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CONSENSUS STATEMENT

EAES recommendations for the management of gastroesophageal reflux disease

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Abstract
Background Gastroesophageal reflux disease (GERD) is one of the most frequent benign disorders of the upper gastrointestinal tract. Management of GERD has always been controversial since modern medical therapy is very effective, but laparoscopic fundoplication is one of the few procedures that were quickly adapted to the minimal access technique. The purpose of this project was to analyze the current knowledge on GERD in regard to its pathophysiology, diagnostic assessment, medical therapy, and surgical therapy, and special circumstances such as GERD in children, Barrett's esophagus, and enteroesophageal and duodenogastroesophageal reflux.
Methods The European Association of Endoscopic Surgery (EAES) has tasked a group of experts, based on their clinical and scientific expertise in the field of GERD, to establish current guidelines in a consensus development conference. The expert panel was constituted in May 2012 and met in September 2012 and January 2013, followed by a Delphi process. Critical appraisal of the literature was accomplished. All articles were reviewed and classified according to the hierarchy of level of evidence and summarized in statements and recommendations, which were presented to the scientific community during the EAES yearly conference in a plenary session in Vienna 2013. A second Delphi process followed discussion in the plenary session.
Results Recommendations for pathophysiologic and epidemiologic considerations, symptom evaluation, diagnostic workup, medical therapy, and surgical therapy are presented. Diagnostic evaluation and adequate selection of patients are the most important features for success of the current management of GERD. Laparoscopic fundoplica-

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tion is the most important therapeutic technique for the success of surgical therapy of GERD.
Conclusions Since the background of GERD is multifactorial, the management of this disease requires a complex approach in diagnostic workup as well as for medical and surgical treatment. Laparoscopic fundoplication in well-selected patients is a successful therapeutic option.

Keywords GERD · Gastroesophageal reflux disease · Laparoscopic fundoplication · Barrett's esophagus · Proton pump inhibitor · PPI

Gastroesophageal reflux disease (GERD) is one of the most frequent benign disorders of the upper gastrointestinal tract. Management of GERD has always been controversial since modern medical therapy is very effective, but laparoscopic fundoplication is one of the few procedures that was quickly adapted to the minimal access technique and developed a large following in surgery. There have been several consensus conferences in the past that parallel the new developments in the diagnostic and therapeutic management of the disease [1–6], including one from the EAES (European Association of Endoscopic Surgery and Allied Techniques) [1]. In view of the expanding amount of literature, the boards of the EAES have decided to renew its guidelines on GERD by establishing a new consensus conference in 2013.

The purpose of this project was to analyze current knowledge on GERD in regard to its pathophysiology, diagnostic assessment, medical therapy, and surgical therapy, and special circumstances such as GERD in children, Barrett's esophagus, and enteroesophageal and duodenogastroesophageal reflux.

Material and methods

Constitution of the expert panel

A group of experts was determined based on their clinical and scientific expertise in the field of GERD. Members were to be independent from industry-driven methods, representative of different subspecialties involved in GERD, and be distributed throughout Europe. Accordingly, the expert panel consisted one gastroenterologist (ES), one pulmonologist (PK), nine surgeons (WB, BD, AF, KHF, EF, FG, PH, RP, and GZ), and one pediatric surgeon (MvH). The project was assisted in Frankfurt by a surgical coworker (BB). The group was finalized in early 2012.

A basic list of important items with respect to GERD was established by the members in Frankfurt and circulated to the others, and a critical response and possible corrections were requested. For the literature research we followed the concept as published in other EAES consensus projects [7, 8].

Initially, in 2012, the core group in Frankfurt (KHF, WB, and BB) performed a systematic search for information in Medline via PubMed and the Cochrane Library using the following items or search terms: GERD epidemiology, pathophysiology, natural course; hiatal hernia; GERD symptoms; GERD indication for surgery, GERD medical therapy, fundoplication; Redo fundoplication; Barrett's esophagus, duodenogastroesophageal reflux, and GERD in children. A total of 18,490 leads were evaluated and, of these, 4,900 abstracts were read and selected for further analysis, following the hierarchy of research evidence and clinical evidence. All articles were reviewed and classified according to the hierarchy of level of evidence [9].

In May 2012 a project plan, together with a literature list and a preliminary list of GERD items, was distributed among the panelists. All panelists were given tasks and asked to focus on certain items according to their subspecialty. They were asked to check the literature list for completeness. A first-draft statement on the different items was created in August 2012 after collecting all the information from the panelists and circulated for evaluation and changes before the first face-to-face meeting.

A revised draft was circulated and the first face-to-face meeting was held in Frankfurt at the end of September 2012. On this occasion, an in-depth discussion on each item began during the one-and-a-half-day meeting. The selected literature underwent critical appraisal in regard to consistency and valid clinical background. This information and the results of these discussions were transformed into statements, along with the level of available evidence and comments for further explanation, as necessary. The resulting document was circulated for further completion of each item, including diagnostics, medical therapy, surgical therapy, failures, and Barrett's esophagus. During the following months a second period of reassessment of the chosen statements, literature review and incoming additional information was performed by email exchange.

A second face-to-face meeting was organized in January 2013 to reevaluate all items, statements, and their corresponding evidence level as well as the possible consensus among the panelists. Again, there was an in-depth discussion on each item and the results were summarized in statements and comments. Some items were dropped and others were included in different sections.

The strength of an item's recommendation was based on the level of evidence and indicated by the word "must," "should," or "can" according to the grade A, B, or C [7–9]. The degree of consensus was expressed as the percentage of agreement for or against a certain item. If the

result of discussion led to controversial standpoints, it was clearly stated in the document. In the Results section, the grade of recommendation was expressed as GoR, the expert panel's consensus as ExC, and the scientific community consensus as SCC, all three as percentage.

The results of the meeting were reformulated and summarized in an updated version of the document which was circulated for a final Delphi round prior to the EAES meeting in Vienna.

During the final consensus conference at the plenary session of the 22nd annual EAES congress in Vienna in June 2013, the consensus statements were presented to the scientific community for further discussion and input. To have measurable and representative input from the scientific community, a questionnaire presenting all items was distributed to the audience for assessment and feedback. The answer for each item was selected from "agree," "partially agree," "indifferent," "partially disagree," and "completely disagree." The questionnaires were collected at the end of the session and evaluated. The results of the community's agreement or disagreement on the items are documented in the Results section. A disagreement of more than 5 % led to revision of the statement.

