Foregut Surgery

Achalasia, Gastroesophageal Reflux Disease and Obesity

Marco G. Patti
Marco Di Corpo
Francisco Schlottmann
Editors

Springer

Foregut Surgery

Marco G. Patti · Marco Di Corpo
Francisco Schlottmann
Editors

Foregut Surgery

Achalasia, Gastroesophageal Reflux Disease and Obesity

Springer

Editors
Marco G. Patti
University of North Carolina
Chapel Hill, NC
USA

Marco Di Corpo
University of North Carolina
Chapel Hill, NC
USA

Francisco Schlottmann
University of Buenos Aires
Buenos Aires
Argentina

ISBN 978-3-030-27591-4 ISBN 978-3-030-27592-1 (eBook)
https://doi.org/10.1007/978-3-030-27592-1

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

To my mentors, Marco G. Patti, Daniela Molena, and Anthony G. Charles, who inspired me to become an academic surgeon.
Francisco Schlottmann

To Giuseppe Spidalieri, for inspiring me to pursue my dreams.
Marco Di Corpo

To my brothers, for showing me the path to excellence.
Marco G. Patti

Preface

In October of 2018, during the congress of the American College of Surgeons, the Department of Surgery of the University of Carolina in Chapel Hill organized a postgraduate course on the treatment of gastroesophageal reflux disease, paraesophageal hernia, achalasia, and morbid obesity. The course was based on lectures given in the morning and hands-on using simulators in the afternoon.

All lectures were given by experts and focused on the preoperative workup, indications, and technical aspects of each operation. We received a very positive feedback from all the participants, and some asked if we could publish the contents of each lecture. *This book* is based on those lectures, and we included several additional chapters we feel could be useful for surgeons who take care of patients with reflux, achalasia, and morbid obesity.

Chapel Hill, NC, USA — Marco G. Patti
Chapel Hill, NC, USA — Marco Di Corpo
Buenos Aires, Argentina — Francisco Schlottmann

Contents

Part II GERD

Part III Bariatric Surgery

Editors

Marco G. Patti Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Francisco Schlottmann Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Marco Di Corpo Department of Surgery, Catholic University of Córdoba, Córdoba, Argentina

Nuevo Hospital San Roque, Córdoba, Argentina

Contributors

Vera Lucia Ângelo Andrade Department of Pathology, Faculdade de Medicina da UninCor, Universidade Vale do Rio Verde, Belo Horizonte, Brazil

Wojciech Blonski Orlando VA Medical Center and University of Central Florida College of Medicine, Orlando, FL, USA

Rudolf Buxhoeveden Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina

Leonardo M. Del Grande Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, SP, Brazil

Marco Di Corpo Department of Medicine and Surgery, University of North Carolina, Chapel Hill, NC, USA

Justin B. Dimick Health Services Research, Division of Minimally Invasive Surgery, Center for Healthcare Outcomes & Policy, Department of Surgery, University of Michigan Health System, Ann Arbor, MI, USA

James Patrick Dolan Department of Surgery, Oregon Health State University, Portland, OR, USA

Amelia Dorsey Department of Surgery, Stanford University, Stanford, CA, USA

Nicolás H. Dreifuss Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina

Timothy M. Farrell Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Michel Gagner Herbert Wertheim School of Medicine, FIU, Miami, FL, USA

Hôpital du Sacré Coeur, Montreal, QC, Canada

Clinique Michel Gagner, Montreal, QC, Canada

Westmount Square Surgical Center, Westmount, QC, Canada

Martín Galvarini Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Hans Gerdes Department of Gastroenterology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Verónica Gorodner Programa Unidades Bariátricas, Buenos Aires, Argentina

A. Daniel Guerron Department of Surgery, Duke University, Durham, NC, USA

Benjamin E. Haithcock UNC Lung Transplant Program, Cardiothoracic Surgery Residency Program, Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Mary Hawn Department of Surgery, Stanford Hospital, Stanford, CA, USA

Fernando A. M. Herbella Gastrointestinal Surgery – Esophagus and Stomach Division, Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, SP, Brazil

