1.1 Prophylactic Surgery

1.1.1 Introduction

Prophylactic surgery (PS), also called preventive surgery, preemptive surgery, or risk-reducing surgery, involves partial or complete removal of organs or body tissues that may appear healthy now, but are likely to become ill due to cancer or other causes in the future. PS has been defined as risk-reducing procedures by the American Society of Clinical Oncology (ASCO) and the Society of Surgical Oncology (SSO) [1]. In the NIH-NCI dictionary of cancer terms, PS is defined as “surgery performed to remove an organ or gland that does not show signs of cancer in order to prevent the development of cancer of that organ or gland” [2].

Environmental and genetic factors play an important role in cancer development. There are germline mutations in hereditary transitions and the risk of developing cancer increases. For example, BRCA1/2 positive women have a 5–40-fold increase in cancer development risk [3]. Besides, mutations can occur in some of the germ cells in the early stages of the organism’s development and cause mosaicism in the gene line. Anatomical and functional problems arise after birth, depending on the location of the gene damage caused by mosaicism. Somatic mutations that play a role in forming sporadic cancers are known to develop spontaneously or due to external (environmental) factors as a natural consequence of aging [4]. For example, in the background of gastroesophageal reflux, Barrett’s esophagus and the risk of developing cancer increase 30 to 40 times [5].

Prophylactic surgery’s application area is genetically transmitted cancers, precancerous lesions, and asymptomatic noncancerous pathologies that can threaten life and function with its complications (Table 1.1). Prophylactic appendectomy and cholecystectomies can also be performed to minimize complications during space travels or prolonged polar voyages and to avoid risking the lives of passengers and crew [6].

Prophylactic surgery has been increasingly used in recent years as a preventive procedure, especially in genetic predisposition cases. In this respect, colon, breast, stomach, thyroid, and ovarian cancer syndromes are classic examples. Much data in the literature on surgical methods to be applied, especially inherited diseases involving the breast and colon. Algorithms containing organ-specific diagnosis and treatment approaches have been developed. Besides, with the advances in imaging and other diagnostic tools, many nonhereditary diseases can be detected in the “in situ” or “high-grade dysplasia” stage, and they have begun to be treated with prophylactic organ/tissue resections and interventional procedures.
Table 1.1 Classification of prophylactic surgery/procedures indications

