only effective treatment to control hypercalcemia and reduce tumor burden, both at initial resection and at the time of recurrence of metastasis. During the first surgery, en bloc resection with microscopically negative margins and an intact tumor capsule is the preferred treatment to achieve the best chance of recovery. It is also another surgical approach in local excision [39]. Local excision involves only pericapsular excision of the affected parathyroid gland. However, most authors agree that expanded en bloc excision at the first operation reduces the need for repeat surgery and improves survival outcomes.

Surgical Principles of Expanded En bloc Excision:

1. All four glands should be investigated thoroughly in terms of concurrent adenomas and cancers. Although rare, multiglandular cancers have been described in the literature.

2. A bloodless surgical field and careful meticulous exploration of adjacent structures ensure that neighboring structures are not injured.

3. Minimal manipulation of the tumor itself is required to avoid rupture of the capsule and spillage of the tumor. This is usually accomplished by total removal of the ipsilateral thyroid lobe with the tumor.

4. Careful exploration enables the determination of the structures that may need to be resected with the mass in terms of evaluating tumor invasion to surrounding strep muscles or other adjacent structures (The structures where local tumor invasion is most common are the ipsilateral thyroid lobe, ipsilateral strep muscles, ipsilateral recurrent laryngeal nerve, esophagus and trachea.).

5. Regional lymph node involvement requires regional lymph node dissection in that compartment. However, it is known that prophylactic lateral neck dissection does not increase survival and it is not recommended because it will increase morbidity.

6. In most cases, the recurrent laryngeal nerve can be spared. However, if there is evidence of nerve involvement, the nerve can be sacrificed and removed with the tumor [40,41].

The management of this cancer recurrent or metastatic disease is primarily surgery; resection of even tiny tumor deposits in the neck, lymph nodes, lungs, or liver can provide significant palliation. If possible, accessible distant metastases should be resected. Localization studies performed before initial surgery or reoperation may include Tc 99m-sestamibi scintigraphy, single photon emission computed tomography, CT-MIBI image fusion, ultrasound, computed tomography (CT), selective angiogram, and selective venous sampling for PTH; CT and magnetic resonance imaging are useful imaging aids for localization of distant metastases [42,43]. Non-surgical treatment modalities for PC generally do not give good results. Some researchers have advocated the use of adjuvant radiotherapy to reduce the local recurrence rate[42]. Patients treated in this way should be monitored very tightly for life, as the risk of disease recurrence may be relatively high in long-term follow-ups [44,45].

9. FOLLOW-UP

Approximately 40% to 60% of patients relapse, typically 2 to 5 years after the first surgery. In most cases, hypercalcemia precedes the physical signs of recurrent disease. In about two-thirds of relapse cases, the location of the relapse is typically in the neck tissues or cervical lymph nodes. Often, local recurrences in the neck are difficult to identify because they can be small and multifocal, as well as caused by scar tissue left over from the previous surgical procedure. Ultrasonography, sestamibi-thallium scintigraphy, and positron emission tomography can help identify lesions that are difficult to detect. Distant metastases have been reported in 25% of patients, primarily in the lungs, but also in the bone and liver. Because of its low malignant potential, the morbidity and mortality associated with parathyroid cancer is primarily due to the metabolic consequences of the disease, not directly from malignant growth[19,22,38].

10. RESULT

Because of its rarity, it is difficult to design clinical trials for the causes of parathyroid carcinoma and new treatments. Surgery remains the most effective therapeutic and palliative option in the light of current knowledge. Pooling the resources of multicenter clinical studies, a multidisciplinary approach with experienced endocrinologists, pathologists, radiologists, nuclear medicine physicians, oncologists and surgeons are required to optimize patient outcomes.

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CHAPTER VI

BENIGN BILIARY TRACTS OBSTRUCTIONS

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ANATOMY OF THE BILIARY TRACTS

INTRAHEPATIC BILIARY TRACT

The liver consists of two primary and one dorsal lobe. Right lobe drains 5th, 6th, 7th and 8th segments, left lobe 2,3,4 segments, dorsal (caudate) lobe drains 1st segment.

The boundary separating the right and left lobes is the line joining the gallbladder bed on the visceral side and the left edge of the inferior vena cava. On the parietal side, this border falls approximately 4 cm right lateral to the falciform ligament. The right hepatic lobe is divided into anterior and posterior segments, and the left hepatic lobe is divided into medial and lateral segments. These segments also consist of superior and inferior subsegments.

A subsegmental bile duct drains each subsegment. Thus, anterior superior and anterior inferior subsegmental ducts combine to form the right anterior subsegmental bile duct. Likewise, posterior superior and posterior inferior subsegmental bile ducts join to form the right posterior subsegmental bile ducts. The posterior of both right segmental canals is longer and is in a higher position. These merge next to the porta hepatis and form the right hepatic bile duct. However, in 28% of cases, these ducts cannot unite and combine with the left hepatic duct separately to form the main hepatic duct.

In the left hepatic lobe, the superior lateral and inferior lateral subsegments form the lateral segmental canal, and the superior medial and inferior medial subsegments form the medial segmental duct. These two segmental ducts form the left main hepatic bile duct.

The caudate lobe also has a separate canal system. It drains into both the right and left hepatic duct systems.

The left hepatic duct is thicker and longer than the right hepatic duct. The left hepatic duct is 4-7 mm, and the right hepatic duct is 3-6 mm

thick. The right and left hepatic bile ducts combine with extrahepatic localization at the porta hepatis level to form the main hepatic bile duct.

EXTRAHEPATIC BILIARY TRACT

Main Hepatic Duct: 3-5 cm long and 4-8 mm thick. It occurs as a result of the union of the right and left hepatic duct. Common hepatic duct moves down and right side, on the right edge of the part of the omentum minus called hepatoduodenal ligament, between both peritoneal leaves, to the right of the proper hepatic artery and the front of the portal vein.

Cystic Duct: Its length is 2.5-4 cm. This duct starts from the neck of the gallbladder and turns slightly to the left. It moves down, back and left, joining the main hepatic duct to form common bile duct. Various variations are observed in this union.

Common Bile Duct: Its length is 10 cm, its diameter is 3-10 mm. This canal runs down, to the left and slightly back, between the two peritoneum leaves on the right edge of the omentum minus. It is divided into four sections:

1. Supraduodenal piece
2. Retroduodenal piece
3. Pancreatic piece
4. Intramural piece

The distal 1/3 of the common bile duct passes through the back of the pancreas and enters into the ampulla of Vater (papilla). The common bile duct can join with the pancreatic duct in 3 ways:

a) The most common form is that the two canals join outside the duodenum and attend as a single canal inside the wall and in the papilla.

b) The two ducts may join in the duodenal wall and attend jointly in a short segment.

c) Rarely, both ducts reach the papilla without ever joining.

A circular muscle mass called the Oddi sphincter surrounds the common bile duct, and this sphincter controls the bile flow.

Gallbladder: It is located under the liver. With this location, it separates the right and left lobes of the liver. It has four anatomical sections:

a) Fundus (front)

b) Corpus (storage area)

c) Infindubulum-Hartmann pouch (located behind the neck and corpus.)

d) Neck (connects the sac with the cystic duct)

The gallbladder has functions such as storing, concentrating and secreting bile. Electrolyte concentration in bile is the same as in plasma. Therefore, bile losses are best met with ringer lactate solutions in the structure of bile:

1- Electrolyte and water

2- Bile pigments

3- Protein

4- Lipids:

a) Phospholipids and lecithin

b) Cholesterol

c) Bile acids; chenodeoxycholic acid, cholic acid, taurine, and glycine

DIAGNOSIS METHODS IN BENIGN BILIARY TRACKS OBSTRUCTIONS

There are many methods used in the diagnosis of benign biliary tract diseases. These are applied preoperatively and intraoperatively.

1- PREOPERATIVE TESTS

A- LABORATORY-BIOCHEMICAL

Serum bilirubin level proves the presence of icterine, gives an idea about its weight and allows monitoring of jaundice. Patients with mechanical icterus typically have a direct increase in bilirubin. Sometimes, indirect bilirubin level may increase as a result of prolonged jaundice and affecting liver functions in prolonged bile duct obstructions. When the total bilirubin level exceeds 10 mg / 100 ml, the cause of obstruction is 80% malignant. Serum alkaline phosphatase level 3 times the normal (if there is no bone pathology) indicates biliary obstruction, but high ALP levels can also be found in non-biliary cirrhosis. If there is an increase in gamma-glutamyl transpeptidase together, the event is of hepato-biliary origin. The elevation of 5' nucleotidase together with ALP indicates the pathology of liver disease. Amylase levels are generally normal. Serum transaminase levels can be as high as several times. During the passage of gallstones through the ampulla, a temporary and rapid rise and fall of transaminases can be observed. In this event, an increase in serum amylase level can also be detected. Low leukocyte count and a relatively mild lymphocytosis

favour hepatocellular icter. Leukocytosis may also be present in cholestatic jaundice with cholangitis.

Hemostasis panel may be impaired. In patients with prolonged prothrombin time, vitamin K corrects PT in patients with cholestasis for three days and does not affect hepatocellular jaundice.

Although laboratory tests cannot reveal the actual disease process, it strengthens clinical judgment in terms of the aetiology of jaundice. The determination of bilirubin fractions is necessary for the differentiation of parenchymal and extrahepatic biliary obstructions as well as in the follow-up of the patient. History, physical examination and routine laboratory tests are an essential guide in the correct evaluation of a patient with jaundice.

B- RADIOLOGICAL STUDIES

FLAT ABDOMINAL GRAPH

Its usefulness is limited in the evaluation of patients with gallstones or jaundice. Since 15% of gallstones contain calcium, they are seen as faceted formations on direct abdominal X-ray. Pigment stones with hemolytic dysfunctions are not radiopaque, but if they have sufficient calcium, they can be visualized on direct abdominal images.

ORAL CHOLECYSTOGRAPHY

It is a simple and effective diagnostic method with limited use today. Reliability is 95%. In this examination, fat-soluble contrast agents (iopanic acid, sodium ipodate; such as Telepak, Biloptin) are used. The gallbladder gives information about the cystic duct. It should not be used in cases where serum bilirubin level is above 3.5-4 mg/dl. It is out of date with the introduction of other examinations.

INTRAVENOUS CHOLANGIOGRAPHY

It is applied if the gallbladder cannot be filled with oral cholecystography or if the oral intake of the patient is not good or unfavourable. It is administered as an iodinated substance IV, such as meglumine iodopamide (Biligrafin). Although it is mostly used in the diagnosis of common bile duct stones, it gives false-negative results in 15%. In cases where serum bilirubin is above 4 mg/dl, the biliary system cannot be displayed.

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC)

It is the visualization of bile ducts in the proximal part of the obstruction. With the Chiba or Skinny needle (22-23 no), the radiopaque material is given to the intrahepatic bile ducts through the skin and liver capsule.

PTC can be applied in the palliative treatment of inoperable primary or metastatic malignancies involving the bile ducts, in biliary obstruction, and in cases of sepsis, for preoperative decompensation. It should be considered primarily in patients with duodenal stenosis, hepaticojejunostomy and Billroth II type surgery.

If there is enlargement due to obstruction in the bile ducts, the chance of success is 90-100%. If there is no enlargement, it varies between 66-80%. Therefore, it should be determined by ultrasonography that the intrahepatic bile ducts are wide. Contrast material is administered percutaneously through a trans-hepatically enlarged bile duct, and the entire biliary tree can be visualized.

In this way, stones in the bile ducts are presented as filling defects, and pancreatic head carcinoma is presented as the mouse tail appearance. In addition, strictures and enlargements in intrahepatic and extrahepatic bile ducts can be easily demonstrated. As a result of being essentially an invasive method, complications such as sepsis, intraabdominal bleeding, bile leakage and biliary peritonitis can be seen. Therefore, patients should be monitored more closely, and the necessary antibiotic prophylaxis should be applied.

With the development of Chiba and Skinny needles, these complications have been minimized. Pregnancy, uncorrected coagulation disorders and the presence of acid constitute a contraindication to its administration.

C- ENDOSCOPIC EXAMINATIONS

ENDOSCOPY OF THE UPPER GASTROINTESTINAL SYSTEM

Especially in periampullary tumours, the upper gastrointestinal system should be evaluated endoscopically. The presence or absence of any infiltrative lesions, the condition of the passage and the bulb are essential. If necessary, a biopsy can be taken from the duodenum and ampoule.

ENDOSCOPIC RETROGRADE CHOLANGIO-PANCREA-TOGRAPHY (ERCP)

ERCP, which can be defined as the imaging of the biliary system and pancreatic duct endoscopically, was first described by Mc Cune et al.