Amy L. Holmstrom Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Salim Hosein Division of General Surgery, Section of GI/MIS, Department of Surgery, University of Nebraska Medical Center, Omaha, NE, USA

Eric S. Hungness Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Aftab Jafri The Metabolic and Bariatric Institute, Cleveland Clinic Florida, Weston, FL, USA

Robert T. Kavitt Center for Esophageal Diseases, Department of Medicine, Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago, Chicago, IL, USA

Rafael M. Laurino Neto Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, SP, Brazil

Francisco Laxague Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina

Victoria Lyo Department of Surgery, Oregon Health State University, Portland, OR, USA

Emanuele Lo Menzo Department of Clinical Research, The Metabolic and Bariatric Institute, Cleveland Clinic Florida, Weston, FL, USA

Jennifer A. Minneman Department of Surgery, University of Washington, Seattle, WA, USA

Daniela Molena Esophageal Surgery Program, Thoracic Surgery Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Charles Muller Department of Medicine, Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago, Chicago, IL, USA

Nabeel R. Obeid Department of Surgery, University of Michigan Health System, Ann Arbor, MI, USA

Dmitry Oleynikov Gastrointestinal, Minimally Invasive and Bariatric Surgery, Center for Advanced Surgical Technology, Omaha, NE, USA

Marco G. Patti Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Joel E. Richter Joy McCann Culverhouse Center for Swallowing Disorders, Division of Digestive Diseases and Nutrition, University of South Florida Morsani College of Medicine, Tampa, FL, USA

Raul J. Rosenthal Department of General Surgery, The Bariatric and Metabolic Institute, Cleveland Clinic Florida, Weston, FL, USA

General Surgery Residency Program and Fellowship in Minimally Invasive and Bariatric Surgery, Cleveland Clinic Florida, Weston, FL, USA

Uma M. Sachdeva Memorial Sloan Kettering Cancer Center, New York, NY, USA

Sarah Samreen Division of General Surgery, Section of GI/MIS, Department of Surgery, University of Nebraska Medical Center, Omaha, NE, USA

Francisco Schlottmann Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Ranjan Sudan Psychiatry & Behavioral Sciences, Department of Surgery, Duke University, Duke University Health System, Durham, NC, USA

Samuel Szomstein Department of General Surgery, The Metabolic and Bariatric Institute, Cleveland Clinic Florida, Weston, FL, USA

Natalie Tapaskar Department of Medicine, University of Chicago, Chicago, IL, USA

Richard Thompson Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Antonio Carlos Valezi Department of Surgery, State University of Londrina, Londrina, Brazil

John Waters Memorial Sloan Kettering Cancer Center, New York, NY, USA

Andrew S. Wright Department of Surgery, University of Washington, Seattle, WA, USA

Part I

Achalasia

Achalasia: History

1

Rafael M. Laurino Neto
and Fernando A. M. Herbella

Introduction

Esophageal achalasia is a primary esophageal motility disorder characterized by the absence of esophageal peristalsis and failure of the lower esophageal sphincter (LES) to relax in response to swallowing. These abnormalities lead to impaired emptying of food from the esophagus into the stomach with resulting food stasis. Most patients experience severe dysphagia and regurgitation that can lead to aspiration and respiratory problems [1].

The pathophysiology of achalasia involves the selective degeneration of inhibitory neurons of the esophageal plexuses, which are needed for peristalsis of the smooth muscle of the esophageal body, as well as relaxation of the tonic LES. The most common form of achalasia is idiopathic, situation in which the etiology of the degenerative process remains unknown. A similar clinical picture can be present in patients with local or distant cancer (pseudoachalasia) or in patients with Chagas' disease, both characterized by the destruction of the plexuses either by infiltrating tumors or circulating autoantibodies or still by *Trypanosoma cruzi* infection [2].

First Treatments

The first reference to achalasia was in 1679 by the English doctor Thomas Willis (Fig. 1.1) who not only described the disability but also reported a successful treatment. He dilated the esophagus by using a sponge at the end of a whale bone, improving patient's symptoms [3, 4].