| Indications                        | Organ/pathologies                                                                 |
|-----------------------------------|-----------------------------------------------------------------------------------|
| Genetic predispositions           | • Breast—hereditary breast cancer                                                 |
|                                   | • Colon—FAP, hereditary non-polyposis colorectal cancer                           |
|                                   | • Stomach—hereditary diffuse gastric cancer                                       |
|                                   | • Pancreas—F-pancreas cancer, MEN syndromes                                       |
|                                   | • Thyroid—MEN1, MEN2, FMTC, Cowden syndrome                                       |
|                                   | • Parathyroid—MEN1, MEN2A, osteitis fibrosa cystica, FHPT                          |
|                                   | • Adrenal gland—MEN2, Von Hippel Lindau syndrome, incidentaloma, etc              |
|                                   | • Syndromes—Li Fraumeni syndrome, Peutz-Jegher’s syndrome, Cowden syndrome, Lynch syndrome, neurofibromatosis syndrome, FAMMM, MEN, etc |
|                                   | • Hematologic—hereditary spherocytosis, cycle cell anemia, t, etc Associated tumors for hereditary cancers (various). |
|                                   | • Skin—soft tissue tumors                                                         |
|                                   | • Ovary—endometrium, etc                                                          |
| Precancerous lesions              | • Breast—LCIS, ADH, ALH, etc                                                      |
|                                   | • Esophagus—Barrett’s esophagus                                                   |
|                                   | • Colitis ulcerosa†                                                               |
|                                   | • Biliary intraepithelial neoplasm (BillN), IPN-B, etc                            |
| Inflammations/infections (precursor lesions) | • Biliary duct strictures, cholangitis, gallstones, hepatolithiasis, etc        |
|                                   | • Cirrhosis—portal hypertension, esophageal varices                              |
|                                   | • GERD—Barrett’s esophagus                                                       |
|                                   | • Colon—ulcerative colitis, etc                                                   |
|                                   | • Pancreas—chronic pancreatitis, etc                                              |
| Cystic/solid lesions (asymptomatic) | • Pancreas—IPMN, pNETs, etc                                                      |
|                                   | • Thyroid nodules                                                                |
|                                   | • Hemangioma, adenoma, solitary lesions (liver)                                   |
|                                   | • Caroli’s disease, choledochal cysts, (biliary tract)                            |
|                                   | • Gallbladder polyps, adenomyomas                                                 |
|                                   | • Mass (previously had radiotherapy), etc                                          |
| Morphologic disorders             | • Pancreaticobiliary maljunction, etc                                              |
| – Anomalia                         | • Gallbladder anomalies, choledochal cysts, etc                                   |
| – Malrotation                      | • Spleen—spleenic artery aneurysm, wandering spleen, etc                          |
| – Ectopy                          | • Hematologic—hereditary spherocytosis, cycle cell anemia, ITP, etc               |
| – Hematologic disorders           | • Colon—volvulus, diverticular disease                                            |
|                                   | • Gastric volvulus, etc                                                           |
| Miscellaneous procedures          | • Transplantation†                                                                |
|                                   | • Embolization [Vascular (aneurysm, bleeding, etc), portal vein, etc]             |
|                                   | • Pringle maneuver, packing, falciform lig. flooring, etc                         |
|                                   | • Bariatric surgery                                                              |
|                                   | • Concomitant surgeries—appendectomy, cholecystectomy, oophorectomy               |
|                                   | • Vagotomy, gastroenterostomy, etc                                                |
|                                   | • Omentectomy, peritonectomy, lymphadenectomy, etc                                |
|                                   | • Diversion procedures, etc                                                        |
|                                   | • Percutan drainage procedures (various), etc                                     |
|                                   | • Compartment syndromes, etc                                                      |
| Others…                           | • Pelvic pain/exploration-appendectomy                                            |
|                                   | • Travel to space/pole-appendectomies, cholecystectomies (?), etc                  |

ADH atypical ductal or ALH atypical lobular hyperplasia, F familial, GERD gastroesophageal reflux disease, HPT hyperparathyroidism, IPMN intraductal pancreatic mucinous neoplasm, IPN-B intraductal papillary neoplasia of the bile duct, ITP idiopathic thrombocytopenic purpura, LCIS lobular carcinoma in situ, MTC medullary thyroid cancer

†The table is designed to give an idea about PS. Exceptions may apply to selected patients
This section will try to explain prophylactic surgical operations and procedures with literature data and clinical practice examples.

1.1.2 Definition

Prophylaxis aims to apply approaches, surgeries, and risk-reducing procedures that will prevent the development of the disease or its complications, depending on the situations that threaten life or organs. The prophylactic procedure is a procedure that should be done naturally and at an early stage (at the most appropriate time). PS, which is the subject of our book, can also be expressed as managing risks by surgical methods. As Lord Moynihan stated as “surgery to prevent the surgery,” PS is a chosen method to prevent more extensive interventions and complications [7].

Various methods are applied to the etiological factor in order to prevent cancer. The majority of cancers due to environmental factors can be prevented and reduced with protective measures. Prevention can be expressed in three different ways. There are some semantic distinctions between them. Primary prevention refers to the actual protection of the development of the disease. In contrast, secondary prevention can be expressed as an intensified early diagnosis and possible treatment options, and tertiary protection means lifetime posttreatment care. Preventive medicine and environmental health studies are essential preventive measures.

Prophylactic surgery is a concept and action developed to eradicate especially hereditary cancers while in situ. However, it is also a preferred method to eliminate complications or clinical symptoms caused by surgical procedures or developed organ pathologies, especially environmental factors that threaten organ functions without a genetic predisposition. Various procedures are made for prophylactic purposes or to reduce the risk in many asymptomatic benign pathologies.