With this method, the water papilla is cannulated with a fiberoptic endoscope with a side-view, and a contrast agent is given to the biliary system as a retrograde so that the biliary system and the pancreatic canal can be visualized. ERCP is a complex procedure with some risks. Diagnostic ERCP is often followed by therapeutic procedures such as

sphincterotomy, stone removal and biliary drainage. Therefore, the indication of only diagnostic ERCP is very limited.

Obstructive jaundice, acute suppurative cholangitis, recurrent episodes of cholangitis and pancreatitis, unexplained ALP elevation, cholestatic enzyme elevation, large coledoc or periampullary tumour in imaging methods, acute biliary pancreatitis, biliary fistula, perforated biliary hydatid cyst and chronic pancreatitis are ERCP indications.

Since ERCP is a complicated and risky procedure, the preparation should be done well, prophylaxis with a broad-spectrum antibiotic 1 hour before and the patient should be hungry for at least 4 hours.

If there is no anatomical anomaly, the technical success of ERCP is 95%. It is selective deep common bile duct cannulation, ideal for performing therapeutic procedures and obtaining quality film. It is not always possible for anatomical and pathological reasons.

Paravaterian diverticulum, bulbs or periampullary tumours, papillary deformities, Billroth II gastroenterostomy or Roux-en-Y choledochojejunostomy, papillary region surgery and Oddi stenosis make ERCP difficult. In this case, the problem of cannulation is tried to be solved by using different types of catheters, guidewires, sphincterotomy, pre-incision, radiological-endoscopic combined intervention. The rate of pre-incision for cannulation is 15-20%.

Complications of diagnostic ERCP are pancreatitis, cholangitis, drug reaction and cardiopulmonary effects.

Therapeutic techniques:

- Endoscopic sphincterotomy (EST)
- Stone extraction
- Nasobiliary drainage
- Biliary stenosis obstruction
- Biliary stent insertion
- Gallbladder techniques

ERCP and Endoscopic Treatment Complications: The general complication rate varies between 5-10%. The rate of severe life-threatening complications is 1%. Early (seen within the first 12 hours) complications; pancreatitis, cholangitis, retroduodenal perforation, bleeding, stone entrapment, stent dysfunction. Late complications are; bleeding, gallstone ileus, cholangitis, acute cholecystitis, EST stenosis, new gallstone formation.

Clinical Use of Diagnostic and Therapeutic ERCP:

- Bile duct disease
- Benign biliary stenosis: Surgical treatment mortality is 10%, re-surgery is required in 35% of cases. Therefore, it is an endoscopic treatment method developed as an alternative to surgery. This treatment includes balloon dilation and stent insertion.
- Biliary fistula
- Endoscopic treatment of bile duct parasite diseases
- In biliary anatomical anomalies

D- ULTRASONOGRAPHY AND COMPUTED TOMOGRAPHY

ULTRASONOGRAPHY (USG): USG, which is widely used in the diagnosis of biliary system diseases, is a non-invasive method. It is superior to other methods in terms of its application in patients with jaundice and showing intrahepatic and extrahepatic biliary tracts. It is possible to differentiate extrahepatic obstruction from hepatocellular with an accuracy of 96%. On the other hand, it may not always be possible to determine the nature and anatomical localization of obstruction with USG. The sensitivity of USG for this purpose is 55-90%, and its specificity is 82-93%. The insufficiency of USG in this regard is due to the inadequacy of imaging the distal common bile duct and stones that may be found in this localization secondary to colon gases.

The most crucial criterion for the diagnosis of the enlarged gallbladder by USG is that the transverse size of the bladder is over 4 cm in adults.

Diagnosis of the contracted gallbladder by USG is made when the transverse bladder size is below 2 cm in adults despite enough hunger.

Even if the common bile duct stone is not defined, ultrasonographically larger than 6 mm, the common bile duct is considered pathological. USG has not yet reached the sensitivity of ERCP in the definition of obstructive jaundice. But; Its usefulness as a first screening study is not discussed. However, if a stone or biliary tract enlargement cannot be shown in USG, obstruction of the common bile duct should not be ruled out immediately, and ERCP or PTK should be performed.

Endosonography: Endosonographic examination of the biliary system is not easy due to the difficulty in anatomical orientation. Visualization of the liver hilum and right intrahepatic bile ducts is difficult due to the problem in the penetration of sound waves.

Currently, the endosonographic examination is not routinely performed to examine primary gallbladder pathologies. Because, with transabdominal sonography, the gall bladder pathologies can be detected with great accuracy. Endosonography is most beneficial in the biliary system in distal biliary tract pathologies, where the transabdominal examination is difficult. It provides beneficial information in determining the nature of the pathology that obstructs the lower end of the common bile duct. In addition, endosonography is very important in TNM staging of pathologies detected by different methods.

COMPUTED TOMOGRAPHY (CT): This method is used less than USG in the diagnosis of biliary system diseases, especially gallstones and acute cholecystitis, because of its more expensive and radiation risk. Compared to the above imaging methods, the success rate of CT in the bile ducts is lower. However, if the occlusion is in the distal common bile duct, there is an indication for use to identify possible pancreatic head carcinoma and to determine surgical resectability. If the width of the common bile duct is more than 9 mm, it is considered pathological.

E- CHOLESCINTIGRAPHY

This method is followed by IV administration of HIDA (dimethyl-acetanilide-iminodiacetic acid) labelled with Tc 99m. and showing the bile ducts with a gamma camera. The most important advantage of this study is that it reveals the mechanical obstruction in the bile flow hours and days before the enlargement of the bile ducts or even an increase in the alkaline phosphatase level occurs. With cholescintigraphy, it is possible to demonstrate mechanical obstructions in the common bile duct, and anastomosis can also be evaluated in cases with a bilioenteric anastomosis.

F- MAGNETIC RESONANCE CHOLANGIOPAN-CREATOGRAPHY (MRCP)

2- INTRAOPERATIVE TESTS

A-OPERATIVE CHOLANGIOGRAPHY AND T-TUBE CHOLANGIOGRAPHY

This technique is generally to visualize the bile ducts by giving radiopaque material from the catheter placed in the cystic canal and the T-tube placed in the cystic canal before the exploration of the bile ducts in the operating room. The main purpose of this examination is to prevent unnecessary common bile duct exploration by showing that the transition from the bile ducts and bile ducts to the duodenum is normal. Otherwise, 2/3 of common bile duct explorations performed only with clinical indications were found negative. Due to the high cost and false-positive results, it is gaining strength to perform the operative cholangiography selectively. Recurrent jaundice in the history, lightening of the stool colour

and pancreatitis attacks, laboratory increases in serum bilirubin, LDH and ALP levels, radiologically, the coledoc is larger than 10 mm, the presence of stones in the common bile duct and palpation of stones in the common bile duct. The presence of one or more of the criteria is an indication for operative cholangiography. In the absence of these criteria, the possibility of leaving stones behind in the common bile duct is 2% or less, and only 1/10 of them cause clinical cases. The recently developed endoscopic sphincterotomy technique has also removed the stones left as a problem.

T-tube cholangiography is performed after T-tube is placed in the common bile duct after choledochotomy and exploration of the common bile duct, or before the T-tube is removed after surgery. This technic declares that the common bile duct was normal, there were no stones left, and the transition from the common bile duct to duodenum was normal.

B- OPERATIVE ULTRASONOGRAPHY

There are publications indicating that it is more sensitive than operative cholangiography in the identification of choledochal stones. Correct identification efficiency is reported as 97.5% and 94.4%, respectively. In addition, since it is not invasive, its morbidity is lower than operative cholangiography. Intraoperative USG is an examination with a higher accuracy rate due to the direct contraction of intraabdominal tissues from percutaneous USG. Intraoperative USG can evaluate invasion to peripancreatic tissues and vessels in pancreatic surgery and gains importance in determining resectability. It is also possible to evaluate impalpable structures in the liver. In the evaluation of the biliary system; The sterile hand-held real-time probe is placed directly over the bile ducts and can be identified with very small millimetric stones. It is a more easily applicable method than operative cholangiography, and its detection rates are almost close. However, USG yields less false-positive results, and unnecessary duct exploration is avoided. However, USG, like cholangiography, cannot reveal the entire ductal anatomy and therefore, variations and anomalies cannot be detected. USG is also important in postoperative evaluation. For example; biloma, hematoma and abscesses can be detected and aspirated under USG control for diagnostic and therapeutic purposes.

THE REASONS OF THE BENIGN BILIARY TRACTS STRICTURES

1. Congenital Strictures

a. Biliary atresia

b. Choledochal cysts

c. Caroli's disease

d. Congenital veils and strictures.

2. Choledoc Stones

a. Primary

b. Secondary

3- Biliary Tract Injuries

a. Postoperative strictures

i.Cholecystectomy and/or biliary tract exploration

ii.Bilioenteric anastomoses

iii.Hepatic resection

iv.Portacaval shunt

v.Pancreatic surgery

vı.Gastrectomy

vii.Other procedures

b. Blunt and penetrating trauma

4- Inflammatory Diseases

a. Cholelithiasis or choledocholithiasis (Mirizzi syndrome)

b. Chronic pancreatitis

c. Chronic duodenal ulcer

d. Liver or subhepatic abscesses

e. Parasitic infestations

5- Benign Tumours of The Bile Ducts

a. Hyperplasia

b. Papilloma

c. Papillomatosis

d. Cystic papilloma

6- Others

a. Sclerosing cholangitis

b. Duodenal diverticula

c. Radiation fibrosis

d. Papillary stenosis

BILIARY ATRESIA

Congenital biliary atresia is an anomaly in which the extrahepatic bile ducts and gallbladder are atretic or hypoplasic. Aetiology is not clarified, and whose treatment is severe and complicated. It occurs in 1 in 12,000 births. Relationship with children with trisomy has been established. Aetiology is also considered in genetic factors. In porta hepatis, it is thought to be due to interruption in remodelling during the period of normal development of the biliary tract. The authors found a significant relationship between Reo-3 virus and biliary atresia.

Howard et al. found cardiac anomalies, malrotation or situs inversus, portal vein anomalies, inferior vena cava and spleen anomalies in 25% of 237 patients with congenital biliary atresia. In studies conducted on children with biliary atresia, low L-Proline levels and an anatomical anomaly in the postnatal biliary tract after decreased hepatic synthesis were found.

In the experimental animal studies conducted by Okamata and Hashimoto, devascularization of all extrahepatic bile ducts, after ligation and devascularization of choledoc; atresia changes in the biliary tract, destruction of the epithelium, and fibrous thickening in the muscles of the ductal wall were observed.

The most important factors which affect the prognosis are recurrent fibrosis and stricture formation.

Atresia can be intrahepatic or extrahepatic. The intrahepatic form is a very severe form, and surgical correction is not possible. Extrahepatic biliary atresia has been defined by the Japanese association of pediatric surgeons with three main types of classification.

Type I- Common bile duct atresia

Type II- Common hepatic ductus atresia

Type III- Right and left hepatic ductus atresia

In extrahepatic biliary atresia, jaundice occurs within the first 2-3 weeks after birth. Urine colour gets dark, and stools become colourless, the

liver and spleen grow. There is an increase in direct bilirubin, ALP and transaminase. Its treatment is surgery. Portoenterostomy is performed between the intrahepatic ductal system and the jejunum in the form of a Roux-en-Y in hilum of the liver. This is called the Kasai procedure.

CHOLEDOCHAL CYSTS AND CAROLI'S DISEASE

Vater described the first choledochal cyst in 1723. In 1959, Alonso-Lej reported two cases and examined 94 cases published so far. Based on this case series, he categorized common bile duct cysts into three main groups. Longmire added 4 and 5 to this classification in 1971.

Type 1; it is the most common congenital cystic dilatation of the common bile duct without intrahepatic dilatation.

Type 2; It is the diverticular enlargement of the common bile duct, and it is the rarest.

Type 3; It is the local enlargement of the intraduodenal common bile duct in the form of a common bile duct with Vater obstruction.

The form first described in 1958, in which intrahepatic bile ducts are included in the disease, and the form defined as "Caroli's Disease" today constitutes the 4th type. There are two types according to this original definition.

1. Simple Type: Recurrent attacks of cholangitis, fever and liver abscesses are prominent in this.

2. Periportal Fibrotic Type: Cirrhosis and portal hypertension are dominant in the liver. Cystic lesions in the liver can be unilateral (focal) or segmental or bilateral (diffuse).

Although its aetiopathogenesis is not fully known, it has been accepted as a congenital malformation. Two main factors have been blamed; distal biliary obstruction and pancreaticobiliary reflux. It has been suggested that both obstruction and the reflux of pancreatic secretions to the bile ducts destroy the common bile duct covering epithelium and cause cystic enlargement.