After consideration of the feedback of the audience and further comments by the panel, an additional and final Delphi process was initiated to achieve a final consensus, which is presented here.

Results

Definition

In spite of some inconsistencies (defined later), for the purpose of this consensus conference, we have adopted the Montreal definition of gastroesophageal reflux disease (GERD). GoR C; ExC 100 %; SCC 95 %

Endoscopic findings in GERD allow one to distinguish between Nonerosive reflux disease (NERD), erosive reflux disease (ERD), and Barrett's esophagus (BE). In addition to normal endoscopy, diagnosis of NERD requires a satisfactory response to PPI therapy and/or an abnormal acid exposure and/or a positive symptom association with documented reflux episodes. GoR C; ExC 100 %; SCC 98 %

In Europe, the two most widely used endoscopic classifications of esophagitis in GERD are the Savary and Miller classification and the Los Angeles Classification. GoR C; ExC 100 %; 95 %

In the Montreal consensus meeting, the disease was classified into esophageal and extraesophageal syndromes. In addition, the group recognized laryngitis, cough, asthma, and dental erosions as possible GERD syndromes [5]. After in-depth discussion, the panel felt that this did not completely reflect the current clinical situation and differentiated the symptomatic presentation of GERD in more detail [4–6]. As endoscopic findings are assessed differently in many European countries, the most widely accepted classifications should be used [10–13].

Pathophysiology

GERD is a multifactorial disorder, related mainly to failure of the antireflux mechanisms. The pathophysiologic components of GERD, which can be involved either alone or combined, are a defective antireflux barrier (mechanically defective LES, inappropriate transient LES relaxations, hiatal hernia), delayed gastric emptying, and impaired esophageal clearance. GoR C; ExC 100 %; SCC 100 %

GERD is a multifactorial process in which esophageal and gastric changes are involved. The major pathophysiologic causes are the incompetence of the lower esophageal sphincter (LES), transient sphincter relaxations, insufficient esophageal peristalsis, altered esophageal mucosal resistance, delayed gastric emptying, and antroduodenal motility disorders with pathologic duodenogastroesophageal reflux as well as altered hiatal and gastroesophageal anatomy [14–19]. Changing and deteriorating hiatal anatomy involves the hiatal crura, the phrenoesophageal ligament, and esophageal shortening [19–21]. Several factors such as stress, obesity, pregnancy, and diet as well as drugs play an aggravating role in this process [4–6].

Epidemiology

Epidemiologic data on GERD are not reliable. Based on symptoms, the prevalence ranges between 0.1 and 20 % in industrial countries. GoR D; ExC: 100 %; SCC 89 %

Data are based merely on subjective symptoms such as heartburn and regurgitation [22, 23].

Natural course

GERD is a chronic disease. The majority of patients with GERD will remain within the initial level of severity of the disease. Only a proportion of patients will progress and develop further complications. GoR B; ExC 100 %; SCC 98 %

The majority of patients with GERD will remain stable over time and within the level of severity of the disease [24, 25]. However, a small proportion (4-7 %) of patients have progressive disease with usually deteriorating anatomy and function as well as increasing severity of symptoms and decreasing quality of life [19, 23, 25]. A few patients with severe GERD can even develop detrimental aspiration, most often associated with advanced age, other comorbidities, and large hiatal hernias, which aggravate the

exposure to reflux, accounting for some deaths related to GERD [26].

Anatomy and hiatal hernias

In GERD, hiatal hernia is a very frequent finding, found in up to 80-90 % of the surgical patient population. GoR B; ExC 100 %; SCC 89 %

Hiatal hernia is defined as an anatomical abnormality consisting of a protrusion or migration of intra-abdominal contents through an enlarged hiatal opening at the diaphragm [14, 27, 29]. When this develops over time, a hernia sac forms while the hiatal phrenoesophageal membrane and mediastinal and abdominal connective tissue deteriorate. Hiatal hernia is found in up to 80-90 % of GERD patients [14, 20, 27–29].

Even though the size and shape of a hernia can very markedly, the surgical principles of dissecting a hiatal hernia are similar for small and large hernias. A surgically relevant classification of hiatal hernia should be used, because indications for certain surgical and endoscopic techniques as well as patient information and informed consent may depend on the presence of symptoms and different types of hernias. GoR C; ExC 100 %; SCC 95 %

There are several classifications of hiatal hernia [14, 27–30]. The most frequently used is a topographic description [14, 27, 29]. Another very useful classification is an endoscopically generated, which allows for a more functional assessment [30]. In a sliding hiatal hernia, a circumferential insufficiency of the phrenoesophageal ligament has caused a complete circular migration of the gastroesophageal junction into the lower mediastinum, which can grow into an intrathoracic stomach translocation. In a true paraesophageal hernia there is a local failure of the phrenoesophageal ligament causing a paraesophageal herniation of the fundus, while the gastroesophageal junction remains at the hiatal level. In a partial or complete upside-down stomach, the stomach has turned into the hernia sac in the mediastinum and herniation of other organs such as the colon can occur.

Since the surgical principles of dissecting and taking down a hiatal hernia are similar independent of the hernia's size and rotational status, the classification of a hiatal hernia is not of major importance with respect to its repair by an experienced surgeon. However, a surgically relevant classification may be useful when certain special surgical and endoscopic techniques are indicated and for patient information and obtaining informed consent, since size and shape still can play a role in the pathophysiology and symptomatic presence.

Surgical requirements are an adapted approximation of the crura to narrow the hiatal orifice with nonresorbable sutures and resection of the hernia sac with care being taken to preserve the vagal nerves. GoR C; ExC 100 %; SCC 98 %

Narrowing the hiatus by adapted crural closure with nonresorbable sutures in addition to resection of the hernia sac after extensive mobilization of the esophagus in the mediastinum has been documented [14, 21, 31]. Relevant surgical problems include careful preservation of the vagal nerves, attention to anatomical variations at the hiatus, and recurrence despite adequate surgical technique due to tissue weakness and failure to establish stable adhesion after surgery. Recently, new efforts to evaluate the hiatus more precisely in order to classify the risk of failure and possibly prevent this failure by the use of meshes have been emphasized [32–35].