Prophylactic interventions are advantageous in that they are more straightforward and more economical. In addition to these, it is other advantages that people increase and provide a healthier and more functional life expectancy. Laparoscopic, radiological, endoscopic, and minimally invasive surgical techniques have been increasingly used in the clinic as a result of such desire and expectation. It can be accepted that any method that provides a more comfortable or more minimal procedure than a more radical surgery has a prophylactic purpose. From this perspective, not only surgeries but also minimally invasive procedures, interventional procedures, or endoscopic procedures that will provide the same result instead of surgery should be evaluated within this framework. For example, treatment of an abscess in the abdomen not by laparotomy but by ultrasonography (USG)-guided percutaneous drainage, treatment of a severe peptic ulcer bleeding with an endoscopic approach instead of surgery, and prevention of bleeding in the spleen by embolization are also prophylactic procedures.

The procedures to be performed in diseases with genetic predisposition are briefly determining the size of the genetic transition feature after the first diagnosis, determining the risk groups, revealing screening and follow-up programs, and finally applying the prophylactic surgical procedure minimize the risk. Some clues should be questioned in order to identify patients with genetic predisposition early. These are early age cancers, cancers seen in many family members, rare tumor histopathologies, presence of the same type of cancer in many family members, presence of multiple primary tumors, bilateral cancer in bilateral organs, some racial characteristics, and unusual tumor presentations (Table 1.2). In addition to general features, clinical, radiological, and laboratory screening criteria should be determined according to its origin. Around 70
germline mutations responsible for cancer development have been identified [8–10].

### 1.1.3 Diagnosis

#### 1.1.3.1 Genetic Testing and Counseling

The first requirement of prophylactic surgical treatment in genetic diseases is the definition of germline transition characteristics. Management of patients with genetic disposition is determined according to the target organ and the mutated exon and codon (location) [11–15]. The clinical picture varies according to the location. Even by looking at the exon and codon location features, information can be obtained about whether the disease will progress aggressively and other organ pathologies. For example, in MEN2 cases, more than 80% of cases are MEN2A, 15% familial medullary thyroid cancer (FMTC), and 5% MEN2B, depending on the location of the mutation [16, 17]. Desmoid tumor is seen more than ever when the mutation in a patient’s APC gene with FAP is localized between codon 1310 and 2011 [18]. Nowadays, as new exons and codons are found in hereditary diseases, more detailed information about the clinic of the diseases continues to be obtained [17]. Another critical issue for diagnosis is the variety of mutations in genes. For example, about 100 different mutations have been reported in the CDH1 gene for hereditary diffuse gastric cancer (HDGC) [19, 20].

Eighty to ninety percent of cancers occur with sporadic, 3–20% with germline-type genetic predisposition. It is estimated that about 15–25% of organ-based cancers are at familiar risk [1, 21–23]. The proportions may vary according to organ, age, breed, and race. As an example, BRCA positivity was reported as 36% in women of Jewish ancestry [24]. Stoltze et al. (2018) reported that germline-transmitted pediatric cancer syndromes are seen more than previously predicted [25]. Genetic predispositions cause FAP in 1–3% of patients with gastric cancer, 1% of patients with colon cancer, and Lynch syndrome in 1–3% [19, 26]. A study done in the USA reported that 5–9% of thyroid cancer cases were MTC and 25% of them had a hereditary predisposition [1, 17]. The presence of genetic predisposition has been detected in 5–10% of breast cancer patients and 10–15% of patients with ovarian cancer [Walsh T]. When considering disease-based, it is revealed that 20–25% of patients with MTC and 20–25% of breast–ovarian patients have a genetic predisposition [17, 27, 28].

Situations related to genetic predisposition can be examined under three main headings.

Patients with genetic predisposition constitute the largest risk group. The sensitivity, specificity, and correct performance of the test are important in determining the chosen treatment. For example, APC gene mutation can only be detected in 80–90% of the patients with FAP clinic [29]. Similarly, the presence of mutations in MLH1 and MSH2 genes can be detected in 90% of patients with Lynch syndrome (HNPCC-Hereditary non-polyposis colorectal cancer). Apart from these two genetic mutations, it has been reported that 10% of the cases have mutations in the MSH6 and PMS2 genes [30–32]. Besides, hormones synthesized in patients with known hereditary cancer syndrome (e.g., calcitonin for MTC) may be considered as a disease-specific marker for diagnostic and follow-up purposes [17, 33].