There are virtually no reports of achalasia and its treatment in the eighteenth century but at the end of the nineteenth and at the beginning of the twentieth century, coinciding with important improvements in surgical conditions with the advent of aseptic surgery, anesthetics with procedures under mechanical ventilation, as well as better understanding of the pathophysiology [3].

In 1887, over 2 centuries after the remarkable description by Willis, J. C. Russell also in England, placed an inflatable rubber balloon covered with silk at the end of a bougie and blew up the balloon to dilate the stricture [5]. H. Plummer, in 1908, opened the cardia using olive-tipped bougies over a swallowed string. Later he used a hydrostatic dilator to effectively

R. M. Laurino Neto
Department of Surgery, Escola Paulista de Medicina, Federal University of São Paulo, São Paulo, SP, Brazil

F. A. M. Herbella (✉)
Gastrointestinal Surgery – Esophagus and Stomach Division, Department of Surgery, Escola Paulista de Medicina, Federal University of São Paulo, São Paulo, SP, Brazil
e-mail: herbella.dcir@epm.br

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_1

relieve symptoms by rupturing the constricting circular muscle fibers. The satisfactory results obtained with dilatation by pneumatic or hydrostatic balloon gave rise to the idea of proceeding to surgical dilation, which could be done under direct vision and not blind [6].

In 1904, Mikulicz, by an abdominal incision, inserted a rubber sheath forceps through a gastrostomy opening and dilated the cardia from below (Fig. 1.2). Barrow, in 1915, used the technique of digital dilation, invaginating the anterior wall of the stomach avoiding the opening of the organ. This technique was later adopted by Kümmel in 1921. Anschütz (1921) dilated the cardia with a balloon but opened the abdomen to correctly place it.

Also procedures to reduce the size of the dilated esophagus such as those of Ressinger (1907) and Meyer (1911) or shortening of the organ by invagination as proposed by Tuffier (1921) and Freeman (1923) gave poor results [6].

Fig. 1.1 Thomas Willis (1621–1675)

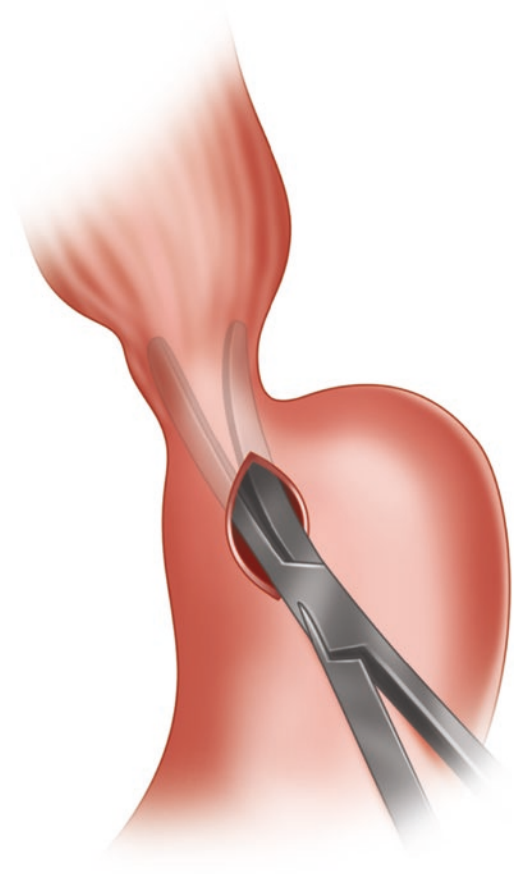


Fig. 1.2 Mikulicz's technique

Operations on the Cardia

Cardioplasties/Cardiectomies

With the observation that the point of obstruction to the progression of food was located in the cardia and with the improvement of the conditions in which the operations were performed, several procedures began to appear for the treatment of achalasia. Cardioplasty began with the operation of Wendel (1909), inspired by the Heineke-Mikulicz pyloroplasty. It consisted of a longitudinal incision of all layers of the wall at the esophagogastric junction and closure of the opening in a transverse direction (Fig. 1.3).