Although it is mostly a newborn and childhood disease, it can be seen at any age. 40-60% of the patients apply in the first ten years of life. Choledochal cysts are four times more common in women than men.

Cardinal symptoms and signs of common bile duct cysts are pain, jaundice, and a palpable mass in the right upper quadrant. Besides, high fever, chills, nausea and vomiting may be seen. USG, CT, ERCP and PTC can be used for diagnosis. Biliary imaging methods are essential in diagnosis. Ductal system anomalies should be defined with ERCP or PTC. 16% of cases have splenic anomalies, including polysplenia or asplenia,

and some of these have preduodenal portal vein anomalies. If there is no cholangitis, biliary obstruction, pancreatic or intrahepatic stones, the patient is kept under observation. Surgical treatment is applied in symptomatic cases.

CHOLEDOCHOLITHIASIS

It is the most common cause of extrahepatic obstructive jaundice. It is also one of the most severe and vital complications of cholelithiasis. Although there are various discussions about the proportion of stones that pass through the cystic duct or directly into the common bile duct after they form in the gallbladder, it is most commonly associated with gallstones. The rate is not known because some of them are overlooked or asymptomatic.

Stones can be single or multiple. It is also proportional to the width of the ductus. Some are larger in diameter than the diameter of the cystic duct and are thought to grow after falling into the bile duct. It is present in 8-15% of patients with gallstones. Its incidence increases with age. In a study conducted, the incidence rate after cholecystectomy was determined as 65% under the age of 40, 42% between the ages of 70-80 and 50% over the age of 80. Bolton and le Quesne found that the rate of stones in the common bile duct after cholecystectomy was 6-19.5%, and Glenn was 8.8%.

It is classified to primary and secondary.

1. PRIMARY COMMON BILE DUCT STONES: These are stones found at least two years after cholecystectomy. Unlike the gallbladder origin, they are oval and brown, without facet and easily crumbly. There are changes in bile structure and infection bile stasis in its aetiology. For this reason, bile duct obstruction is seen. This obstruction may be due to post-traumatic biliary stricture, narrowed biliary-enteric anastomosis, Oddi stenosis, and sclerosing cholangitis.

The beta-glucuronidase enzyme secreted by the bacterial population that increases as a result of stasis (such as E.coli) convert conjugated bilirubin to unconjugated bilirubin. Stones are formed by the precipitation of this bilirubin in the form of calcium salt. For this reason, primary colloid stones are composed of calcium bilirubinate.

Saharia et al. suggested the following criteria for a stone to be considered as primary common bile duct stone; the previous exploration for cholelithiasis, previous cholecystectomy, an asymptomatic period of two years after cholecystectomy, characteristic morphological features, long cystic duct stump was not left, and there was no stricture development in a previous surgery.

2. SECONDARY COMMON BILE DUCT STONES: These are originated from the gallbladder. They pass through the cystic duct in the gallbladder and clog up the common bile duct. They are seen within two years postoperatively. The fact that the stone originates from the gall bladder is understood by the presence of multiple faceted stones in the bladder, the large cystic duct and the presence of stones similar to the common bile duct. Without a fistula, very few stones can pass into the common bile duct, but once this happens, the stone grows with the soft accumulation of pigment and debris. The stone formed by these events is of a cylindrical structure. In the cross-sectional study of these stones, the presence of a small, hard and faceted stone to be detected that the stone originated from the gallbladder. On the other hand, the determination of soft bile sludge suggests that the stone originates from the common bile duct. Stones in the common bile duct leading to acute and chronic intermittent obstruction. Acute obstruction develops as a result of the stone settling in the terminal intrapancreatic segment of the common bile duct and the development of oedema in the common bile duct wall, partly with sphincteric spasm. Bile flow is not completely cut, and there is some bile pigment in the stool, some urobilinogen in the urine. Therefore, although the colour of the stool may lighten, it returns to normal later. Closing and jaundice occur. After a while, the stone either falls into the common bile duct, or oedema regresses, and bile flow begins, jaundice disappears. Temporary and recurrent jaundice occurs in chronic intermittent obstruction. Due to chronic obstruction, the common bile duct progressively expands, doubling on average, and as a result of obstruction, infection, biliary cirrhosis and fibrosis develop in the liver lobules. The changes return to normal if the blockage is removed in the early period.

CLINIC

Small stones can pass spontaneously into the duodenum without any symptoms, as well as cause pancreatitis episodes. Stones with diameters of 1-12 mm were found in studies in 12% of patients without biliary symptoms. Common bile duct stones that do not pass into the duodenum can remain in the ductus for a long time. After a symptom-free period, a clinic of biliary colic, jaundice, cholangitis or pancreatitis may develop. Sometimes it can be detected in elective cholecystectomies for gallstones. If the stones obstruct the common bile duct and the bile becomes infected, acute cholangitis may occur. Classical triad is fever, jaundice and pain. In this case, common bile duct stone should be suspected, and if there are stones in the gallbladder, possibly choledocholithiasis should be considered. If this triad is accompanied by hypotension and mental confusion, it means that acute obstructive suppurative cholangitis has occurred due to bacteremic shock (Reynold's pentad). Pancreatitis is the second most common complication of the

common bile duct stone. Apart from that, it can be seen in the choledochoenteric fistula and common duct structure.

A careful history, physical examination, serum bilirubin, ALP, GGT, AST, ALT values and abdominal USG are generally sufficient for diagnosis. Characteristically, serum bilirubin and alkaline phosphatase levels are increased. Serum bilirubin level is approximately 9 mg per 100 ml. If there is a complication of pancreatitis, serum amylase is usually twice as high as normal, so it should be checked in all cases of bile duct stones. In USG, if common bile duct is larger than 9 mm in diameter, there is no normal liver function and a history of pancreatitis, jaundice, and if there is suspicion of choledocholithiasis, MRCP or ERCP can be applied. If there is no stone, laparoscopic cholecystectomy is performed. If there is stone, it is extracted in ERCP.

BILIARY DUCT INJURIES AND POSTOPERATIVE BILIARY STRICTURE

Extrahepatic bile ducts can be injured in any upper abdominal operation. Iatrogenic biliary injuries are critical because they cause preventable morbidity and mortality. Although it is often after cholecystectomy, it may occur in other operations (liver, stomach, pancreas operations). Stenosis may also occur after a reconstructive or by-pass bilioenteric anastomosis.

The most common abdominal operation is cholecystectomy. In Blumgart's series, surgical mortality under 65 years of age is almost zero; bile duct injury is around 0.2% in these operations. With the increase of laparoscopic procedures over time, the injury occurred about 1-2% (1984). Operative traumas were the most common cause of benign biliary obstruction after all cholecystectomies in 1973. 80-90% of the strictures have been found to be due to compound biliary tract injury in routine cholecystectomy operations. It can be observed after primary common duct surgery, biliary enteric anastomoses, sphincterotomy, and sometimes gastric and pancreatic procedures. In addition to operative traumas, external trauma and stone compression can also cause stricture. Postoperative strictures emergence time In a study by Lillemoe et al.; Symptoms resulted in 10% in the first week, 70% in the first six months, and 80% in a year.

CAUSES OF INJURY DURING CHOLECYSTECTOMY

Anatomical variations are a subject that the surgeon should know very well in advance and pay attention to during the operation. It can be examined in two groups. Among the canal variations, the most frequently observed differences between the cystic canal and the main biliary canal. In cases of doubt, it should be imaged with radiological examinations. With

20% of the arterial variations, the most common right hepatic artery originates from the superior mesenteric trunk completely or partially.

Pathological factors should also be taken into account. In the case of acute cholecystitis, the dissection of the porta hepatis and Callot triangle will be difficult due to excessive oedema. If the dissection cannot be performed safely, cholecystostomy may be a better option. In acute cases, the indication to return to laparotomy for laparoscopic operations should not be omitted.

In the long-term presence of largely impacted gallstones, the presence of a cholecystocholedochal fistula should be kept in mind if there is inflammation in the contracted fibrotic gallbladder, often embedded in the liver (Mirizzi 1948). Stenosis is often associated with the cystic duct. Instead of cholecystectomy, the stones in the canal are removed by partial wall excision, the inside of the gallbladder is observed, and cholecystocholedocoduodenostomy is applied as a treatment option.

SURGICAL TECHNIQUE AND PREVENTION OF COMPLICATIONS

Clear monitoring of compound hepatic duct, compound duct, cystic duct and the cystic artery is important in open or laparoscopic cholecystectomy. Due to the frequent variations of the bile ducts, good anatomy knowledge and slow dissection are required, especially in the presence of inflammation. Technically, in every operation, before the cystic canal is connected, its junction with the common hepatic should be clearly monitored. While connecting the cystic duct, care should be taken to avoid tenting. Blind clamping, clipping and cauterization should be avoided. Operative cholangiography is useful in anatomical differences and possible damage.

The surgeon's predisposition to the operation is essential. Although injuries are often performed by incompetent persons, most of the cholecystectomies where trauma occurs are easy cholecystectomies. In laparoscopic approaches, the surgeon's laparoscopic experience should be sufficient. Failure to distinguish the cystic duct from the main bile ducts in laparoscopic cholecystectomies is the most common cause of injury. In laparoscopic operation, Callot dissection should be started from the neck of the gallbladder, lateral to the Hartmann's pouch, and the entrance of the cystic duct. Dissection of the cystic duct where it joins the compound bile duct increases the risk of duct injuries, especially in the presence of anatomical variation. Again, the most common injuries of the right hepatic artery are observed (Davidof et al., 1992).

Partial cholecystectomy and drainage should be considered in the presence of dense fibrous adhesions in the Callot triangle. Dissection

should be started from the fundus, and if progression cannot be achieved when the neck of the bladder is reached, partial excision should be made, and a drain should be placed. Bile leakage is extremely rare, as there will usually be a complete obstruction in the fibrotic cystic canal. Segmental resection of the compound bile duct 87ajö can 87ajö with common bile duct tenting due to excessive traction.

Bleeding should be carefully controlled during the operation. Finger pressure should be applied to the hepatic artery, and appropriate hemostasis should be provided by distinguishing the bleeding site. Blinding increases the risk of cauterization or clamping damage.

In cholecystectomy operations, supraduodenal choledochotomy should be done carefully in the exploration of the compound biliary tract. When stone forceps or metal spark plugs are used, care should be taken not to cause postinflammatory papillary stenosis, pancreas or duodenum wrong passage by causing excessive difficulty. Postoperative jaundice or cholangitis occurs in the case of an iatrogenic choledochoduodenal fistula. Postoperative pancreatitis may arise together with bile duct stenosis when the device enters the pancreas.

Obstruction or stenosis may 87ajö in the distal bile duct after surgical or endoscopic sphincteroplasty or sphincterotomy. Side-to-side choledochoduodenostomy occurs in cases of multiple 87ajör87, primary stasis 87ajör87, or papillary stenosis. 87ajör87e anastomosis, the compound bile duct should be at least 15 mm in diameter, and a stoma of at least 20 mm should be created. The results of this operation are good, obstruction or cholangitis is rare (Lyoidakis 1981).

DIAGNOSIS

Although bile duct injuries can be noticed during the operation, it often presents with biliary fistula or stenosis after months. Premature bile leakage from a wound or drain indicates 87ajör injury. Peritonitis, limited bile collection, jaundice, fever and chills are observed in delayed patients. The presence of an internal or external fistula or complete obstruction affects the presence and pattern of jaundice.

Cholestatic liver function results are exhibited in the laboratory; serum bilirubin and serum alkaline phosphatase increase. If there is cholangitis, liver enzymes are increased.

USG is excellent in demonstrating intrahepatic dilatations. CT also shows accompanying parenchymal events. Percutaneous transhepatic cholangiography has the advantage of revealing the distal anatomy. ERCP is useless at complete and highly localized strictures. Arteriography or delayed phase portography is indicated if there is excessive bleeding during the operation.

CLASSIFICATION AND FACTORS AFFECTING THE RESULT

Treatment modality, operative risk, and expected prognosis vary significantly in benign biliary strictures. In the series obtained from 34 publications conducted in the 1900s, the operative mortality was 8.3% after 7643 procedures performed on 5586 patients (Warren et al. 1982).

Results are better in young people and those without comorbidities. Hepatocellular disease and liver fibrosis worsen the situation. Stenosis of compound bile ducts or sub-compound hepatic ducts is easier to treat than higher strictures.