Clinical presentation of GERD: typical and atypical symptoms

GERD can cause a variety of gastroesophageal (typically heartburn and regurgitation) and extraesophageal symptoms. GoR B; ExC 100 %; SCC 100 %

Although heartburn and regurgitation are characteristic of GERD, they overlap substantially with other disorders such as dyspepsia or somatoform disorders. GoR C; ExC 100 %; SCC 100 %

Patients with GERD can also present with dysphagia, upper gastrointestinal bleeding, chest pain, and epigastric pain. These symptoms ("red flag" symptoms) attest to severe acute disease and should be clarified by immediate appropriate diagnostic investigations. GoR C; ExC 100 %; SCC 97 %

The multifactorial pathophysiologic background of GERD accounts for the manifold clinical presentation [14, 17, 19, 27, 36–40]. In addition, symptoms suggestive of GERD show a considerable overlap with other disorders such as functional heartburn, esophageal hypersensitivity, functional dyspepsia, irritable bowel syndrome, respiratory disorders, eosinophilic esophagitis, and disorders of the mouth and throat [41–47]. Thus, symptoms are not reliable for confirming the diagnosis of GERD.

In the Montreal consensus meeting [5], clinical manifestations of GERD were differentiated in only two syndromes, esophageal syndromes and extraesophageal syndromes, subject to the criticism of the panelists. The panelists found evidence to claim that there are esophageal, gastrointestinal, and extraesophageal (respiratory and oropharyngeal) symptoms associated with GERD [36–53]. Esophageal symptoms are heartburn, regurgitation, and thoracic pain. Heartburn (also known as retrosternal burning and substernal burning) from the epigastrium upward is the most typical and frequent symptom in GERD. Heartburn can be present in 6-20 % of dyspepsia patients [36–38]. Regurgitation of refluxed gastroduodenal contents

from the stomach into the hypopharynx and/or mouth is the second most important symptom in GERD, with a prevalence of 33-86 % [36–38, 53].

Among the gastrointestinal symptoms, epigastric pain is present in 70.5 % of patients with foregut symptoms and in 12-67 % of those with documented pathologic acid reflux. The overlap with dyspepsia and somatoform disorders is large [38, 41–47].

Dysphagia is also potentially related to GERD, indicating an impaired passage throughout the esophagus. It can also be a "red flag" symptom, potentially caused by a tumor, requiring immediate evaluation [5].

Extraesophageal symptoms (EES) (e.g., cough, hoarseness, globus, and shortness of breath) can be associated with syndromes such as reflux cough syndrome, reflux laryngitis syndrome, reflux asthma syndrome, and reflux dental erosion syndrome. Further potential extraesophageal manifestations include idiopathic pulmonary fibrosis, pharyngitis, sinusitis, and otitis, which are currently under scrutiny. GoR C; ExC 100 %; SCC 98 %

Extraesophageal symptoms (EES) include respiratory and oropharyngeal symptoms such as chronic cough, hoarseness, sore throat, and pharyngeal burning. In addition, a burning sensation of the tongue and mouth, a globus sensation, and dental erosions can be related to GERD [5]. The term extraesophageal reflux (EER) is used for respiratory-related symptoms. Although there is no consensus definition of EER, common sense leads to define EER as related to lesions and/or symptoms caused by gastroesophageal reflux that reaches structures above the upper esophageal sphincter [5].

The Montreal consensus proposed several syndromes and association of syndromes in GERD [4]. The level of evidence, particularly for the latter, is low. Established associations are reflux-cough syndrome [54–56], reflux-laryngitis syndrome [57, 58], reflux-asthma syndrome [59, 60], and reflux-dental erosion syndrome [61], while the proposed associations include pharyngitis [62, 63], sinusitis [62], idiopathic pulmonary fibrosis [64, 65], and otitis [62].

Today EER can be regarded as an important contributing factor to EES [66]. Of note, by far not all patients with reflux suffer from such syndromes. For example, in reflux-chronic cough syndrome, hypersensitivity of the anatomically closely related cough reflex circuit to the LES innervation may play a crucial role [67]. This changing paradigm of understanding reflux-respiratory disease correlations makes it very difficult to collect epidemiologic data [67, 68]. Sampling gaseous, aerosolized reflux in the pharynx might be more appropriate for the assessment of laryngopharyngeal reflux (LPR), further complicating sampling of epidemiologic data on EER [68–70].

Diagnostic investigations

The most important diagnostic investigations to prove the presence of GERD are endoscopy and long-term impedance pH monitoring (or pH monitoring). For accurate placement of the impedance pH probe, manometry measurements are recommended. The test should be performed after adequate washout of PPI or antisecretory drugs (discontinuation 2 weeks before testing). GoR B; ExC 100 %; SCC 97 %

It is essential to differentiate between the investigations necessary to establish the diagnosis of GERD and those necessary to establish the indication for surgery or any other invasive therapy [5, 11, 17, 37, 71, 72]. Upper gastrointestinal endoscopy is an important investigative tool to document GERD when there is endoscopic visualization of mucosal damage such as signs of reflux esophagitis [11, 73, 74]. The other important diagnostic investigative tool is pH monitoring or impedance pH monitoring, which is necessary to objectively document pathologic acid exposure and/or other pathologic reflux activities [75–79]. Impedance pH monitoring increases the diagnostic value of these functional studies by quantifying acid and nonacid reflux [80] and by providing a correlation between symptoms and documented reflux episodes [81–84]. In addition, esophageal pH monitoring has important prognostic value in patient selection for antireflux surgery [85].

Esophageal manometry is not important in establishing the diagnosis of GERD. It does, however, have some value as a marker of severity of the disease in that LES incompetence is associated with more severe disease and long-term progression [15–17, 19, 86]. Manometry studies are important prior to any surgical procedure to evaluate motility disorders, especially spastic motility disorders or achalasia [31, 71, 72, 83, 86–90].

When atypical symptoms are predominant, a symptom correlation with proven reflux episodes should be considered for accurate diagnosis. GoR B; ExC 100 %; SCC 92 %

The more atypical symptoms present in a given patient, the more detailed diagnostic assessment should be performed prior to surgery to detect all functional defects [72, 90]. When extraesophageal symptoms are present or, especially, are the chief complaints, it is extremely important to correlate the atypical symptoms with the reflux episodes to justify invasive antireflux therapies [91].