People in the second group have a genetic predisposition in their family, but no genetic mutation. Different genetic screening and surveillance

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**Table 1.2** The suggestive features of genetic predispositions

| Mutation | Predictors |
|----------|------------|
| Germline | • Cancers seen at an early age (<40)  
• Cancer in many family members (first- or second-degree relatives)  
• Rare tumor histopathologies  
• Same type of cancer seen in many family members  
• Presence of multiple primary tumors  
• Bilateral cancer in double organs  
• Racial characteristics  
• Unusual tumor presentations  
• Known familial genetic predisposition |
| Somatic  | • Radiotherapy/exposure to radiation  
• Exposure to chemical compounds  
• Infections/inflammation  
• Old age  
• Chemotherapy?  
• Alcohol?  
• Smoking? |
programs are needed in these patients. According to this, some algorithms define the risk assessment tools and how the follow-up will be in people with genetic predisposition [4, 34]. The third group is the patients with familial cancer history but no data on genetic predisposition. These patients need enhanced surveillance. Algorithms that revealed the risk should be introduced. The way of surveillance varies according to the location of malignancy development. For example, 20–25% of high-grade serous ovarian carcinomas have a germline or somatic BRCA1/2 mutation. Genetic testing should be performed in all ovarian cancer cases [35].

In general, somatic mutations are usually low frequency and are only detectable by amplification of the genome. Mutations that involve less than 10% of cells in the tissue sample are generally not detectable using genome amplification strategies [4, 36, 37].

Lesions without genetic inheritance but with precancerous features are frequently encountered in the clinic. The risks of these lesions, in terms of health, should be evaluated (Fig. 1.1). For example, endoscopic and histopathologic surveillance studies demonstrate the risk of developing Barrett’s esophagus due to gastroesophageal reflux and subsequent cancer development. While prophylactic esophagectomy was performed in more patients due to Barrett’s esophagus and the risk of cancer development in the 1990s, today the success of endoscopic eradication reaches 95% and prophylactic esophagectomy is performed only in complicated patients. In short, the need for surgery has decreased with the development of endoscopic follow-up and diagnostic

![Algorithm for prophylactic surgery](image)

**Fig. 1.1** Diagnostic and therapeutic approach algorithm for prophylactic surgery
tools [38]. The opposite situation is seen in the pancreas, and with the widespread and effective use of diagnostic tools, more precancerous lesions are detected in the pancreas, and PS is applied.

1.1.3.2 Histopathologic Evaluation
Histopathologic evaluation is important in determining the method (concurrent resections) to be applied in diagnosis, surveillance, and PS (see Chap. 27). During the diagnosis phase, sampling from an appropriate location and sufficient amount are necessary for an accurate diagnosis. Deficiencies in diagnosis and monitoring devices and biopsy are the most significant problems. For example, in the HDGC series of 23 cases by Hebbard et al. (2009), endoscopic surveillance was insufficient in detecting cancer in 91% of the cases [39]. However, in very young patients with HDGC mutation, it is recommended to take six random biopsies (minimum 30 biopsies) from the stomach parts every year until the age of surgery [40]. A definitive diagnosis can be made in 80–90% of clinically suspected patients with genetic predisposition syndrome [1, 4, 19].

1.1.3.3 Misdiagnosis
Deficiencies in the genetic analysis may cause errors and inadequacies in diagnosis and treatment. There are some studies indicating that resection may not be required in patients with incomplete mutations detected in genetic examinations performed on patients undergoing prophylactic resection [41]. Moreover, traditional mutation analysis may overlook some of the mutations that can only be detected when the two alleles are studied separately using more sophisticated techniques [17]. For example, it has been reported that in patients who underwent total gastrectomy due to HDGC, the penetrance of CDH1 mutation was incomplete and unnecessary resection was performed in up to 20–30% of these patients. The unnecessary resections may be due to diagnostic errors due to inadequate biopsies and the unclear surgery date for HDGC [4, 37, 42]. There are “missense mutations” in 26% of MLH1 mutations and 16% of MSH2 mutations defined in Lynch syndrome. Clinically, APC mutation cannot be detected in 10–30% of patients with FAP [41]. Misdiagnosis may be due to deep intrinsic mutations, genomic rearrangements, missense mutations, and mutations in other genes that have not yet been identified or further characterized. Such situations make it difficult to evaluate the data [43, 44].