The Bismuth classification (1982) is the classification accepted and used in this sense:

1. Downstream compound hepatic duct stenosis - hepatic duct stump > 2 cm

2. Middle compound hepatic duct stenosis - hepatic duct stump < 2cm

3. Hilar stenosis where there is no compound hepatic bile duct - hilar junction is intact

4.Hiler junction is distorted - right and left canals are separate

5. Stenosis of the aberrant right sectoral canal, which also involves the single or combined channel

Treatment should be provided in the first and only operation. Any subsequent intervention will adversely affect the result. Proximal location of the stenosis, intrahepatic or multiple stenoses, accompanying cholangitis or hepatic abscess, intrahepatic stones, external or internal biliary fistula, intraabdominal abscess or bile collection, portal hypertension, hepatic parenchymal disease, lobar liver atrophy and/or hypertrophy, old age or poor general condition are factors affecting biliary stenosis repairs.

PATHOLOGICAL STAGES

FIBROSIS: Biliary obstruction is associated with the formation of concentrated local bile salts in the canalicular membrane, and this initiates pathological changes in the liver (Schaff-ner et al. 1971). Acute and chronic inflammation causes fibrosis and scar formation around the canal and canalicular with collagen deposition. Subsequent damage to hepatocytes is mostly reversible. It takes 4-5 years for liver fibrosis and portal hypertension to occur.

ATROPHY: The liver mass is preserved by a poorly understood balance of bile flow, portal venous flow and hepatic venous flow. Since

atrophy of one lobe is followed by hypertrophy of the other lobe, it creates difficulties in diagnosis and treatment. The most common symptoms are left lobe hypertrophy and right lobar atrophy (Czerniak et al. 1986). In this case, the hilus and left hepatic canal will be difficult to dissect due to rotational deformity of the hilus.

PORTAL HYPERTENSION: Portal hypertension develops secondary to liver fibrosis or with the direct involvement of the portal vein. Liver biopsy is indicated because liver diseases may accompany. Hospital mortality in portal hypertension cases can be around 40% -80% (Bulumgart et al. 1984).

TREATMENT

Preoperative preparation; while the necessary diagnostic tests are performed in the preoperative period, the general condition for the operation should be adjusted. Culture should be produced from the bile that will be taken with PTC. If there is no culture result obtained, an antibiotic effective against anaerobic and enterococcus is used. Although there is not enough information available, the general acceptance is that antibiotics should be used between 48 hours and five days postoperatively, depending on the presence of biliary infection and bacteremia.

If there is anaemia, it should be resolved by transfusion. For coagulation disorders manifested by prothrombin time, vitamin K or fresh frozen plasma should be given. Since oral intake will be insufficient, parenteral nutrition is required. Nevertheless, no results have been obtained in terms of short-term preoperative nutritional support in terms of decreasing the operative risk in prospective studies conducted to date.

Bile strictures; biliary reconstruction is essential because of complications such as biliary peritonitis, subphrenic and subhepatic abscess, liver fibrosis, portal hypertension, hematemesis and liver failure. Percutaneous transhepatic biliary drainage is the appropriate choice for emergency drainage in case of sepsis due to biliary obstruction.

Surgical treatment; the aim of the surgical treatment of bile duct stenosis is to drain bile into the proximal gastrointestinal system; prevention of cholestasis, cholangitis, mud or stone formation, and reoccurrence. This is achieved by tension-free anastomoses of healthy tissues. The operative method changes when the canal injury is noticed during the operation, in the early postoperative period or at the late stage.

DETECTION AND TREATMENT OF TRAUMA IN OPERATION

Detection in operation provides the chance to intervene in the same session. Detection of injury during cholecystectomy has been reported as 12-41%, 19% in various series. The surgeon should seek the opinion of a

more experienced person, if necessary, taking into account his own experience. Dissection should be done into the canal to reveal the extent of the injury. Excessive skeletonization of the bile ducts impairs blood supply. Damaged canal diameter 3 mm and if it is below, a drain is placed and followed. 4 mm and above strictures will drain more than one lobe, they do not close spontaneously and require further intervention.

While turning to laparotomy in laparoscopic operations, in those performed with laparotomy, the incision is extended, and the field is enlarged. An additional assistant may be required for retraction. Operative cholangiography is useful for revealing the anatomy and type of injury.

Regardless of the localization of the lesion in the biliary tree, there are two purposes in the repair of the injury recognized at the time of cholecystectomy; to leave a ductal structure under the hilus without causing tissue destruction, and to prevent uncontrolled postoperative bile leakage. In order not to risk the patient and the next operation, the operation can be terminated by providing external drainage. If the compound duct or hepatic compound duct is connected, it should be opened immediately, and a T-tube drain should be provided away from it. T-tube should be kept for up to 6 months. An anastomosis is required if the crushed clamp is placed or cut. There are two major options for complete canal incision. First, if the ends are brought together without stretching, end-to-end anastomosis can be made. The duodenum and pancreatic head are completely mobilized with the Kocher manoeuvre to relieve tension in the anastomosis. The anastomosis is made with a single layer of absorbable suture and protected by a T-tube placed away from this line. Second, Roux-en-Y hepaticojejunostomy can be performed as 50-60% stenosis or reduction in length can occur in anastomoses. The second may be the first choice for high-level incisions (Bismuth et al. 1978). Also, if the proximal duct is short or the wall is thin, hepaticojejunostomy is preferred.

Although the loss of length is uncommon in lateral injury, its recognition is important because it can be sutured primary over a T-tube. In long lateral injuries, it is almost impossible to sew without narrowing the lumbar. Some authors recommend the use of vein patches, cystic duct stump, or pedicle jejunum flap. The use of the Roux-en-Y jejunal loop as a serosal patch and external drainage with a T-tube is the most recommended method.

Although the literature does not contain many publications about the repair of canal trauma in the same session, success was found to be 40% in the follow-up from Sweden for 3-13 years (mean eight years) (Browder et al.) They reported a rate of 100% in 8 cases in 2.5 years of follow-up.

INJURIES DETECTED IN THE EARLY POSTOPERATIVE PERIOD

The postoperative clinic is variable in injuries that could not be detected intraoperatively. Excessive leakage of bile from the wound or drain within a few days after the operation is manifested by bile peritonitis or progressive jaundice. If there is complete obstruction, it will become yellow on the 2nd or 3rd day. In partial occlusion, jaundice develops following the fistula from the drainage tube. In patients, serum bilirubin increases with the degree of stenosis, with a marked increase in liver enzymes alkaline phosphatase and gamma-glutamyl transferase. Other liver enzymes tend to be minimal or slightly increased.

Trauma to the biliary tree is considered in the presence of external fistulas that drain hundreds of millimetres of bile per day. In the presence of an external fistula, it is necessary to show the enteric continuity of the biliary system rather than being hasty. If there is a passage, the pressure is reduced with sphincterotomy. If there is bilioenteric continuity, external fistulas generally tend to close spontaneously for a long time. In the presence of obstruction, the expansion of the proximal bile ducts over time facilitates the possible operation. Compound bile duct stones, bile duct tumours, suture slippage from the bile stump or clip opening should be considered in the differential diagnosis.

In the case of bile peritonitis, if there is an infection, the picture can be very serious. Sterile bile can be collected in large quantities without symptoms. The drainage and collection of bile should be prevented. Since definitive operation will be very difficult under these conditions, external drainage is the best approach.

A special case occurs in only one lobar lobe occlusion. Fever, which may be accompanied by a slight increase in serum bilirubin, is observed in the patient. Slight jaundice and itching may be observed, but the stool is in its normal colour. There may be no other finding except a slight increase in serum alkaline phosphatase. A clinic may not be given only in a segmental branch occlusion. Ipsilateral atrophy and contralateral hypertrophy are observed in prolonged lobar occlusion.

Imaging is important in making the diagnosis and determining the treatment path to follow. Endoscopic retrograde cholangiography and percutaneous transhepatic cholangiography are essential examinations. Although the first is less invasive; The latter is also valuable as it gives better information about the proximal bile ducts in case an anastomosis is required.

If there is progressive jaundice with cholangitis, the injury is as described below. Injuries occurring long after the first operation

Treatment should be initiated in all patients following diagnosis. The first postoperative days following cholecystectomy provide an easy appearance due to the fact that rigid adhesions have not yet formed in the subhepatic area, and dense adhesions increase parallel to the delay.

Although it is said that percutaneous transhepatic cholangiography does not affect the mortality and morbidity of stenosis treatment, it should not be preferred, except for patients with serum bilirubin levels above 30 mg/dl.

In addition to surgical treatment, percutaneous transhepatic or endoscopic retrograde dilatation and stent placement are among the choices. Surgical dilations in general; it is preferred in cases of segment stenosis longer than 0.5 cm, when there is no traceable lumen (tied or clamped ductus), in cases where percutaneous or endoscopic dilatation fails.

Dilatations are often performed by inflating a balloon used with a flexible guide. After dilatation, 12 or 14 French catheters are placed and kept for 2 to 6 months. Adding endoscopic sphincterotomy is preferred in endoscopic dilatations. This procedure is not preferred in high biliary strictures. However, complications are not common in these procedures, bleeding and sepsis.

If an end-to-end anastomosis is performed in strictures after liver transplantation, percutaneous or endoscopic dilatation is the best treatment.

The treatment principles in delayed biliary stenosis or obstruction are as follows:

1. Visualization of intact proximal bile ducts providing drainage in all bile ducts of the liver,

2.Adjustment of a distal mucosa suitable for an anastomosis,

3. Anastomosis of the biliary system between the mucosa and mucosa so that it can reach the enteric system.

In the presence of an intraabdominal abscess, portal hypertension, or poor condition of the patient, stepwise therapy should be preferred. Percutaneous transhepatic drainage approaches are preferred, especially in patients with portal hypertension. (Pelligrini 1984) If a portosystemic shunt is required, this operation should be performed before the stenosis operation.

OPERATIVE TECHNIQUES IN THE TREATMENT OF STENOSİS

- Direct end-to-end canal repair: It is applied by placing anastomosis and a T-tube.

- Bilioenteric repairs:

NON-OPERATIVE APPROACHES IN THE TREATMENT OF STENOSIS

Observation of stenosis or occlusion in a small area in cholangiography does not mean an indication for operation. The formed internal fistula can provide good long-term drainage. Although it gives mild symptoms in elderly or high-risk patients, close follow-up and antibiotic prophylaxis can be applied in cases where drainage is provided. The superiority of balloon dilatation to close follow-up approach is controversial due to the lack of long-term results. Mueller et al. followed 61 patients for three years by performing bolon dilatation, and in their results, they achieved 67% success in anastomotic stenosis and 76% in iatrogenic injuries. Although there are no long-term consequences, balloon dilatation has a high re-stenosis rate in the short term. Mean, while 77% of patients had success after dilatation in 30 months, the rate decreases to 55% in 59 months. (For those whose stenosis was resolved without open surgical intervention, good results were achieved at a rate of 67% to 55% as a result of 59 months follow-up.) Complications of transhepatic balloon dilatation are also frequent; in a publication from Mayo Clinic, 29% of 65 patients had more than 2-gram haemoglobin loss, and 11% are transfused. Again, 24% of patients had sepsis with positive blood culture. Patients with successful endoscopic dilatation are those with primary bile duct stenosis and choledochoduodenal anastomosis stenosis. There is a need to replace the stent periodically.

RESULTS:

The reasons affecting the prognosis of the patients have been stated before. Factors that are effective in satisfactory repair are the presence and number of previous operations, the type and level of stenosis, and the method of treatment. Those affecting mortality are previous operations, level of stenosis, preoperative liver function, liver fibrosis and portal hypertension.

Operative mortality and morbidity: 10% of patients who undergo biliary reconstructive surgery experience one or more major complications. This rate is even higher in those with reoperation. The most common complications are subphrenic, subhepatic and pelvic abscess, wound infection, cholangitis, bacteremic shock, postoperative haemorrhage, biliary fistula and pulmonary infection. Operative mortality has been given between 5-8% in various series. The most common causes are uncontrolled haemorrhage, hepatic and/or renal failure. Biliary fistula, bacteremia and pulmonary causes have been reported rarely. Mortality in abscess drainage, portosystemic shunt and stenosis operations was 8.3%, whereas it was only 3.2% in stenosis operations. There were no deaths in 63 patients who

underwent hepaticojejunostomy and choledochoduodenostomy with a mucosa-to-mucosa anastomosis. In 1993 Chapman et al. had reported zero mortality as a result of mucosa-to-mucosa anastomosis in 108 patients, 97 of whom were left canal hepaticojejunostomy. In the mean 7.2 (1-13) year follow-up of the patients, 80% of the patients did not have biliary symptoms, and no further intervention was required.