Further diagnostic investigations may be needed to verify functional abnormalities and establish the indication for surgery or other invasive therapies. Investigations that can evaluate the status of esophageal and gastric function include high-resolution manometry (HRM), video-radiography, scintigraphy, and others. GoR B; ExC 100 %; SCC 93 %

HRM facilitates the procedure for the patients. Dynamic barium sandwich videography is important in evaluating patients with dysphagia. In cases of large hernias, a barium study can provide information about the possibility of a short esophagus [21]. In GERD patients with nausea and vomiting as the major complaint, gastric emptying studies and duodenogastroesophageal reflux assessment should be done to evaluate the presence of a gastroduodenal motility disorder such as delayed gastric emptying [92–95].

Medical therapy

The goal of medical therapy in GERD is to control heartburn, heal gastroesophageal mucosal injuries, and improve quality of life. GoR A; ExC 100 %; SCC 100 %

GERD, both ERD and NERD, is associated with significant impairment of quality of life [3, 4, 96–101]. Thus, the goal of medical therapy in GERD is to control heartburn, heal gastroesophageal mucosal injuries, and improve quality of life [96–98].

Lifestyle and dietary modifications may benefit some selected patients with GERD, but alone they are almost ineffective in relieving reflux symptoms. GoR B; ExC 100 %, SCC 97 %

Patients should avoid large meals and lying down within 3 h after eating. Moreover, ingestion of fatty or spicy foods, chocolate, coffee, peppermint, citrus fruits and juices, tomato, carbonated drinks, and alcohol may favor the occurrence of reflux events and GERD symptoms [3–5, 102, 103]. Changes in lifestyle may include sleeping with the head elevated and stopping smoking [103, 104]; however, there is little or no evidence for the efficacy of these interventions. Conversely, recent data suggest that a high BMI is an independent risk factor for the development of GERD and that the clinical efficacy of medical therapy seems to be influenced by the patient being overweight/obese. Weight loss or avoidance of weight gain should be considered to reduce the risk of GERD and to obtain a better outcome from acid suppressant therapy [104–106].

Antacids are well tolerated, safe, and effective in reducing heartburn and controlling acid regurgitation (typical symptoms of GERD) in patients with mild reflux disease. GoR B; ExC 100 %; SCC 96 %

Antacids such as alginate-based preparations are well tolerated and effective in reducing heartburn and improving quality of life [107–110]. However, they are less effective in controlling nonacid reflux and regurgitation [111].

Acid suppressive drugs are safe and effective in patients with esophageal syndromes. Proton pump inhibitors (PPIs) are more powerful than H_2 *receptor antagonists in providing mucosal healing and symptomatic relief. GoR A; ExC 100 %; SCC 100 %*

H_2receptor antagonists (H_2RAs) Acid suppression represents the mainstay of GERD medical treatment. H_2RAs have shown lower efficacy than PPIs in acid suppression, but given in divided doses they may be effective in some patients with less severe forms of GERD [112, 113]. Moreover, as gastric acid is still secreted particularly during the night, despite twice-daily PPIs, it has been suggested that the addition of a nighttime H_2RA might be helpful in suppressing this acid reflux, but insufficient data are available to recommend it [114]. However, it is important to note that continuous use of H_2RAs is associated with the development of tolerance to them, limiting their long-term use and efficacy as add-on therapy [115].

Proton pump inhibitors (PPIs) By inhibiting the H^+-K + adenosine triphosphatase pump of the parietal cell, PPIs potently reduce gastric acid secretion and provide the most powerful symptomatic relief and heal esophagitis in the majority of the patients [3–5, 116, 117]. Moreover, they are safe and have been used world-wide for more than a decade [116, 118, 119]. Standard doses of omeprazole, lansoprazole, pantoprazole, esomeprazole, and rabeprazole for the most part have shown comparable rates of healing and remission of erosive esophagitis [119, 120], although there are several physiologic studies showing a mild to moderate benefit of one drug over another [121, 122]. Since PPIs are best absorbed in the absence of food, patients should be advised to take their PPI between 30 and 60 min prior to eating, usually before breakfast or prior to the evening meal [123].

In patients with a partial or unsatisfactory response to once-daily PPI dose, twice-daily PPI may be of help to improve symptom relief. Nonresponders should be further investigated. GoR B; ExC 100 %; SCC 98 %

Data supporting twice-daily PPIs (or H_2RAs) rather than a standard dose for improving mucosal healing and symptom relief are weak [124, 125], even though the pharmacodynamics of the drugs logically supports twice-daily dosing [119, 126]. Expert opinion suggests twice-daily dosing of PPIs in patients with an esophageal syndrome and unsatisfactory response to once-daily dosing or in patients with "atypical" or "extraesophageal symptoms" [119, 127, 128]. Nonresponders to twice-daily PPI therapy should be considered treatment failures and further investigated [129, 130].

Promotility drugs as monotherapy or add-on therapy are not recommended for the routine management of GERD. Prokinetics may be used in selected patients in conjunction with antisecretory agents. GoR C; ExC 100 %; SCC 93 %

Esophageal and gastric motility abnormalities are relevant in the pathogenesis of GERD. Therefore, promotility drugs such as metoclopramide, bethanecol, and domperidone, given as mono- or add-on therapy, usually before a

meal, may be useful to control reflux symptoms. However, the frequent side effects have largely limited the regular use of these drugs [131, 132].

Indication for surgical therapy in GERD

Prior to the indication for surgery or any other invasive therapy, it must be proven that patients are in need of long-term treatment of GERD. GoR B; ExC 100 %; SCC 98 %

Patients with continuous reduced quality of life, persistent troublesome symptoms, and/or progression of disease despite adequate PPI therapy in dosage and intake should be offered laparoscopic antireflux surgery after proper diagnostic testing. GoR A; ExC 100 %; SCC 98 %

The aim of therapy is to resolve the symptoms, treat and prevent complications, and improve the patient's quality of life. If symptoms and a reduced quality of life persist despite an adequate PPI dosage and proper intake, patients should undergo further testing to evaluate the severity and complexity of the disease and possible indication for antireflux surgery. The basis for this is the available evidence that laparoscopic antireflux surgery can improve quality of life in patients with altered anatomy, massive acid exposure, nonacid reflux, severe reduction in quality of life, and progressive disease with need to increase PPI dosage over the years [31, 71, 72].

PPI therapy is always the primary therapy for acute GERD. If a patient needs long-term treatment, both medical and more invasive options must be considered. Several randomized trials comparing PPI therapy with antireflux surgery have been conducted. Three of these trials [133–135] showed an advantage for surgical therapy in outcome and cost-effectiveness after a few years, whereas one showed an advantage for PPI therapy after 5 years [117]. The conclusion from these studies and other large case-control series from experienced centers is that patients should be well selected for surgery so that they benefit from an increase in quality of life [117, 133–138].