Another type of cardioplasty used by many surgeons was that described by Heyrowsky

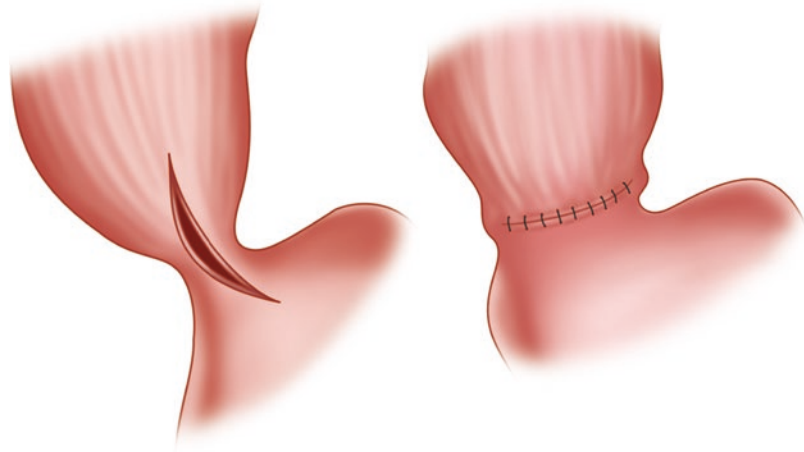


Fig. 1.3 Wendel's technique: It consisted of a longitudinal incision of all layers of the wall at the esophagogastric junction and closure of the opening in a transverse direction

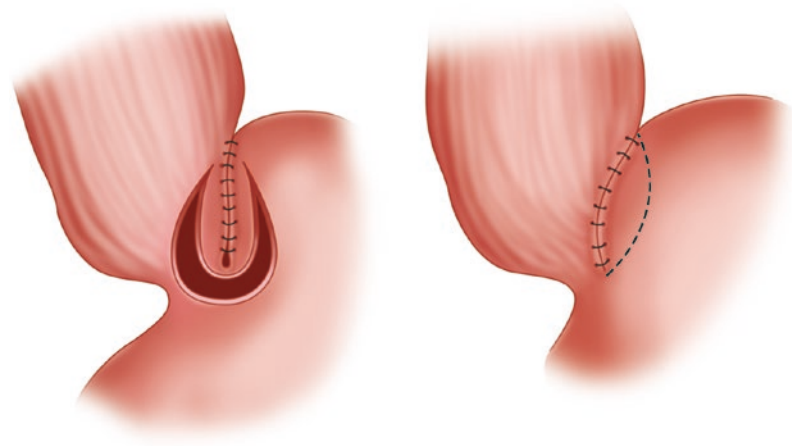


Fig. 1.4 The Backer-Gröndhal technique: the longitudinal incision was replaced by a curved incision passing through the esophagogastric junction

(1913), which consisted of an anastomosis of the lateral wall of the distal esophagus with the gastric fundus. This, however, was associated with retention of food between the lateral esophagogastric anastomosis and the cardiac orifice. The most widespread variant to correct such problem was described by Backer-Gröndhal (1916), in which the longitudinal incision was replaced by a curved incision passing through the esophagogastric junction (Fig. 1.4) [6].

The immediate result of the cardioplasty was satisfactory from the clinical point of view, with improvement or even disappearance of the regurgitation and dysphagia. However, long-term follow-up of the patients operated showed reflux esophagitis, which was particularly severe because of the lack of peristalsis to clear acid refluxed from the stomach, with a long contact time with the esophageal mucosa [6].

Authors such as Thal (1965), Frejat (1974), and Guarner and Gaviño (1983) proposed the association of various cardioplasty with a fundoplication or developed procedures that created valvular mechanisms in the gastro esophageal area. Serra Dória et al. (1968), aiming to solve the problem of reflux esophagitis in megaesophagus operated patients, associated Gröndhal's cardioplasty with the subtotal gastrectomy with Roux-en-Y transit reconstitution [7] adapting the Holt and Large operation for stenosis.