Hypoalbuminemia, elevated serum bilirubin levels, presence of liver disease and portal hypertension are parameters that affect the outcome. Although Bismuth type 4 stenosis is a factor that affects the operation badly on its own, it affects the result of three or more previous operations. Bismuth (1982) has described only one perioperative mortality in 186 cases since 1956 with left-sided hepaticojejunostomy. In summary, operative reconstruction is a very reliable technique for stenosis in competent hands.

LONG-TERM RESULTS AND FOLLOW-UP: Long-term well-being parameters differ according to the authors. In the classification of Terblanche et al.;

Grade 1: No biliary symptoms,

Grade 2: There are temporary symptoms,

Grade 3: Presence of obvious symptoms requiring medical treatment,

Grade 4: Recurrent stenosis requiring intervention is indicated as. Bismuth describes the absence of stenosis as good, with a symptom-free period of at least five years, preferably ten years, and normal liver function. Recurrent strictures occur between two and ten years postoperatively. In clinically good patients, ongoing elevations of serum alkaline phosphatase levels are due to accompanying hepatocellular disease or inadequate opening of the obstruction. The operation cannot be considered perfect until the alkaline phosphatase is normalized.

BILIARY TRACTS INJURY IN OPERATIONS EXCLUDING CHOLECYSTECTOMY

BILIARY RECONSTRUCTION

Stenosis or fistula may be encountered as a complication in bilioenteric anastomosis operations. These operations include pancreaticoduodenectomy, bile duct tumours, and common bile duct cysts. The reason for these is the narrowing of the average diameter lumen used in anastomosis over time due to fibrosis. In side-to-side anastomoses, if the lumen diameter and anastomosis diameter are provided above 15 millimetres, stenosis is very rare (Degenshein 1974). If Sump Syndrome develops after choledochoduodenostomy, cholangitis and stenosis may

develop due to stone or debris. Although endoscopic approaches can be tried, the consensus of the authors is that they prefer end-to-side Roux-en-Y hepaticojejunostomy for intestinobiliary regurgitation and permanent elimination of the Sump (Matthews 1993). Recurrent episodes of cholangitis after biliary-enteric anastomosis often lead to anastomotic stenosis. Intrahepatic stenosis or intrahepatic stone may have been missed while attached (Matthews 1993). Lillemoe states that one should not be in a hurry for leaks from the anastomosis, and it will be highly spontaneous.

GASTRIC RESECTION

If the pyloric region and duodenal bulb are oedematous and distorted during gastrectomy, bile duct injuries are more common. It is mostly seen in Billroth II operation and rarely in Billroth I. The differential diagnosis of jaundice or biliary fistula in the postoperative period from duodenal stump leakage should be made. Anastomosis to the duodenal stump is easy in repair after Billroth II. Blumgart buried the pancreatic head with an open jejunum, bringing in the retro colic Roux-en-Y segment in three cases he encountered.

HEPATIC RESECTION

In liver resection, especially if hilar dissection is performed, bile ducts may be damaged. A T-tube is not routinely placed in partial liver resection. If trauma to the bile ducts is suspected, intraoperative cholangiography is performed. Choledochostomy is opened, and right and left canals are evaluated with spark plugs. If the choledochostomy is opened, a T tube is placed. Since the treatment of injuries after partial hepatectomy will be quite difficult, permanent fistula or; if jaundice or cholangitis is superimposed, it should be dealt with.

OTHER PROCEDURES

Stenosis may develop after exposure of portocaval shunt or paraaortic structures to radiation. There is no consensus on the treatment of strictures that may occur after liver transplantation.

BILIARY TRACTS INJURIES DUE TO DRILLING-CUTTING OR BLUNTED TRAUMA

The gall bladder or bile ducts can be damaged during blunt abdominal trauma, piercing knife or gunshot wounds. Late problems are bile fistulas formed from the injured section. If there is accompanying distal stenosis, the fistula will be permanent. The best approach is an anastomosis to a well-formed track jejunum (fistulojejunostomy) or gallbladder. Fistulojejunostomy can provide permanent healing, and stenosis or obstruction may develop in the late period. Direct suturing of the fistula is rarely successful.

POST INFLAMMATORY BILIARY TRACT STRICTURES

PROLONGED CHOLELITHIASIS

As a result of recurrent attacks of cholecystitis, fibrosis and shrinkage of the gallbladder occur, this occludes the Calot triangle. Jaundice and cholangitis develop if the inflammatory process progresses to the environment and involves the combined hepatic ducts. Cholecystocholedochal fistula may occur as a result of erosion due to chronic inflammation. For this reason, preoperative percutaneous or endoscopic cholangiography should be performed in patients presenting with prolonged stone, previous attacks, jaundice and cholangitis.

CHRONIC DUODENAL ULCER

Chronic periampullary duodenal ulcer may erode and damage the entire periampullary area over time, resulting in stenosis or choledochoduodenal fistula. Standard ulcer treatment is sufficient for healing.

GRANULOMATOUS LYMPHADENITIS

This may cause stenosis in common hepatic or common bile ducts with which it is in contact. Often the causative agent is tuberculosis. Since liver damage and atrophy due to stenosis will accompany, its treatment is difficult. Regular biliary reconstruction is not always possible.

RECURRENT PYOGENIC CHOLANGITIS

There are intrahepatic calcium bilirubinate stones and intrahepatic strictures in the disease, which is frequently seen in far east Asia. Hepatectomy and Roux-en-Y hepaticojejunostomy are used to the affected lobe. There are authors who use interventional radiological approaches alone or in combination with surgery.

CHRONIC PANCREATITIS

It is frequently seen in alcoholic pancreatitis. The cut affected is the retropancreatic bile duct. It is accompanied by pain. While the diagnosis is often made by ERCP, it can also be noticed during the operation. It is very difficult to differentiate from carcinomatous occlusion. The presence of stenosis findings in the course of pancreatitis is not an indication for treatment. If cholestasis or cholangitis occurs, biliary by-pass occurs. Almost all of the strictures heal with the passage of pancreatitis. Biliary enteric anastomoses provide excellent long-term results in treatment.

BENIGN TUMORS OF THE BILIARY TRACTS

It is thought to occur in response to an inflammatory process. It can be a gallstone, non-absorbed suture material, or a T-tube. It likes papilloma clinically and histologically, and can be distinguished only in typical cases by the presence of chronic inflammatory infiltration of the hyperplastic epithelium. Usually, at the lowest part of the biliary tract, papillae are located in the covering epithelium. This process can lead to papilla's fibrotic stenosis.

PAPILLOMA: It is the most common benign tumour of the biliary tract, located in the Ampulla of Vater. It has a polypoid structure and is histologically covered with columnar cells and goblet cells.

MULTİPLE PAPILLOMA AND PAPILLOMATOSIS: They are the rarest ones, and they are clinically and histopathologically similar to papillomas. However, the risk of recurrence and malignant transformation is high.

CYSTIC PAPILLOMA: It is rare, cystic lesions that have arisen from papillary extensions within the cyst. They have been detected in intrahepatic bile ducts and hepatic ducts.

CLINICAL SYMPTOMS AND DIAGNOSIS

Benign tumours of the biliary tract may not give symptoms. Symptoms are usually seen due to obstruction, so jaundice, pain, and cholangitis are the most common complications. There is a high probability of having common bile duct stones with them.

DIAGNOSIS

PTK, ERCP and biliary scintigraphy are used. Often they are overlooked or even not noticed during surgery.

TREATMENT

Local excision and evaluation of the piece pathologically with a "frozen section" is recommended.

SCLEROZAN CHOLANGITIS

Sclerosing cholangitis is an inflammatory disease of the biliary tract, characterized by progressive fibrosis and obliteration, involving the entire biliary tract. Although the clinical picture indicates the event, intrahepatic multiple strictures and dilatations, multiple extrahepatic strictures, and major stenosis in the common hepatic duct completing the diagnosis are observed on x-ray. Rarely, a solitary nodule may be found in the distal biliary tract, mimicking its primary carcinoma. If this condition is not after surgery, trauma, or stone, it is qualified as "primary sclerosing cholangitis". Inflammatory bowel disease, often accompanied by

ulcerative colitis, in almost all patients. It may accompany cholangiocarcinoma.

Sclerosing cholangitis is often manifested by jaundice, cholangitis and pruritus in young or middle-aged adults. Upper abdominal pain may be a symptom. Although the aetiology of primary sclerosing cholangitis is unknown, showing the same antigenic structure as some autoimmune diseases supports the autoimmune aetiology. An increase in sclerosing cholangitis was observed in patients with AIDS, possibly as a result of opportunistic infection due to criptosporoidea.

Biliary cirrhosis and portal hypertension become evident in the course of the disease. The formation of acid and oesophagal varices indicates progressive liver failure. Although the clinical study may cause death in one or two years, it may be relatively slow or nonprogressive. Medical treatment of the disease is controversial. Response to steroids, immunosuppression and copper-binding agents was not satisfactory. In the presence of inflammatory bowel diseases, colectomy has no effect on the progression of the biliary disease. Surgery gives the best result in removing dominant strictures in the extrahepatic ductal system. These strictures can be removed, or intestinal anastomosis can be made following resection. Surgical interventions are not satisfactory in recurrent strictures. Although some surgeons recommend leaving a long-term bilateral transhepatic tube, good results are obtained in percutaneous dilation with enlarged dilatation.

Liver transplantation is inevitable after the development of cirrhosis and portal hypertension in these patients. As a result of early transplantation, the risk of carcinoma development, which is between 6-20%, is prevented.

DUODENAL DIVERTICULES

Duodenal diverticula can be intraluminal or extraluminal. Extraluminal diverticula are often located in the head of the pancreas and rarely cause symptoms. As such, they have been reported in cases of perforation, bleeding, infection, and obstruction of the biliary tract or duodenum. The treatment consists of closing the neck following excision or inverting into the lumen.

Intraluminal diverticula, on the other hand, were previously a congenital web in the development process, but gradually become a long diverticulum due to pulling. They are difficult to differentiate from type 3 common bile duct cysts and can only be distinguished by the presence of duodenal mucosa on its wall. The mouth of the diverticulum can take the Vateri into the ampulla.

Symptoms may be due to biliary obstruction, duodenal obstruction, pancreatitis or ulcer bleeding. The diagnosis is usually made

by barium X-ray, and its treatment is surgically duodenotomy and excision of the diverticulum. Endoscopic removal of the debris by widening the neck or partial excision of the diverticular wall endoscopically can relieve symptoms. Duodenojejunostomy may be useful in cases where the duodenal obstruction is the main problem.

MIRIZZI SYNDROME

Mirizzi syndrome is the entity determined by the obstruction of the common hepatic duct, Hartmann pouch or the stone attached to the cystic duct, by compression of the sac wall and ductus wall and the resulting obstruction. The table is similar to carcinoma by imaging techniques, and its symptoms are similar to wearing jaundice.

In delayed patients, cholecystocholedochal fistulas may develop from the damaged wall of the common hepatic duct. The necessary treatment is cholecystectomy following careful dissection of the Calot's triangle and, if any, the defect in the common hepatic duct is closed with Heineke-Mikulicz or a patch from the sac wall. An anastomosis of the proximal ductal system to the jejunum may rarely be required.

RADIATION FIBROSIS

In primary biliary tract tumours, there is a pause of the disease after intraoperative administration of 6000 rad, intracavitary radiation, or external beam radiation, and radiation fibrosis and subsequent implantation in the ductal system develop. This occurrence gains importance in the operative evaluation of patients who receive radiation therapy and those who have recurrent jaundice. Treatment consists of stenting or tube placement and operation or percutaneous balloon dilatation. The biliary enteric by-pass is indicated in some patients.

PAPILLARY STENOSIS

Benign papillary stenosis is being reported at an increasing rate, but its presence is difficult to detect. It is characterized by intermittent recurrent upper abdominal pain in patients with cholecystectomy. The syndrome includes structural abnormalities caused by intraoperative trauma, adenomyosis, or chronic inflammation and fibrosis due to migrating stones. As a result of manometric studies, a functional component due to increased pressure without structural anomaly was defined in the Oddi sphincter. This component is thought to be due to the denervation or spasm of the sphincter muscle.

Most of the patients are women with or without stones undergoing cholecystectomy. Almost all patients describe episodic upper quadrant pain radiating to the back, similar to those before cholecystectomy. Recurring pancreatitis is rarely defined. For the diagnosis, a good history should be taken, and Oddi sphincter dysfunction should be demonstrated

with ERCP. Intravenous administration of cholecystokinin is valuable for further investigation. Administration of IV cholecystokinin provokes pain. Pancreatitis, peptic ulcer, common duct stones, and ampulla neoplasms should be ruled out.