The following list of criteria drawn from the literature contains the most important and most frequently mentioned features leading to the indication for antireflux surgery:

- Typical symptoms for GERD [85]
- Documented symptom-reflux correlation [83]
- Year-long reflux history [14, 16, 86]
- Reduced quality of life [31, 71, 72]
- Positive PPI response [85]
- Need for PPI dosage increase [25, 117, 133, 134]
- Hiatal hernia [14, 19, 20]
- Documented esophagitis (in the past before PPI) [14, 19, 134–136]
- Proven LES incompetence [14–17, 19, 86]
- Documented acid reflux [14, 17, 19, 71, 72, 77, 92]

GoR B; ExC 100 %; SCC 95 %

These criteria should be evaluated in each patient who is a candidate for antireflux surgery to verify as much as possible the need for long-term therapy and surgical correction [14–17, 19, 20, 25, 31, 37, 71, 72, 77, 83, 85–87, 92–94, 117, 133–135].

Patients with proven GERD, good response to PPI, dependent on PPI, and acceptable quality of life under adequate PPI therapy may be considered for surgery if she/he so desires. Information about the side effects and risks of antireflux surgery is particularly relevant in this category of patient. GoR C; ExC 100 %; SCC 91 %

Patient with documented GERD and sufficient quality of life under adequate PPI therapy can continue medical treatment. However, some patients may want surgical therapy. The indication for surgery—the patient's wish—is a critical issue since 5-10 % of these patients run the risk of reduced quality of life postoperatively [31, 71, 72, 117]. This risk should be part of the information presented to the patient before he/she gives informed consent.

In patients with proven GERD and impaired esophageal motility, a fundoplication (partial or total) can be performed without an increased risk of dysphagia. In cases of severe hypomotility, the data are controversial, but a partial fundoplication might be considered. GoR C; ExC 100 %; SCC 91 %

The influence of esophageal motility disorders on postoperative results was investigated in several randomized trials [139–141]. Keeping the different definitions of esophageal motility disorders in mind, laparoscopic fundoplication can be either partial or total. However, for patients with aperistalsis, the results in the literature are controversial [139–145].

In NERD patients and those with hypersensitive esophagus, antireflux procedures can improve quality of life if adequate indication criteria are fulfilled. GoR C; ExC 100 %; SCC 95 %

Limited evidence from preliminary data has shown good results from laparoscopic Nissen fundoplication in patients with NERD and in patients with normal acid exposure and positive symptom association with acid and/or nonacid reflux episodes (hypersensitive esophagus), if the patients are selected very carefully [146, 147].

Patients with documented pathologic laryngopharyngeal reflux (LPR) and positive symptom correlation may benefit from a laparoscopic fundoplication. There is only limited evidence on the efficacy of antireflux surgery in patients with documented LPR associated with nonacid reflux. GoR C; ExC 100 %; SCC 93 %

Several case-control studies have shown good results for laparoscopic Nissen fundoplication in carefully selected

patients with LPR or GERD-related respiratory symptoms [67, 148–153].

Patients with GERD and who are obese can benefit from a bariatric procedure rather than from an antireflux procedure. Indications according to BMI and the best procedure to use (gastric bypass, sleeve, others) are currently being debated. GoR C; ExC 87 %; SCC 89 %

In obese patients with BMI >35 kg/m^2 and GERD, a traditional antireflux operation may not be sufficient. In moderate cases, a combination of sleeve gastrectomy with sphincter and hiatal repair can be considered. In more severe cases, both problems can be solved by bariatric surgery [154, 155].

Standard technique of primary laparoscopic fundoplication

The rationale for surgery is to create a functional antireflux barrier. The reconstruction of the antireflux barrier consists of three fundamental components: (1) proper length of the intra-abdominal esophagus, (2) crural repair, and (3) fundoplication. GoR B; ExC 100 %; SCC 98 %

The operative strategy of mechanical augmentation of the cardia, as introduced by Nissen [156], is still valid and successful [31, 71, 72, 117, 133–135, 157]. Several modifications to fundoplication (complete, posterior, or anterior partial wraps) have been shown in randomized trials to efficiently reduce gastroesophageal reflux and improve quality of life over years [31, 71, 72, 117, 133–135, 157–160]. Both partial and total fundoplications must meet the basic standard of being efficient and providing longevity by restoring the intra-abdominal segment of the esophagus, using only the fundus to create the wrap, placing the valve at the level of the gastroesophageal junction, and adequately approximating the crura [157].

Laparoscopic partial and total fundoplications are currently the best available surgical techniques to treat severe GERD. GoR A; ExC 100 %; SCC 99 %

Randomized controlled trials (RCTs) have shown that partial fundoplication has fewer short-term side effects. However, the available RCTs are of limited quality and power. Due to the heterogeneity with respect to the definition of dysphagia and outcomes and/or different poorly defined technical details of the procedures, results are difficult to compare. As a consequence, experienced surgeons in high-volume centers may decide between total and partial posterior fundoplication according to their own experience and outcome. GoR B; ExC 100 %; SCC 97 %

Controversy exists about the optimal shape of the wrap, whether to use complete (360°) or partial, anterior or posterior, and whether the latter should cover 240°, 180°, or 90° of the esophageal circumference. Several randomized trials [159–174] and meta-analyses have been published [175–182].

The two major competing procedures are the laparoscopic Nissen fundoplication and the posterior partial Toupet hemifundoplication. Meta-analyses show a similar success rate at 5 years but a higher rate of side effects (dysphagia, bloating, and flatulence) and a higher reoperation rate in the Nissen group compared to the Toupet group [160, 162, 170, 176, 179]. In contrast, large case-control studies from experienced centers show a low level of side effects with minimal enduring dysphagia, a high long-term durability, and a low reoperative rate for the Nissen procedure [31, 71, 72, 157, 183–189]. Since the data are controversial, consensus is difficult and the choice of which fundoplication technique to use should be left to the individual surgeon according to his/her expertise.

Hiatal repair (approximation) is obligatory in the surgical treatment of hiatal hernia. GoR B; ExC 100 %; SCC 100 %

There is only indirect evidence indicating that hiatal repair should be performed during antireflux surgery [1, 2, 117, 128]. In addition, whether a radiologic hiatal hernia recurrence is clinically relevant and requires therapeutic measures is controversial [190].