1.1.4 Surveillance
Patient follow-up should be considered in various aspects. It will be necessary to prepare and implement separate follow-up programs in basic issues such as the follow-up of patients who will be operated, patients with low genetic risk, patients without surgery, and their relatives. The surgical age of patients with genetic predisposition is generally recommended as 5–10 years earlier than the youngest patient in the family. It should be determined at what age patients will be operated and how to follow until this age [42]. However, the recommended surgery ages may vary depending on the sick organ and its genetic (exon codon) characteristics [19, 45–48]. Besides, it is known that patients with hereditary cancer syndrome have a high risk for second primary tumor [28, 45].

There are surveillance programs that specify how monitoring will be done. For example, it is recommended to perform surgery for MTC in the first months after birth in patients with MEN2B, before 5–6 years of age in children with MEN2A mutation, and between 5 and 10 years of age in familial-type MTC cases, or according to calcitonin level [15, 49, 50]. In families diagnosed with DHGC, prophylactic gastrectomy is recommended at the age of 5 years younger than the youngest patient for certain hereditary transmission [19, 51]. In families with FAP, endoscopic control is recommended from the age of 10 to 12, and from the age of 25, an annual gastroduodenoscopy, thyroid USG from the age of 10, and abdominal USG and AFP level follow-up for hepatoblastoma from the age of 5 are recommended [52, 53].

In the lifetime follow-up of patients with Lynch syndrome, it was reported that 54% of the
cases developed endometrial cancer and 10–12% of them developed ovarian cancer [45]. Patients with Lynch syndrome to have a colonoscopy every 1–3 years before the age of 20–25 for the follow-up of colonic pathologies, transvaginal USG, and pathologic examination of endometrial aspiration once a year before the age of 30 for extracolonic organ scanning, especially for the endometrium and ovary, and the examination of CA-125 in blood recommended [8, 9, 54]. Jarvinen et al. (2000) reported that mortality decreased 65% in families with Lynch syndrome in which they applied a 15-year surveillance program [55]. It has been reported that retained rectum cancer developed in 12% of the patients who preferred subtotal colectomy for Lynch syndrome during the 10–12-year follow-up [56].

While high-risk patients with a genetic predisposition are operated, patients considered low-risk should also be followed up. For example, a low-risk thyroid patient should be followed up with USG and biopsy when necessary, and risk analysis should be performed. Similarly, periodic colonoscopy for colorectal carcinoma, endoscopy for the stomach, MRI for breast cancer may be required. There are surveillance programs established for each organ, and developed algorithms should be followed [2, 9, 34].

The prophylactic surgical procedure is aimed to be curable. However, a complete cure may not be achieved in patients whose target organ is removed. Surveillance programs should also be made for patients undergoing surgery. For example, the risk can be reduced up to 95% in people who undergo prophylactic mastectomy. In cases where the resection is thought to be incomplete, it may be necessary to follow the risky areas (chest wall for breast cancer) [2, 34]. Similarly, in patients planned to undergo an ileorectal anastomosis due to FAP, periodic control of the mucosa left in the anorectal part is required [57].

There is a risk of malignancy development in other organs in some patients who undergo surgery for hereditary cancer. The risky organs should be followed up. For example, it is reported that the lifetime risk of developing hyperparathyroidism as 95%, pancreas-NET development as 40–70%, and pituitary-NET development as 30–40% in the follow-up people with MEN-1 syndrome (Wermer syndrome), which is very rare [58]. Adrenal cortical tumors, carcinoid tumors, lipomas, angiofibromas, gastrinomas, and meningiomas may also develop in these patients [58–60]. While MTC develops in 100% of the patients with MEN2A syndrome, pheochromocytoma may develop in 50% of all MEN2 cases, and hyperparathyroidism may develop in 25% [15, 50]. According to The American Thyroid Association (ATA) criteria, patients with risk for pheochromocytoma and high-risk alleles should be followed at age 11 and patients with moderate risk at the age of 16. Plasma-free metanephrine and nor-metanephrine and urine nor-metanephrine levels should be monitored during follow-up. MRI and CT scanning are also recommended for people with average blood values [60].