Priority in treatment is endoscopic sphincterotomy. This procedure eliminates phasic wave contractions and the gradient between common bile duct and duodenum. Still, the risk of re-stenosis is high. Although success with the operation is good, the chances of recruitment remain high.

Medical treatment should be applied until the patient capacity is exhausted in patients with upper quadrant pain after cholecystectomy. The dysfunction of the Oddi sphincter should be confirmed by rigid criteria and ERCP before operative or endoscopic sphincterotomy. Complaints can last for a long time in patients who cannot provide the necessary improvement after treatment.

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CHAPTER VII

RELIABILITY, REPRODUCIBILITY AND TIME-EFFICIENCY OF VOLUMETRIC EVALUATION OF LUNG TUMORS BY 3D-SLICER SEGMENTATION WIZARD

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1. INTRODUCTION

The treatment response evaluation of lung cancers can be detected in tomography images based on their size changes.[1,2] Therefore, it is crucial to make the measurements precisely.[1,3] Diameter measurement is preferred because of its simplicity. This method is based on measuring the longest diameter of mass which has been standardized by RECIST criterias and used for follow-up imaging of multipl metastatic diseases in daily practice. Malign lesions are ill-defined and have an asymmetric configuration which causes obstacle for defining lesion borders from normal surrounding parenchyma. This could results in observer dependent variability and subjectivity in the measurements. [4] Theoretically, the most ideal follow-up method is the detection of volumetric changes.[1,5] One of the volume calculation methods is the manual 3 dimension volume calculation (M3D), multiplication of longest three diameters in three different anatomic dimensions with the coefficient of 0.523. Repeatability and objectivity are not expected in this method because of the reasons mentioned earlier.[6] The necessity of a reliable and reproducible volumetric measurement prompts the development of computer software allowing automatic and semi-automatic segmentation of lesions.[7,8] This segmentation method allows us to extract the tumor from the surrounding parenchyma, obtain 3-dimensional (3D) images, and detect volumetric changes in asymmetric tumors more precisely.[9]

The segmentation method can be applied manually, semi-automatically or automatically. In the manual segmentation method, the volume measurement is performed by manually drawing the tumor boundaries in each section and then automatically calculating the volume.[10] Therefore, slice thickness and observer dependency affect the reliability of measurements.[11–13] Also, it is not practical for daily routine owing to being a time-consuming method depending on the size of the lesion and difficulty in defining borders of subsolid nodules.[14] Osirix perimeter method (PM) used in a manual segmentation volume calculator software.[10]

Although semi-automatic segmentation methods has decreased measurement mistakes, they are time-consuming methods and most of them are not public domain softwares. Thus, they are not suitable for daily practice. There are ongoing studies, trying to make these methods suitable for daily practice by adding new modules allowing faster and more objective measurements. [14]

3D-Slicer is a public domain software, that can make semi-automatic volume measurements.[15] Volumetric measurements of this software are more precise and reliable than manual segmentation methods, but this is a time-consuming method.[16] Several modules have been developed to reduce the time. One of them is the 'SegmentationWizard' (SW) module.[1]

This study aimed to investigate the reliability, reproducibility, and time-efficiency of 3D-Slicer SW (3DSSW) software for volumetric assessment of lung tumors in routine clinical practice, by comparing it with the PM methods.

2. MATERIALS AND METHODS

2.1 STUDY POPULATION AND MR EXAMINATION PARAMETERS

Multi-detector Computed Tomography (CT) images of 50 histopathologically proven lung tumors obtained prior to therapy were evaluated retrospectively. The study plan was approved by the Faculty of Medicine Ethics Committee of our university (Decision date: 13 December 2018, Decision no: 218). Thorax CT scans were performed with Siemens Somatom Definition AS (Erlangen, Germany) a 128 slice CT machine. Imaging parameters were as follows; automatic effective mA, 120 kVp, gantry rotation speed 0.5 sec, slice thickness 1 mm. 90 ml of 300 mg/ml iodinated contrast agent with 50 ml saline solution was administered to all of the patients intravenously. Reconstructed images were evaluated by

[1]Documentation/Nightly/Extensions/SegmentationWizard-SlicerWiki. https://www.slicer.org/wiki/Documentation/Nightly/Extensions/SegmentationWizard. Accessed 3 Oct 2019

Picture Archiving and Communication System (PACS), OsiriX MA v. 10.0.2 (UCLA, Pixmeo), GPL licensed free to access resource code and commercially licensed, FDA approved Mac OS X radiology workstation.

2.2 IMAGE ANALYSIS AND VOLUMETRIC MEASUREMENTS

Two radiologists, H. A (observer 1) with 15 years and, A.S (observer 2) with 3 years of experience in Thorax radiology evaluated the images independently. Firstly, two observers decided together which tumors should be measured. Thus, the measurement was provided to both observers from the same lesions. Parenchyma window settings were fixed at WL 1800 HU and WW 600 HU to be able to evaluate subsolid and ground-glass nodules and standardize the assessments. Lesions were classified according to size (nodule <3 cm, mass >3 cm), density (solid, subsolid, ground-glass), and location (intraparenchymal, mediastinal/hilar, and chest wall invasion) [17]. Later, both observers calculated tumor volumes, independently of each other, using PM methods and 3DSSW. Three months later, measurements were repeated and the time period was recorded during the second measurements.

In the PM method, lesion borders were drawn manually for each slice and automatic volume calculation was done. Finally, the 3DSSW method was used for measurements.

3D-Slicer 4.8.1 version was used in this study. The 3D-Slicer program uses Image Qualification, Image Extraction or Image Segmentation methods for volumetric calculations of geometric objects and extracting mass from normal structures in routine practice. Image Qualification, is image processing with digitizing the images. A digitized image is the representation of the image with binary coding. Each cell is represented as pixel in coding[18,19]. There are two major characteristics of a pixel. One of them is the radiometric characteristic, which shows grey tone value in the electromagnetic spectrum. The other one is, geometric characteristics which shows the coordinate value in the imaging matrix. In grey scale 0 value represents black and 255 value represents white. Grey tones are formed between these values. With the development of hardware and software technologies, a scale coding between 0-4096, showing grey tone difference more sensitive is being used. The representation of this coding in CT imaging is density. Tissues with different densities are coded in grey color tones. A supplementary method called Thresholding is used for the radiological volumetric and area calculations with Image Extraction. Distinction from surrounding structures is provided by identifying and coloring the grey color scale range corresponding to the mass[20,21] (Figure 1).

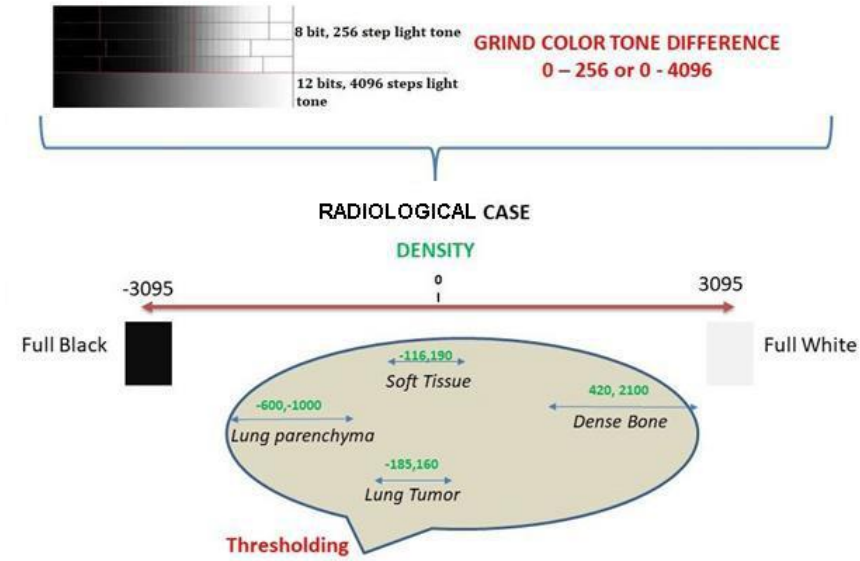


Figure 1: Thresholding with densities used in medical imaging.

Thresholding is not enough for image extraction on its own. Therefore, segmentation is used with thresholding. Segmentation totally depends on the initiative of the expert. 3D-Slicer method marks the circumference of the lesion with a few marking orders differently from other volume calculation methods. Thus, volume calculation processing steps decrease and the time period shortens. Thresholding is used together with segmentation in 3D-slicer software. Firstly, density settings should be performed for thresholding borders. This setting also improves the sharpness of the area to be calculated. Then, in the type-1 method the area to be extracted volumetrically is marked or selected (segmentation). Thus, areas with the information content of density and border information are transformed into three dimensions. It is possible to erase some undesired parts of the 3D solid model. In type-2, after entering density information, all of the regions having this information contained in the area, are transformed into the solid model. Later, plain volumetric information of the desired region can be obtained by extracting from this solid model (Figure 2).

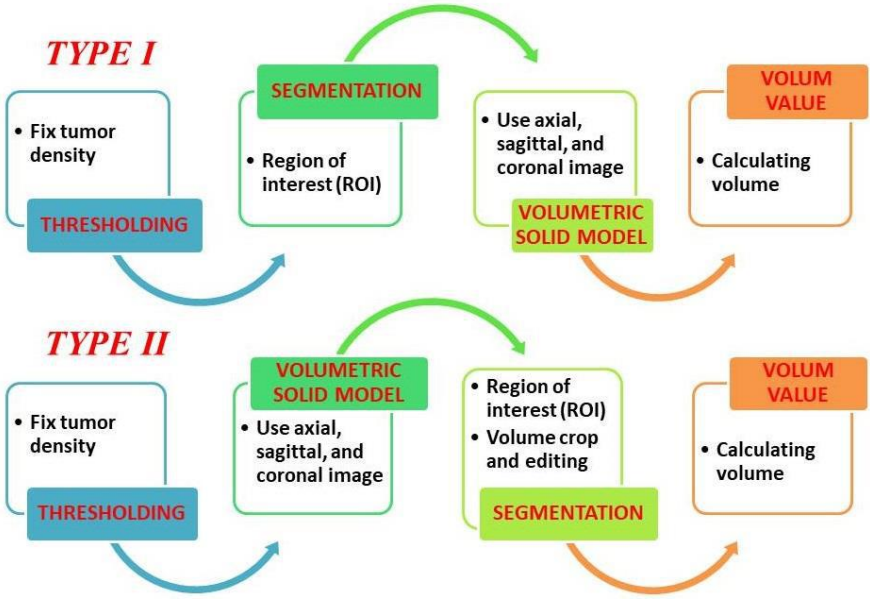


Figure 2: Flowchart of two different volume calculation method.

Both methods are time consuming for routine application and are insufficient to distinguish regions with similar densities [14]. Andrew Beers (Massachusetts General Hospital), developed a coding called SegmentationWizard(SW), which does semi-automatic high resolution extraction, to make this program more suitable for routine practice. SegmentationWizard module processing steps are performed as follows[1] (Figure 3);

Firstly, the 3D-Slicer software is launched and the lung file document is loaded.

Step1: Volume selection (Figure 3a). The CT or MRI image is selected to calculate volumetric data or to create a solid model.