Hiatal repair with mesh reinforcement may reduce hernia recurrence. However, mesh-related complications have to be considered. GoR A; ExC 100 %; SCC 98 %

Frequent recurrences, especially in patients with a large hiatal hernia, have stimulated interest in mesh reinforcement as a possible solution [191–198]. Two randomized trials and other reports have shown an advantage in the use of mesh reinforcement regarding the postoperative recurrence rate of hiatal hernias.

There is increasing evidence of mesh-related complications. As a consequence, indications for mesh should be limited to patients with weak crurae and a large hiatal defect. GoR C; ExC 100 %; SCC 95 %

More recently, clinical experience has shown that the use of mesh at the hiatus can cause severe problems (e.g., recurrent dysphagia and pain, mesh dislocation and penetration) sometimes requiring major resections [197–201].

Collis gastroplasty in the short esophagus

A short esophagus (SE) is a rather rare phenomenon with reports showing it ranging from 1 to 20 %. Although the final diagnosis of SE is made intraoperatively, the presence of peptic strictures, Barrett's esophagus, and large hiatal hernia are considered preoperative indicators of SE. When there is a suspicion of SE, the patient should be investigated with barium studies. GoR C; ExC 100 %; SCC 95 %

In an anatomically normal adult, the intra-abdominal segment of the esophagus is 2–3 cm long, depending on the body's length. In a patient with long-standing GERD and persistent or recurrent esophagitis, the esophagus can be

shortened [21]. If the esophagus cannot be mobilized from the mediastinum in a tension-free fashion to obtain a 2-3-cm intra-abdominal segment during an antireflux procedure, it is classified as a "short esophagus." While most authors consider this a rare phenomenon, the incidence reported in literature is controversial, ranging between 1 and 20 % [21, 202–206].

If sufficient length of the intra-abdominal esophagus cannot be obtained after extensive esophageal mobilization, a lengthening procedure using Collis gastroplasty should be considered, since patients can benefit from it. There is limited evidence on the technical aspects of a Collis gastroplasty. A Collis gastroplasty should be performed by an experienced surgeon in this field. GoR B; ExC 86 %, SCC 78 %

Two meta-analyses and several case-controlled studies have shown that patients with SE can benefit from antireflux surgery combined with a Collis gastroplasty [22, 202–207]. An alternative to gastroplasty can be esophageal lengthening by dividing the posterior and, if necessary, anterior vagal nerves [208].

New emerging techniques for antireflux therapy

There is not enough evidence available to recommend an alternative option to fundoplication for severe GERD. GoR B; ExC 100 %; SCC 97 %

Several endoscopic antireflux techniques have been developed beginning in the late 1990 s. Due to limited effectiveness and/or severe complications, most of these procedures, such as Endocinch™ suturing (C.R. Bard, Inc., Murray Hill, NJ), the Stretta® procedure (Mederi Therapeutics Inc., Norwalk, CT), the Enteryx® injection (Boston Scientific, Natick, MA), the plicator, and the Esophyx™ plication (EndoGastric Solutions, San Mateo, CA), have not survived. Some procedures have had limited success [209–213]. A new laparoscopic antireflux procedure using a device to reinforce the cardia has been introduced in recent years, the magnetic scarf LINX™ (Torax® Medical Inc., Shoreview, MN). The initial clinical experience has produced promising results in patients with moderate GERD with or without small hiatal hernias [214, 215].

Failures of surgical therapy and management of redo surgery

Failure is usually defined as persistent, recurrent, or new-onset symptoms. Antireflux surgery has a failure rate of 10-15 %. The main symptoms of failure are recurrent reflux symptoms and/or dysphagia. GoR A; ExC 100 %; SCC 100 %

Persistent and recurrent reflux can be due to intrathoracic wrap migration, disruption of the wrap, slipping, and/or telescoping. Pain and/or dysphagia can be caused by intrathoracic wrap migration, slipping, telescoping, paraesophageal herniation, mesh migration, excessive fibrosis (mesh-related or not), and/or an overly tight wrap or overly tight crural repair. Dysphagia can also be due to initially unrecognized esophageal motility disorders such as achalasia. A variety of symptoms (gas-bloat syndrome, inability to belch, gastric fullness, early satiety, diarrhea, nausea, and vomiting) can occur postoperatively, some due to an overly tight wrap or an overly tight crural repair, others secondary to vagal damage. GoR B; ExC 100 %; SCC 98 %

Primary antireflux surgery has a successful outcome in 85-90 % of patients up to 5 years after surgery [31, 71, 72, 117, 133–135, 157, 183–188]. Consequently, that means there is a failure rate of 10-15 %. Redo antireflux surgery is required in 3-6 % of all patients who undergo primary antireflux surgery [216–220]. Recurrent reflux symptoms such as heartburn and regurgitation are the main complaints after unsuccessful antireflux surgery and are found in 61 % of patients with failure [219, 220]. Troublesome dysphagia is the second most frequent symptom in failed antireflux surgery (24 %). Combined recurrent reflux and dysphagia is reported in 6 % of patients. Symptoms should be the primary indication for redo antireflux surgery.

All patients seeking treatment for symptomatic failure after antireflux surgery should be evaluated to identify the causes of failure. Investigative techniques include endoscopy, manometry (HRM), esophageal 24-h (impedance) pH monitoring, barium studies, and scintigraphy. Severe dysphagia requires early endoscopic exploration and, whenever appropriate, endoscopic dilatation. If symptoms persist, revisional surgery is recommended. Excessive dysphagia and intractable pain and/or dyspnea in the early postoperative course require immediate revision after appropriate investigations. In all other failure scenarios, first-line therapy should be medical and/or supportive. GoR B; ExC 100 %; SCC 98 %

The main reason for functional failure after primary antireflux surgery is misdiagnosis. These patients usually have a primary functional disorder other than GERD such as achalasia, diffuse esophageal spasm, nutcracker esophagus, eosinophilic esophagitis, or scleroderma [219–221]. Another possible cause for failure after primary antireflux surgery is the wrong procedure was used in patients with severe esophageal dys- or motility [219].

All patients with symptomatic failure after primary antireflux surgery should be extensively evaluated with several procedures to identify the cause of the failure [219–227]. This diagnostic program should include manometry, possibly a high-resolution manometry, (impedance) pH monitoring, radiographic studies such as a barium sandwich, and scintigraphy in selected cases, as well as assessment of outcome and quality of life [216, 229–233].