While adenomatous polyps develop in 95% of APC gene mutation carriers for FAP before 35, cancer develops in 90% of the cases before the age of 50. Total colectomy to be performed in patients with FAP is very important for the cure. However, it should not be forgotten that the upper gastrointestinal system malignancies and progression of desmoid tumors encountered during the patients’ course are the most important causes of mortality [1, 61]. Patients will need to be followed up by endoscopic and radiological imaging methods.

The lifetime risk of developing breast cancer in BRCA1/2 positive individuals is 50–85%, and the risk of developing ovarian cancer is calculated as 10–46% [62–64]. Similarly, it has been reported that 20–60% of patients with Lynch syndrome who are followed up for life develop endometrial cancer, and 5–12% of them develop ovarian cancer [45].

People with E-cadherin/CDH1 gene mutations have a lifetime risk of HDGC development of 70–80%. Also, 67% of male patients and 83% of female patients risk developing breast cancer [62, 63]. Surveillance programs are recommended because of the increased incidence of lobular breast carcinoma (lifetime risk 40–60% for females), colorectal, and prostate cancer in patients undergoing total gastric resection due to
HDGC [65]. Similar follow-ups are performed for nonneoplastic pathologies. It is essential to use diagnostic methods such as MRI and EUS to follow-up for cystic lesions of the pancreas. In contrast, endoscopic follow-up is vital for patients with Barrett’s esophagus. The algorithms developed and recommended by international organizations (e.g., ATA, AGA-American Gastrointestinal Association) within the framework of evidence-based medicine in this regard are instructive.

In addition to the diagnosis, follow-up, and PS of hereditary cancers, it should also be evaluated in terms of environmental, familial, economic, social, and psychological dimensions.

1.1.5 Chemoprevention

Chemoprevention is an option that can be applied to protect other target organs in the nonoperative, low-risk group, or postoperative period. There are different medications and approaches for each disease. For example, selective COX-2 inhibitors and nonsteroidal anti-inflammatory (Sulindac) drugs are the most commonly used drugs in patients with FAP [66–68]. In the series by Tonelli et al. (2000), it was reported that the number of polyps decreased by 28% with the use of COX-2 inhibitors for 6 months. However, the diameter of the polyps increased, and the number increased within 4 years after discontinuation of the drug [69].

Prophylactic surgery can be delayed with chemoprevention. Special conditions of the patients may require this. For example, tamoxifen is the most used drug in breast patients. Whether the woman has a child, her age, and her fertility age are important for use. Due to BRCA2 positivity, women who do not have children and who are of childbearing age may request the surgery to be delayed. In such patients, periodic diagnostic screening programs are also applied in addition to tamoxifen treatment for chemoprevention [42, 70, 71].

Elective surgical interventions were postponed worldwide due to the global Covid-19 pandemic in recent months, except emergency and tumor. PS for cancer and noncancer cases had been deferred for 3 months in the USA and UK [72–74]. In patients with genetic predisposition, chemoprevention can be applied as an option in similar cases where surgery will be delayed. Longer follow-up and surgery can be performed in patients who can be followed closely with diagnostic tools. The issue of chemoprevention in non-tumor cases is more comprehensive and controversial. Prophylactic procedures for many nonneoplastic pathologies are described in detail in the chapters.

1.1.6 Prophylactic Resections

In order for resections performed to get rid of hereditary cancer to be prophylactic, the entire target mass should be removed. For this purpose, defined surgical protocols are needed for each organ. The surgeon and pathologist should cooperate very closely in this regard. For example, total thyroidectomy with posterior capsule and central lymph node dissection is recommended for MEN2 patients as prophylactic. Because of the risk of hyperparathyroidism, parathyroid glands are also recommended to be removed in the same surgery and transplanted into the forearm muscle (autotransplantation) [11, 15, 75].