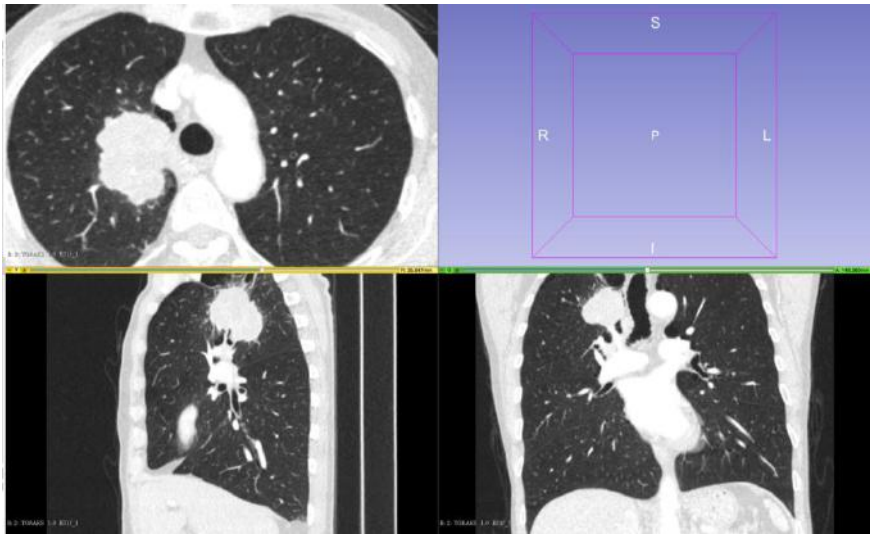
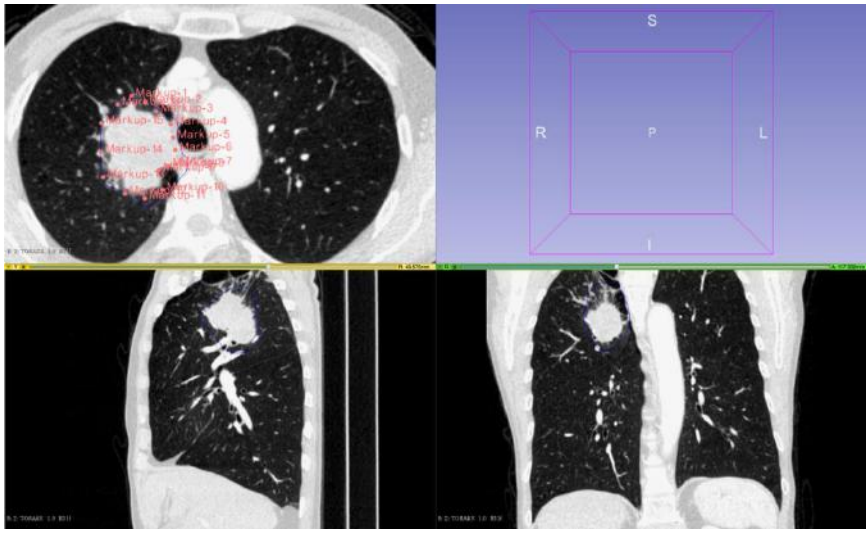


Figure 3a: Image selection. Selection of the slice of the lesion to be measured from the loaded images (ca. 25-30 sec).

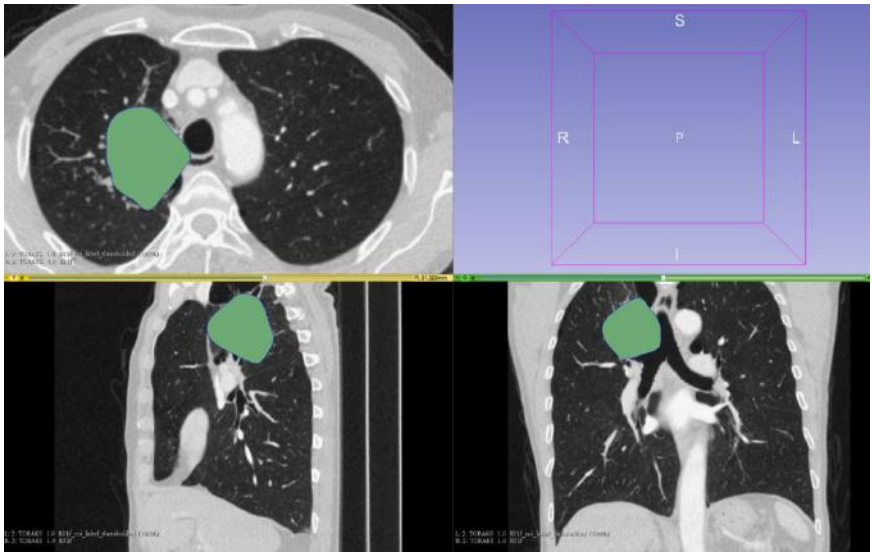
Step 2 (optional): Record. This provides a recording of the studied images as a solid model.

Step 3 (optional): Normalizing and extraction. This reflect changes on the extracted model or protection of original images. Also, image filtration and normalizing are provided by the Gaussian method. Gaussian normalization is a method of calculating unknown equations using a specific matrix and solving unknown equations. It is generally used to locate the views and for filtering.

Step 4: Marking (Segmentation). This is used for marking the region to be extracted. Borders are drawn with points on axial, sagittal, and coronal images (Figure 3b, 3c) because at least three points selection is necessary. The formation of the solid model will be seen directly after the selection. At this stage, a field is set by creating a curve passing at least three points in each CT image. The volumetric image of the objects remaining within these areas will be taken into account.



3b



3c

Figure 3b,c: Marking (segmentation). Borders are drawn with points on axial, sagittal, and coronal images (ca.50-60 sec).

Step 5: Extraction (thresholding). At this stage, the density range of the extraction desired lesion is defined (Figure 3d). Using the simple slider in the previously marked volume enables the user to enter the density of the desired tissue in a range. This adjustment is decided at the moment when the tumor is clearly seen by the user. The adjustment range of the image at this stage is presented by calculating and narrowing the intensity

value within the limit determined in the previous step by the software. This enables the user to make thresholding more sensitively.

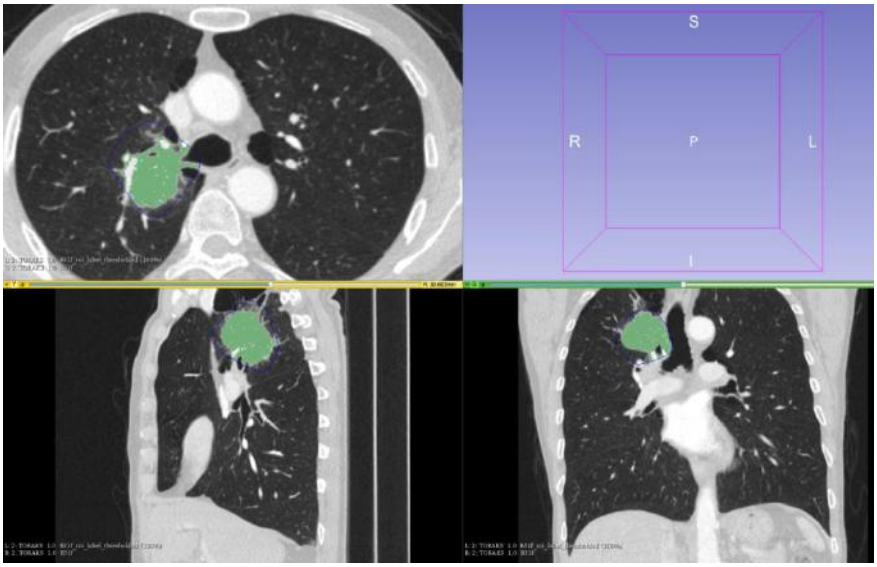


Figure 3d: Extraction (thresholding). The density range of the extraction of the desired lesion is defined (ca. 15-25 sec).

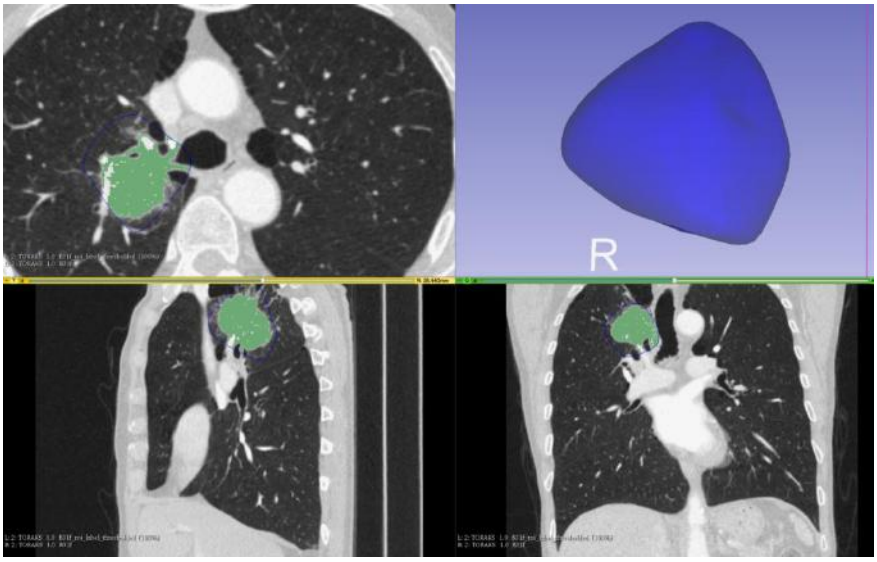


Figure 3e: The volumetric mode will be seen in solid form.

Step 6: Imaging. The volumetric mode can be seen in solid form (Figure 3e). If change or extraction is wanted in this stage, it is possible to switch to present segmentation or editor toolbar of 3D-Slicer. Later, the numeric value of volume can be seen and recorded by the 'volume information' order of 3D-Slicer (Figure 3f).

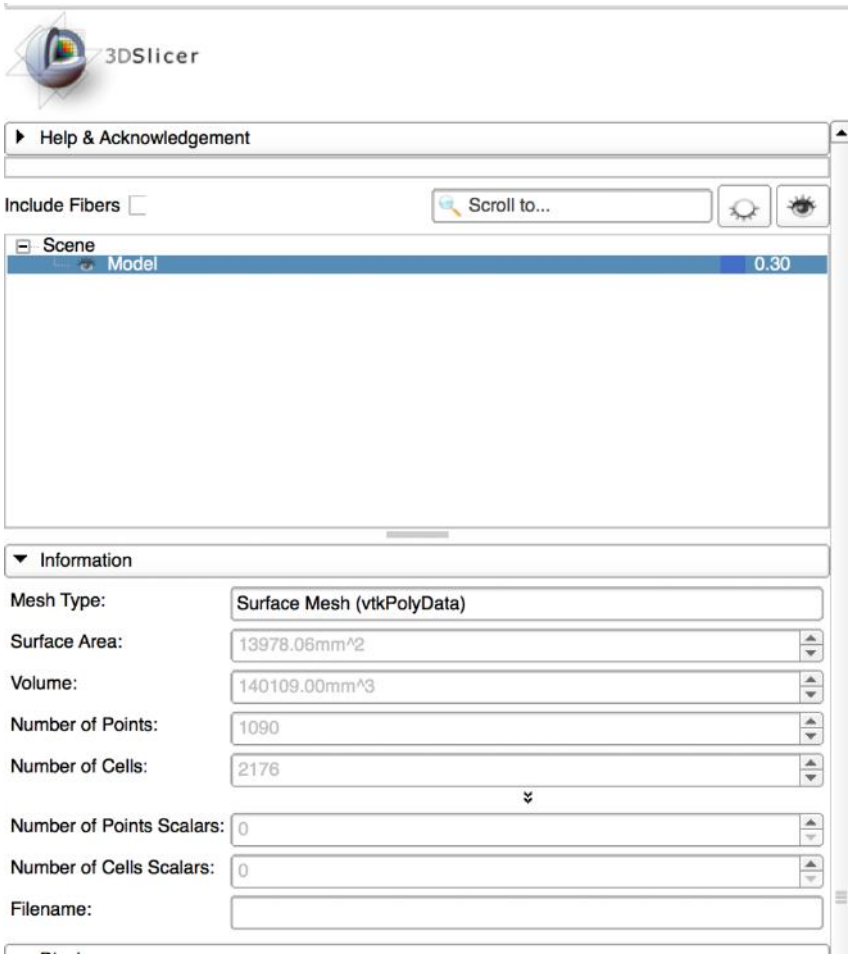


Figure 3f: Numerical value of volume can be seen (ca. 5-10 sec)

Of the above steps, only the 4th and 5th steps require the user to perform manual operations. We skipped the optional second and third steps to achieve results faster in this study. Volumetric change of the mass in one year was olso presented visually. The solid models of the mass from both of the tomography images in STL format were recorded, and printed solid model by a three dimension laser printer using Fused Deposition melting

technology with polylactic acid (Figure 4). These concrete visuals can be used especially for research and education purposes.

Figure 4: The volumetric change of the mass in one year is presented visually. Solid patterns of the mass from both tomography images were saved in STL format, and the solid models were created with a three-dimensional laser printer using Fused Deposition melting technology with polylactic acid.

2.3 STATISTICAL ANALYSIS

Statistical analyses of the study were performed by SPSS (IBM Inc.) with version 20.0. Descriptive statistics were presented as frequencies (percentage) for categorical variables; as median (Q1-Q3) for numerical variables. Continuous variables were analyzed for normality by the Kolmogorov-Smirnov test. Since the distributions of the measurements were not normal, the Mann-Whitney U test for two independent samples and the Kruskal-Wallis test for multiple samples were used for group comparison. Wilcoxon signed rank test for paired samples and Freidman's Two-way Analysis of Variance test for repeated measures wwere preferred. Intraclass Correlation Coefficient (ICC) and the Coefficient of Variation (CV) were calculated for inter- and intra-observer agreement. A p value of less than 0.05 ($p<0.05$) was considered statistically significant by taking 5% for type-I error. Power analysis was performed by GPower software (Universitaet Kiel) to compare the measurements done by different methods. The mean tumor volume was found as 38±45 mm in the pilot study. By taking the power as 80% and error as 5%, the sample size for repeated measures was calculated as n = 43. However, 50 cases were measured to increase power.