Redo antireflux surgery should always begin with a clear definition of the anatomy. Surgeons undertaking revisional laparoscopic surgery should be able to perform total and partial fundoplication, Collis gastroplasty, and resections as necessary. Revisional antireflux surgery should be performed by a well-experienced surgeon in the field. GoR C; ExC 100 %; SCC 86 %

Anatomical alterations such as recurrent hernia or a bilobed and twisted stomach have been described as reasons for failure and subsequent redo antireflux surgery [216–229]. However, an anatomical disturbance without symptoms should never be the only reason for redo surgery. Symptoms should be the primary indication for redo antireflux surgery. Conversely, postoperative anatomy as evaluated by endoscopy and/or barium studies can be normal in patients who still have symptoms.

Anatomical changes after laparoscopic antireflux procedures can be classified into several categories, including intrathoracic wrap migration, wrap disruption, telescoping, paraesophageal herniation, a tight wrap or a tight crural repair, and a bilobed or twisted stomach. With all of these conditions there has to be dissection and proper rearrangement before creating a new fundoplication [216, 219, 220].

Revisional surgery should be performed by specialized gastrointestinal surgeons with extensive experience in the field. The surgeon's technical armamentarium for revisional surgery should include all laparoscopic, endoscopic, and thoracoscopic procedures as well as all open procedures, including major resections, as necessary to solve the problem.

Barrett's esophagus

Barrett's esophagus (BE) is defined as "the presence of columnar mucosa and intestinal metaplasia in the distal esophagus" and is the final consequence of long-standing (duodeno-) gastroesophageal reflux disease (GERD). BE is associated with a 30-150-fold increase in the risk of esophageal adenocarcinoma. GoR B; ExC 100 %; SCC 97 %

There are two definitions of BE currently in use. One, adopted in the US and continental Europe, requires the presence of intestinal metaplasia (goblet cells) in biopsies from the columnar epithelium lining the distal esophagus [234]. In the UK, on the other hand, all histological types of metaplastic epithelium (cardiac or fundic) are defined as columnar epithelium lining the esophagus (i.e., Barrett's esophagus) and the presence of intestinal metaplasia is not essential to the diagnosis [235]. Since intestinal metaplasia is the only type of esophageal columnar epithelium clearly predisposed to malignancy [236], we prefer to use the first definition. The incidence of BE progression to high-grade noninvasive neoplasia or invasive neoplasia is estimated to be between 1 and 5 per 1,000 patients/year, which is 40-50 times higher than in the normal population [237, 238].

The aims of medical or surgical therapy in Barrett's esophagus are to control symptoms, heal any mucosal lesions (esophagitis), prevent complications, and limit progression of BE to neoplasia. Although medical therapy is highly effective in controlling symptoms, it may be less so in abolishing gastroesophageal reflux and the progression to neoplasia. GoR B; ExC 100 %; SCC 98 %

The current treatment for BE [proton pump inhibitors (PPIs) or antireflux surgery] aims to control GERD-related symptoms and to prevent complications such as ulcer, bleeding, and stricture. There have been anecdotal reports of acid suppression therapy being able to revert intestinal metaplasia to cardiac/fundic metaplasia or squamous epithelium (and thereby reduce the cancer risk) [239].

The usual therapy for BE consists of PPI in single or double doses. It is generally believed that BE patients are more difficult to manage with medical therapies than other GERD patients, and higher PPI doses may be required. Abnormal acid exposure in the distal esophagus of BE patients is particularly evident at night when nocturnal regurgitation and related respiratory symptoms (nocturnal acid breakthrough) may occur [240].

Antireflux surgery may be more effective than medical therapy for BE and should be considered, particularly for young patients. GoR C; ExC 100 %; SCC 89 %

Antireflux surgery is a valid alternative to PPI and has the advantage of correcting the LES failure and the frequently associated hiatal hernia, as well as controlling abnormal gastric and duodenal reflux in 80-90 % of patients. One controlled study [241] and several noncontrolled studies [242–246] have demonstrated better symptom control and a lower incidence of stricture after surgery compared to medical therapy. Subgroup analysis of patients with BE enrolled in the recently reported LOTUS trial showed a comparable rate of symptom control between surgery and escalating doses of PPI [247]. Since BE is frequently found in older patients, surgery should be considered for younger and fit patients, particularly in cases at high risk of progression with large hiatal hernias, severe reflux symptoms, and a long history of disease [248, 249].

There is limited evidence to show that antireflux surgery can reduce the extent of BE and the risk of progression to cancer. After antireflux surgery, endoscopic surveillance has to be maintained. GoR C; ExC 100 %; SCC 98 %

There are conflicting data regarding the influence of surgical therapy on the regression or progression of BE [243, 245, 250–257]. Epidemiological studies have recently shown that progression to cancer after antireflux surgery is due mainly to subsequent recurrence of reflux, which remains the Achilles heel of antireflux surgery [259].

Given such conflicting data, endoscopic surveillance should be maintained even after a patient has undergone antireflux surgery [258, 259].

Gastroesophageal reflux and antireflux surgery in children

Although most children with gastroesophageal reflux (GER) no longer have this condition by the age of 1 year, clinically troublesome GERD can occur in a significant proportion of children and adolescents. Contrary to adults, GERD symptoms are often nonspecific. The majority of pediatric GERD patients have neurological impairment. GoR C; ExC 100 %; SCC 100 %

Gastroesophageal reflux (GER) is a normal physiologic process and can occur in up to 70 % of completely healthy newborns and infants. This GER resolves spontaneously in 95 % of the individuals by 12–14 months of age [260, 261]. When GER causes troublesome symptoms and/or complications, the diagnoses of GERD can be raised, according to the Montreal Definition of GERD in adults. This definition also applies to children but with several limitations [5].

Symptoms

Clinical diagnosis cannot be used in infants, young children, or neurologically impaired adolescents because these individuals cannot reliably report their symptoms. Although the verbal child can communicate pain, descriptions of the intensity, location, and severity may be unreliable until the age of at least 8 years, and sometimes even later [262–264].

In infants and younger children or older children with neurologic impairment, symptoms and signs associated with reflux are often nonspecific and include vomiting, excessive regurgitation, refusing to eat, anorexia, unexplained crying, choking, gagging, coughing, disturbed sleep, and abdominal pain [265].