It has been reported that total gastrectomy and D1 lymph node dissection are sufficient for HDGC carrier, and D2 lymph node dissection is not required [76]. The surgery can be done more easily by the laparoscopic or robotic method. However, in order to understand that the procedure is complete, it is recommended to confirm by the frozen section that the specimen has a ring consisting of the duodenal mucosa at the lower end and the esophageal mucosa at the upper end. Implementation of this protocol is required to prevent future relapse [51].

Prophylactic surgeries’ protection rate varies between 80 and 95% despite all the resections performed [1, 19, 77, 78]. Inadequate processing, diagnostic deficiencies (unknowns), and accompanying other organ pathologies are the most important causes of morbidity and mortality.
Many organ resections are performed for non-neoplastic reasons. Among these, prophylactic esophagectomies, which were performed extensively in the 1990s to prevent adenocarcinoma due to Barrett’s esophagus, have decreased today due to the success of endoscopic eradication. Prophylactic/incidental appendectomy is the most common PS performed for nonneoplastic reasons (see Chap. 18). Although pancreatic IPMNs are closely monitored due to the high risk of malignancy, prophylactic pancreatic resections have to be performed in cases where the risk increases (see Chap. 10).

1.1.7 Concurrent Surgeries

It should be questioned whether other target organ resections will be added to the procedure in patients with genetic predisposition undergoing PS. For example, prophylactic mastectomy and oophorectomy should be planned together in BRCA2-positive individuals. Adding hysterectomy to the procedure during prophylactic colectomy in patients with Lynch syndrome is one of the most common concurrent surgeries. Especially in patients with MSH6 mutation, the risk of developing endometrial cancer is higher, and concurrent prophylactic hysterectomy is recommended [30, 45]. In ovarian tumors with a hereditary transmission characteristic up to 20%, oophorectomy may not be sufficient, and tumors can be seen in the tubules. In such cases, additional resections will be added to the process, and close follow-up of patients will be required for cases that cannot be added to the process. The situation is similar for uterine cancers [27]. There are similar situations for MTC, and parathyroidectomy is added to the procedure. It is described in more detail in the sections on organs.

Incidental (concurrent) organ resections or procedures are added to the process in some interventions performed for cancers or noncancer reasons. For example, some authors recommend prophylactic cholecystectomy because of the increased risk of cholelithiasis and choledocholithiasis in cases where duodenum is bypass or Roux-en-Y [79, 80]. Incidental appendectomy is one of the most common procedures performed in patients undergoing exploration due to pelvic pain [81].

1.1.8 Postoperative Evaluation

Histopathological examination is essential in understanding whether the prophylactic procedures performed are sufficient or not. For example, endoscopically eradication can be achieved in 87–96% of Barrett’s esophagus cases, which is the main cause of esophageal adenocarcinoma [38]. In cases with endoscopic mucosal resection, it should be evaluated whether the specimens removed are sufficient or not, especially in terms of the risk of remaining buried mucosa [82]. The risk of inadequate resection also applies to patients undergoing total prophylactic colectomy or total gastric resection for genetic predisposition. It is well known that the risk of tumor development continues in cases with insufficient resection.

Pathologists should investigate whether there is a tumor focus in each case. Occult cancer foci can be detected in some cases with careful examination of the specimens after PS. In a study of 90 cases conducted in the USA, 15% of the patients who underwent prophylactic mastectomy and oophorectomy due to BRCA2 positivity had ductal carcinoma in situ, 8% invasive ductal carcinoma, 3% fallopian tube adenocarcinoma, and 3% ovarian adenocarcinoma [83]. In another example, Groot et al. (2006) operated 20 MEN2 patients (mean age 10) with RET mutations and found C-cell hyperplasia in 19 patients, MTC (70%) in 14 cases, and lymph node involvement in 3 patients on histopathological examination [84]. In another FMTC series of 16 cases, it was reported that the tumor was multifocal in 13 cases, bilateral in 11 cases, and desmoplastic stroma in all cases. It has also been reported that lymph node metastasis is more common in cases with desmoplastic stroma [85]. These results indicate that the patients with genetic predisposition should be operated at a much younger age.
1.1.9 Recommendations for Prophylactic Surgery

Since prophylactic surgical procedures will not involve some radical tumor surgery procedures, they will be more easily applicable procedures. Most prophylactic procedures can be performed using laparoscopic, endoscopic, and radiological interventional procedures depending on technological developments. PS may become a separate discipline in the future.