3. RESULTS

20 (40%) lung nodule and 30 (60%) lung mass were included in this study. 38 (76%) of the lesions were solid and 12 (24%) were subsolid. There was no lesion with pure ground-glass density. 19 (38%) lesions were intraparenchymal, 10 (20%) were mediastinal/hilar localized, and 21 (42%) showed chest wall invasion.

The segmentation times at the 3DSSW method were 1.54 (1.03 - 2.33) min and 1.23 (1.10 -1.34) min, whereas in the PM method were 7.35 (1.17 - 12.45) min and 7.3 (0.32 -11.49) min for the two observers, respectively.

The intra-observer coefficients were significantly higher in methods for both observers. Among the ICC values of the first observer, the highest value belonged to the PM (0.999) whereas the 3DSSW (0.996) coefficient was close to PM method. When the values of the second observer were examined, the agreement value of the PM method was highest (ICC: 0.999) and the value of the 3DSSW method was 0.980. The inter-observer agreement values were high for both methods (ICC > 0.984). The highest inter-observer agreement was observed in the second measurements of 3DSSW (ICC > 0.996). The inter-observer agreement value for PM method was 0.984 (Table 1).

Table 1: Intra- and inter-observer agreements and significance of differences between 1st and 2nd measurements for three methods

	Method	**ICC**	**CV**	***p****
Intra-observer Agreement				
1st observer	*PM*	0.999	0.75	*0.414*
	3DSSW	0.996	9.58	*0.302*
2nd observer	*PM*	0.999	1.37	*0.816*
	3DSSW	0.980	10.66	0.099
Inter-observer Agreement				
PM	*1st measurement*	0.985	17.86	0.154
	2nd measurement	0.984	16.67	0.089
3DSSW	*1st measurement*	0.987	39.26	0.214
	2nd measurement	0.996	9.40	0.382

**Wilcoxon Signed Rank Test*

According to the comparisons performed by Wilcoxon test, no significant difference was found between the first and second measurements for both observers since the median values of the measurements were close to each other in both methods.

The percentage change between the first and second measurements for each method was calculated according to tumor size, location, and internal structure (Table 2).

Table 2: Measurements of 1st and 2nd observers according to tumor density, size and location.

Tumor	Measurement	1st Observer		2nd Observer	
		Difference in PM (%)	***Difference in 3DDSSW (%)***	***Difference in PM (%)***	***Difference in 3DDSSW (%)***
Density	Solid (n=38)	0.56 (-0.10 - 1.32)	6.09 (-1.01-16.47)	0.17 (-0.1- 0.87)	-5.49 (-38.95 - 0.22)
	Subsolid (n=12)	1.15 (0.45 - 3.82)	9.44 (-1.80 - 22.09)	0.51(-0.28-1.23)	0.18 (-18.28 - 4.70)
	p*	**0.048***	0,467	0,555	0,203
Size	Nodüle (<3 cm) (n=20)	0.88 (0.38 - 2.19)	8.96 (-1.20 - 20.07)	0.53 (-0.65 - 1.55)	-14.70 (-28.2 - 1.44)
	Mass (>3 cm) (n=30)	0.56 (-0.18 - 1.32)	2.09 (-1.46 - 11.3)	0.24 (-0.04 - 0.81)	1.55 (-4.71 - 9.65)
	p	0,113	0,301	0,692	0,104
Location	Parenchymal (n=19)	0.94 (-0.24 - 2.13)	2.41 (0.22 - 12.5)	0.01 (-1.64 - 1.22)	0.38 (-6.61 - 9.31)
	Hiler/ Mediastinal (n=10)	0.64 (0.31 - 0.96)	3.82 (-1.84 - 8.19)	0.46 (-0.04 - 1.17)	-2.90 (-21.02 - 3.82)
	Chest Wall invasion (n=21)	0.51 (0.14 - 1.37)	2.43 (-3.53 - 13.47)	0.46 (0.09 - 1.36)	-4.87 (-24.94 - 2.16)
	p	*0,728*	*0,279*	*0,296*	*0,372*

**Significant in P< .05 level according to Mann-Whitney U test*

Among the measurements of the first observer, only the percentage change between the first and second PM method measurements was found

to be slightly significant between solid and subsolid groups (p = 0.048). The percentage change of the second observer did not differ significantly according to the internal structure. The percentage change of PM and 3DSSW methods for the first observer were low in the large tumor group. Especially, in the masses, the percentage change of 3DSSW (2.09%) was closer to PM method (0.56%). This shows the consistency between the 3DSSW and the PM methods. Similarly, the percentage change of 3DSSW (1.55%) for the second observer was quite low in masses. On the other hand, the percentage change of 3DSSW in nodules was higher than the PM method for both observers. However, the percentage changes between the nodules and masses for 3DSSW were not statistically significant. There was no significant difference according to location between the measurement groups of both observers. The percentage changes of 3DSWW (ca. 3%) for both observers were low, and close to PM method (ca. 0.7%) (Figure 5).

The percentage change in measurements of intraparenchymal located tumors for 3DSSW was lower than the other locations.

Volumetric measurements according to the methods were also compared ((Table 3).

Table 3: Comparison of the measurements between three methods for two observers

	PM	**3DSSW**	***p***
1st Observer			
1st measurement	14.77 (2.21 - 55.17)	13.49 (2.61 - 53.43)	*0.432*
2nd measurement	14.61 (2.16 - 55.26)	12.82 (1.74 - 52.59)	*0.223*
2nd Observer			
1st measurement	13.54 (1.73 - 44.44)	12.20 (1.70 - 51.44)	*0.515*
2nd measurement	12.83 (1.91 - 42.58)	11.04 (1.94 - 52.15)	*0.384*

Data expressed as Median (Q1-Q3) (mm^3)

**significant in P<.05 levels, according to the Wilcoxon Signed-Rank Test*

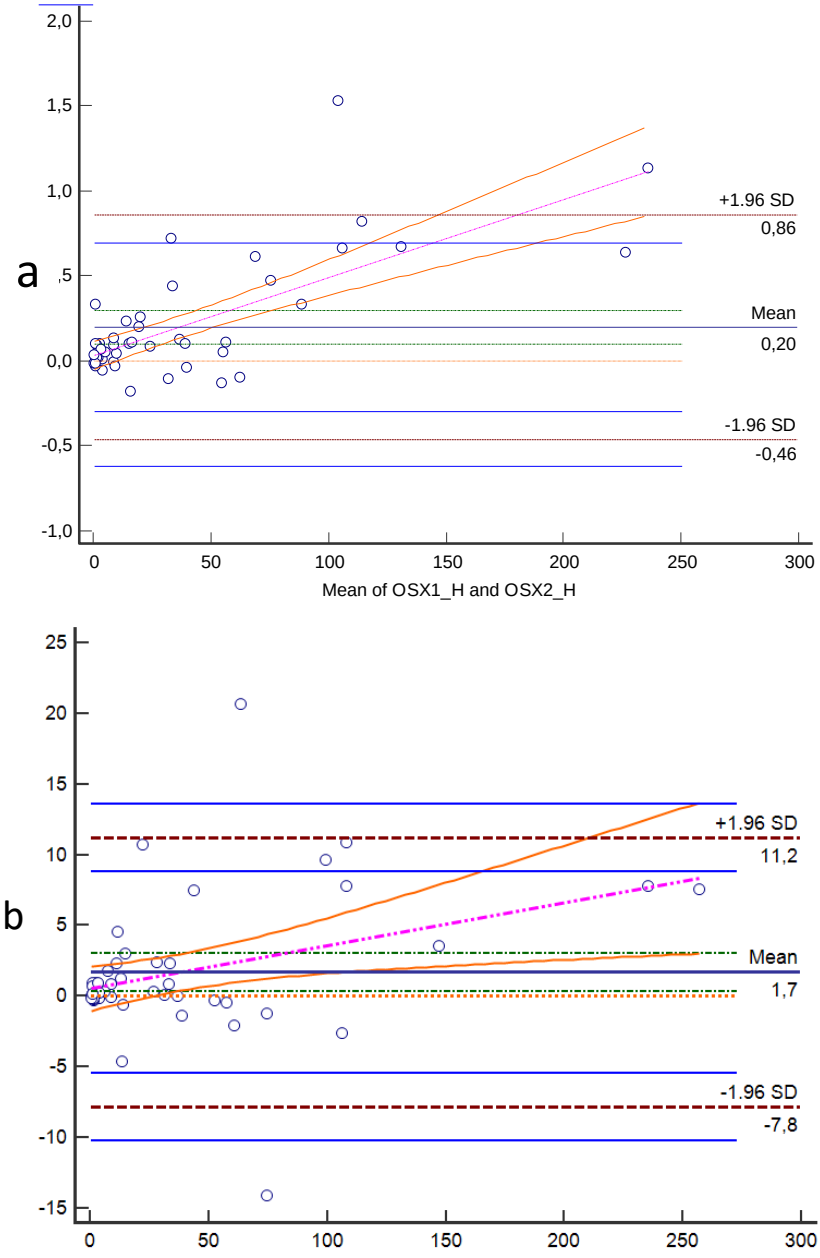


Figure 5: a) Bland-Altman plot of PM method of 1st observer *(OSX: Osirix perimetrik manual segmantation method).* **3b)** Bland-Altman plot of 3DSSW method of 1st observer.

There was no significant difference in volumetric measurements between the two measurements of both observers. The percentage change of 3DSSW was close to PM method.

4. DISCUSSION

The inter- and intra-observer agreement values for the 3DSSW method were generally close to the agreed values for the PM method in this study. Even the inter-observer agreement of the second 3DSSW measurement (ICC: 0.996) was higher than the PM method (ICC: 0.985). This shows that the 3DSSW method is repeatable and reproducible method that could be used in routine practice.

In the 3DSSW method, the measurement time is less than 2 minutes regardless of size, internal structure and location. SegmentationWizard module has significantly accelerated the 3D-Slicer semi-automatic segmentation method. This shows that the 3DSSW method is a fast method that can be used in routine practice. However, the time period recorded for PM method measurement, a manual segmentation method, was 29 min for the largest tumor with a volume of 236 cm^3 and 50 sec for a nodule with a volume of 1.5 cm^3 in this study. This shows that the time period for volume measurement increases by the increase in lesion size.[22–27] Velazquez et al. observed that 3D-Slicer Growcut semi-quantitative method was more powerful and stable than manual segmentation.[16] Yip et al. stated that the 3D-Slicer Chest Imaging Platform (CIP) segmentation method provides more precise results.[14]

In the current study, there was no significant difference in percentage change between the first and second 3DSSW measurements according to the size, location, and internal structure of the tumor. The percentage change between the first and second 3DSSW measurements of both of the observers was lower than the nodules and similar to the PM method, but they were not statistically significant. Yip et al. stated that CIP segmentation methods give more reliable results in larger lesions.[14]. Nishino et al. stated that the tumor location didn't affect the percentage change in volumes as in our study.[28] However, Colombi at al. noticed that the percentage change of volumes was higher in centrally localized masses.[27] In the current study did not find a significant difference for the percentage change of 3DSSW measurements according to tumor location. In the literature, the reliability of segmentation methods for subsolid lesions is reported to be lower than for solid lesions. This is because there are differences between observers in delineating the subsolid lesions and window settings.[14,29,30] However, contrary to the literature, there was no significant difference between 3DSSW and PM method measurements of solid and subolid lesions in this study.

According to these results, it shows that the repeatibility, reproducibility and relaibility of 3DSSW is at least as good as PM method. Moreover, the SW module has reduced the volume segmentation

processing time to less than 2 minutes, making the volume segmentation method, which is normally time-consuming, more routinely available.

The limitations of our study were as follows; 1) Our most important limitation is that we have no gold standard reference measurement. However, it has been reported in the literature that the volumetric calculation made by manual segmentation methods is more reliable than the calculation of the longest dimensions in three different anatomical plans. Therefore, the PM method was accepted as the reference method (although it is prone to observer-dependent measurement errors). 2) Only two observers measured the volumes, this could have caused controversial results. Further studies with more observers and a larger patient population is needed. 3) There was a difficulty in determining a standard range for thresholding and make a consensus for that among the observers. Further studies providing determinant factors for standardization are needed.

4. CONCLUSION

3DSSW is an innovative, reliable, reproducible, repeatable, and time-efficient semi-automatic segmentation method, which can be used for the volume measurement regardless of size, location and internal structure of the lung tumors in routine practice.

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