Authors such as Bier (1920), Radlinski (1936), and Wangensteen (1951) proposed resection of

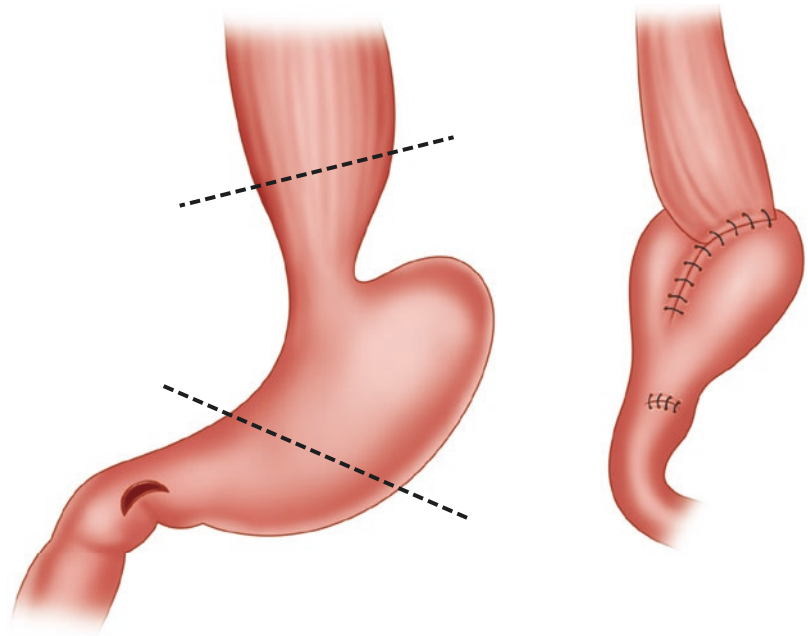


Fig. 1.5 Resection of the cardia and esophagogastrostomy

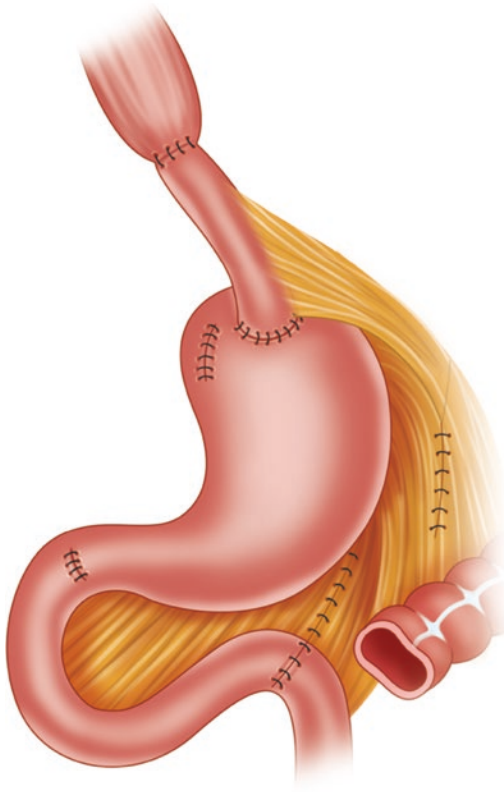


Fig. 1.6 Merendino technique: resection of the esophagogastric junction with intestinal interposition

the cardia and esophagogastrostomy as a therapeutic modality for this disease, with encouraging initial results but with the disadvantages of a high-risk resection and anastomosis for that time (Fig. 1.5). Others, like Merendino and Dillard (1955), adopted the resection of the esophagogastric junction with intestinal interposition (Fig.1.6) [8, 9].