Typical symptoms of GERD in children include recurrent regurgitation with or without vomiting, swallowing difficulties that lead to weight loss or failure to thrive, respiratory problems (wheezing, asthma, or recurrent pneumonia), abdominal pain, irritability, and sleeping problems. Anorexia or refusing to eat is significantly ($p < 0.05$) more common and severe in children aged 1–5 years than in older children or adolescents [266]. Sandifer's syndrome (torticollis) is a specific manifestation of GERD in neurologically intact children and entails abnormal posturing (e.g., head tilt, torticollis), because of GERD [267, 268]. When assessing GERD, rumination should be distinguished from regurgitation. Rumination is common in infants and children with neurological impairment, but it can also occur in subjects without obvious neurologic deficits and is considered by some to lie within the spectrum of eating disorders [269]. Older children are more likely to experience symptoms similar to those in adults such as chronic heartburn, regurgitation with reswallowing, and dysphagia.

Pathophysiology

GERD pathophysiology in children differs from that in adults in that nearly 50 % of pediatric GERD patients are neurologically impaired. In these patients prolonged supine position, spasticity, and generalized gastrointestinal dysmotility contribute to GER [270]. The higher frequency of GERD in infants is associated with transient esophagogastric immaturity [271]. Although the pathophysiology of GERD has still not been completely unraveled, it is known to be a multifactorial disorder, even in childhood [271, 272].

Eosinophilic esophagitis (EE) is a chronic disease characterized by eosinophilic infiltration of the esophageal mucosa and associated with clinical and endoscopic manifestations [273, 274]. The incidence of EE appears to be increasing for as yet unknown reasons. EE can occur at any age, with a clinical presentation ranging from gastrointestinal symptoms (vomiting, feeding difficulties, dysphagia, or food bolus impaction) to coexisting atopic conditions (asthma, allergic rhinitis, or eczema).

Certain underlying disorders such as neurologic impairment, esophageal atresia, chronic lung disease, and genetic disorders predispose pediatric patients to the most severe and chronic GERD, and its complications [275–277].

Normal values for most gastroesophageal functional tests are lacking, which limits diagnostic accuracy. Diagnosis is established by evaluation and interpretation of symptoms and results of diagnostic assessment. GoR C; ExC 100 %; SCC 98 %

Established tests for assessing symptoms of GERD in adults may be used in children. However, there are several differences and limitations. For symptom evaluation, the reliability and validity of two age-specific reflux questionnaires have been described to diagnose GERD, the infant gastroesophageal reflux questionnaire (I-GERQ) and the GERD symptom questionnaire (GSQ) [278–280]. Normal values for children over 18 months of age using pH monitoring have not been established. Reflux assessment should be performed by 24-h impedance pH monitoring [280–282].

Barium swallow X-ray is useful to detect anatomic abnormalities but not for the diagnosis of GERD, since sensitivity and specificity are limited [282, 283]. Gastric emptying is measured by the ^{13}C-octanoic acid breath test, for which normal values in children have been established

[283]. Esophagogastroscopy with esophageal biopsy should be performed to diagnose or rule out other conditions, including eosinophilic esophagitis, infection, and Crohn's disease.

The therapeutic approach should start with medical therapy. The efficacy of pediatric antireflux surgery (ARS) has a wide range, which explains why the best approach is still under debate. Although there is a lack of well-designed studies, partial fundoplication shows less severe postoperative dysphagia while maintaining similar reflux control compared to complete fundoplication. GoR B; ExC 100 %; SCC 100 %

Most symptomatic children respond well to medical treatment. Either H_2 antagonists or PPI may be used in children over 1 year of age [284–286]. However, when medical treatment fails, ARS may be considered [285–287]. ARS is one of the most frequently performed major operations in children. A systematic review of prospective studies on pediatric ARS showed a good overall success rate (median 86 %) in terms of complete relief of symptoms [288].

A systematic review and meta-analysis comparing the laparoscopic versus open approach in children showed a shorter hospital stay, less morbidity, and earlier feeding time after laparoscopic ARS. Recurrence of reflux after either procedure was similar [289].

Several different types of fundoplication (Nissen, Toupet, and Thal) can be performed in pediatric patients with GERD. The results of several studies are controversial as some reports show a higher risk of postoperative dysphagia with the Nissen procedure compared to partial fundoplication [290–292]. Recently, a first randomized trial with pediatric GERD patients was performed comparing Nissen to Thal fundoplication [292]. A meta-analysis showed that reflux control was similar after both types of fundoplication. However, partial fundoplication required significantly fewer dilatations to treat postoperative dysphagia [292]. In summary, ARS in pediatric patients with GERD shows good reflux control.

Enteroesophageal and duodenogastroesophageal reflux

Duodenogastroesophageal reflux is associated with more severe esophageal mucosal damage and BE. Fundoplication can prevent both gastric and duodenal reflux and is indicated in BE with documented enteroesophageal reflux. GoR B; ExC 100 %; SCC 96 %

The damaging effect of combined acid and duodenal juice and its components has been proven and documented in several conditions such as GERD, BE, and postoperative syndromes [14, 17–19, 93, 94, 293, 294]. Fundoplication can reduce gastroesophageal reflux very effectively and is therefore indicated in patients with severe mixed pathologic reflux.

Refluxate from the small bowel into the esophagus in patients with previous gastric surgery can cause severe damage in the esophagus. As a consequence, symptomatic patients after gastric surgery with reduced quality of life and enteroesophageal reflux should undergo functional diagnostic workup. If indicated by a positive correlation between functional defects and symptoms, surgical therapy can be resection and/or duodenal diversion eventually combined with fundoplication. GoR C; ExC 100 %; SCC 89 %

Refluxate from the stomach and the duodenum/jejunum contains a mixture of acid, bile, and pancreatic enzymes, which can have a toxic effect on the esophageal mucosa and other structures of the esophageal wall [14, 17, 18, 85, 93, 94]. The damaging potential of enteroesophageal reflux was studied in the past by studying the effects of different reconstruction methods after gastric and esophageal resections [294–297]. In patients after gastric resection with a short (<50 cm) jejunal limb reconstruction, in patients with a small gastric remnant, or in patients with a distal esophagectomy and gastric pull-up with an anastomosis in the lower mediastinum, there is a high probability of excessive enteroesophageal reflux with symptoms and/or esophagitis, which should be investigated by the proper methods followed by surgical correction [297–299].

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