The following rules should be followed in patients undergoing PS due to genetic predisposition [1, 21, 42]:

1. Must have a high genetic predisposition (independent from environmental factors).
2. The diagnostic test must be reliable.
3. Cure with surgery should be possible.
4. Surgery should be performed with minimal morbidity and mortality.
5. In the absence of organ/tissue, insufficiency (disability) should not be seen, or its maintenance should be provided.

Rules to be followed in patients who are planned to undergo PS for non-tumor reasons:

1. A definite diagnosis should be made.
2. Especially life-threatening complications and their consequences should be anticipated/known.
3. It should be done with minimal morbidity and without mortality.
4. In the absence of organ/tissue, insufficiency (disability) should not be seen, or its maintenance should be provided.
5. Surgery should be able to cure or prevent complications.

Rules to be followed by the surgical team and center:

1. The decision for surgery should be taken with the knowledge and approval of the patient and his family.
2. A decision should be made with a commission consisting of experts from different disciplines (surgeon, radiologist, pathologist, psychiatrist, and related branches).
3. The operation center must be experienced (especially for genetic predisposition).
4. Must have the infrastructure to manage complications.

1.1.10 Cost-Effectivity

There are many studies on the cost-effectiveness of screening and surgeries to be performed due to genetic predisposition. For example, Ramsey et al. (2001), in the genetic screening study conducted in families with Lynch syndrome, performed the cost analysis of patients who underwent screening study with a standard approach. Savings of $ 7556 per patient were reported for each year earned as a result of screening [86]. The general opinion is that PS is cost-effective (see Chap. 4).

1.1.11 Quality of Life (QoL)

Prophylactic surgery can protect patients from the impending danger in 80–95% of cases. It affects the quality of life (QoL) psychologically and, in general, positively. However, it should be kept in mind that the procedure is irreversible and has many side effects and complications in the long and short term. Razdan et al. (2016) reported that 61–100% of the patients in various series undergoing prophylactic mastectomy and oophorectomy considered PS satisfactory [87]. The QoL was found to be lower in those who had surgery due to FAP due to the size of the surgery and accompanying bowel habit problems [88]. Postoperative morbidity and 0–4% mortality are seen in 60% of the patients who undergo total gastrectomy for HDGC. Mental, emotional, and physical problems encountered in the first months of the operation return to normal within 6 months to 1 year in most patients [89, 90].

Education and psychological support of patients and families can provide better diagnosis and treatment [91, 92]. Eliminating the
complications that may develop due to the disease with PS especially the anxiety that occurs due to the risk of cancer relieves and the QoL increases.

1.2 In Conclusion

Prophylactic surgery aims to eliminate the target organ before the life-threatening disease develops, increase the expected survival, and prevent the decrease in the quality of life. The term “prophylactic surgery,” which indicates preventing the probable event before it occurs, has become more popular and gained importance by the current advances in medical literature, surgical techniques, and biomedical equipment.

Experienced centers should follow up the patients with genetic predispositions, and advanced diagnostic tools and specialist doctors.

Early diagnosis will result in a higher chance of cure, more comprehensive surgery, fewer complications, less mortality, lower cost, longer survival, and improved quality of life.

Increasing the detectability of mutant genes, mainly in genetically inherited cancers, will result in high surveillance, prevention, and surgical interventions for prophylactic purposes will become more important.

Surgical resections will begin to be performed in a different size, with a minimally invasive surgery technique. As the pathophysiology of the diseases is well understood, PS will find more application areas in our future lives and surgical clinics with its wide variety of dimensions.

Prophylactic surgery will take its place in the future as a discipline with a corporate identity that adopts a multidisciplinary approach.

The cost-effective dimension of PS will appear as new problems that should be evaluated in the future by insurance companies and health service providers.

Legal, ethical, social, and psychological dimensions of prophylactic initiatives will need to be examined with wide and multicentric center participation.

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