Myotomy

In 1913, Ernst Heller (Fig. 1.7) introduced an operation consisting of a posterior and anterior myotomy, extending from 2 cm above the constrictions down over the cardia (Fig. 1.8). Despite the simplicity of execution and its efficacy, the cardiomyotomy was not immediately accepted as a solution for the surgical treatment of achalasia, and surgeons, mainly in Germany where Heller worked, continued to prefer cardioplasty [10]. Several modifications of Heller's original technique were proposed. The first of these is credited to Girard (1915) and consisted of closing the incision transversely as in Heineke-Mikulicz pyloroplasty. Groenveldt, in the Netherlands, proposed performing only one incision in the

Fig. 1.7 Ernst Heller (1877–1964)

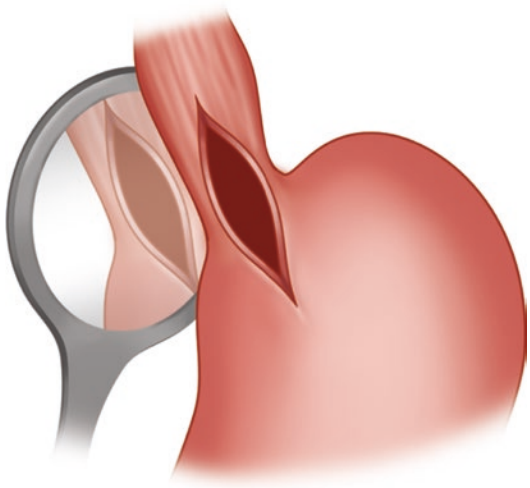


Fig. 1.8 Heller's technique: posterior and anterior myotomy, extending from 2 cm above the constrictions down over the cardia

anterior wall of the esophagus, obtaining results equivalent to those of the double incision of Heller (Fig. 1.9).

Although the incidence of postoperative reflux esophagitis is lower with cardiomyotomy than

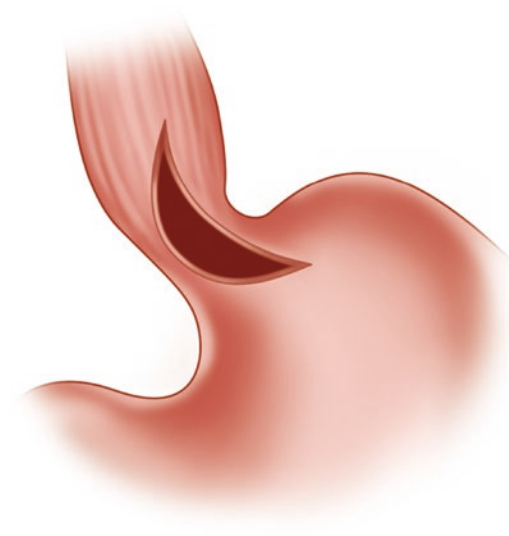


Fig. 1.9 De Bruine Groenveldt's technique: performing only one incision in the anterior wall of the esophagus

with classic cardioplasties, the number of patients presenting with this complication was still significant, which led surgeons to complement the myotomy with some antireflux procedure.

Lortat-Jacob (1953) was the first to emphasize the accentuation of the angle of His for the prevention of reflux in patients who underwent a cardiomyotomy, recommending the fixation of the gastric fundus to the left border of the esophagus. Dor et al. (1962) from Marseille described a partial fundoplication technique covering the area of the myotomy. Toupet (1963) described an analogous operation, which differs from Dor's operation by performing a fixation of the gastric fundus on the posterolateral side of the esophagus and not on the anterior face associated with its fixation to the diaphragm.

Jekler and Lhotka (1967) modified Dor's technique, adding to it the fixation of the gastric fundus to the esophagus, 1–2 cm above the superior commissure, in order to further accentuate the angle of His (Fig. 1.10). Pinotti et al. (1974) developed a posterolateral anterior procedure enveloping the esophagus in about two-thirds of its circumference [11].

In 1991, Cuschieri's group from the University of Dundee, United Kingdom, reported the first laparoscopic Heller myotomy (LHM) [12], which

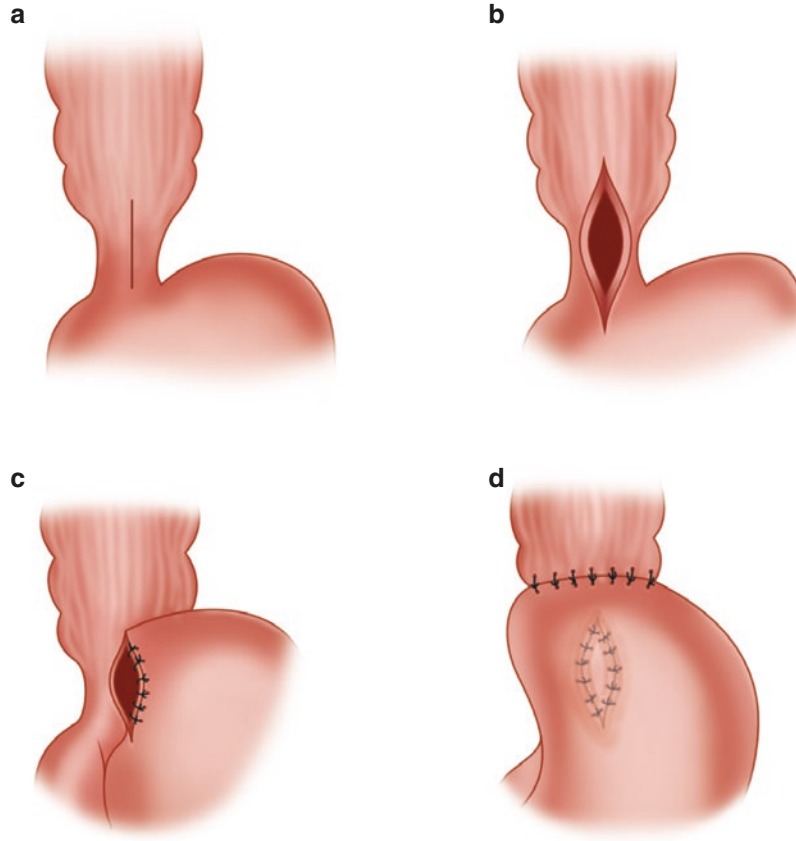


Fig. 1.10 Jekler and Lhotka's technique: fixation of the gastric fundus to the esophagus, one to two cm above the superior commissure, in order to further accentuate the angle of His. (**a**) Myotomy. (**b**) Esophagostomy. (**c**) Fixation of the gastric fundus to the esophagus. (**d**) Tranversal closure of the anastomosis

brought improvements due to the advantages of this surgical access route such as shorter hospitalization time, early mobilization, and absence of extensive abdominal scarring.

In 1992, Pellegrini et al. from the University of California, San Francisco, described the results of 17 patients who underwent a left thoracoscopic myotomy with excellent relief of dysphagia [13]. However, the thoracoscopic approach had significant drawbacks such the need for a double lumen endotracheal intubation to exclude the left lung, the need for a chest tube, and the inability to add a fundoplication to prevent reflux. The same group later compared the results for thoracoscopic myotomy versus laparoscopic myotomy with a Dor fundoplication. Similar results were found in regards to resolution of dysphagia, but with remarkable superiority of laparoscopy considering regarding the incidence of postoperative reflux (from 60% to 17%) [14].

LHM for esophageal achalasia continues to present excellent results today, as demonstrated by Zaninotto et al. [15] that studied more than 400 patients who underwent LHM and Dor fundoplication and reported a 90% success rate at a median follow-up of 30 months. A recent European multicenter randomized trial [16] showed a success rate of 84% after 5 years of LHM, and another randomized trial [17] found that at a follow-up of 5 years, only 8% of the patients after LHM had recurrence of symptoms.

More recently, achalasia surgery has been performed in the robotic-assisted way [18]. Advantages of robotic-assisted surgery include improved visibility of the operative field with three-dimensional imaging, increased degrees of freedom of surgical movements, and improved ergonomics. Retrospective studies [19–21] have shown that with this technique there are lower rates of esophageal mucosa perforations, with success rates similar to conventional LHM. On

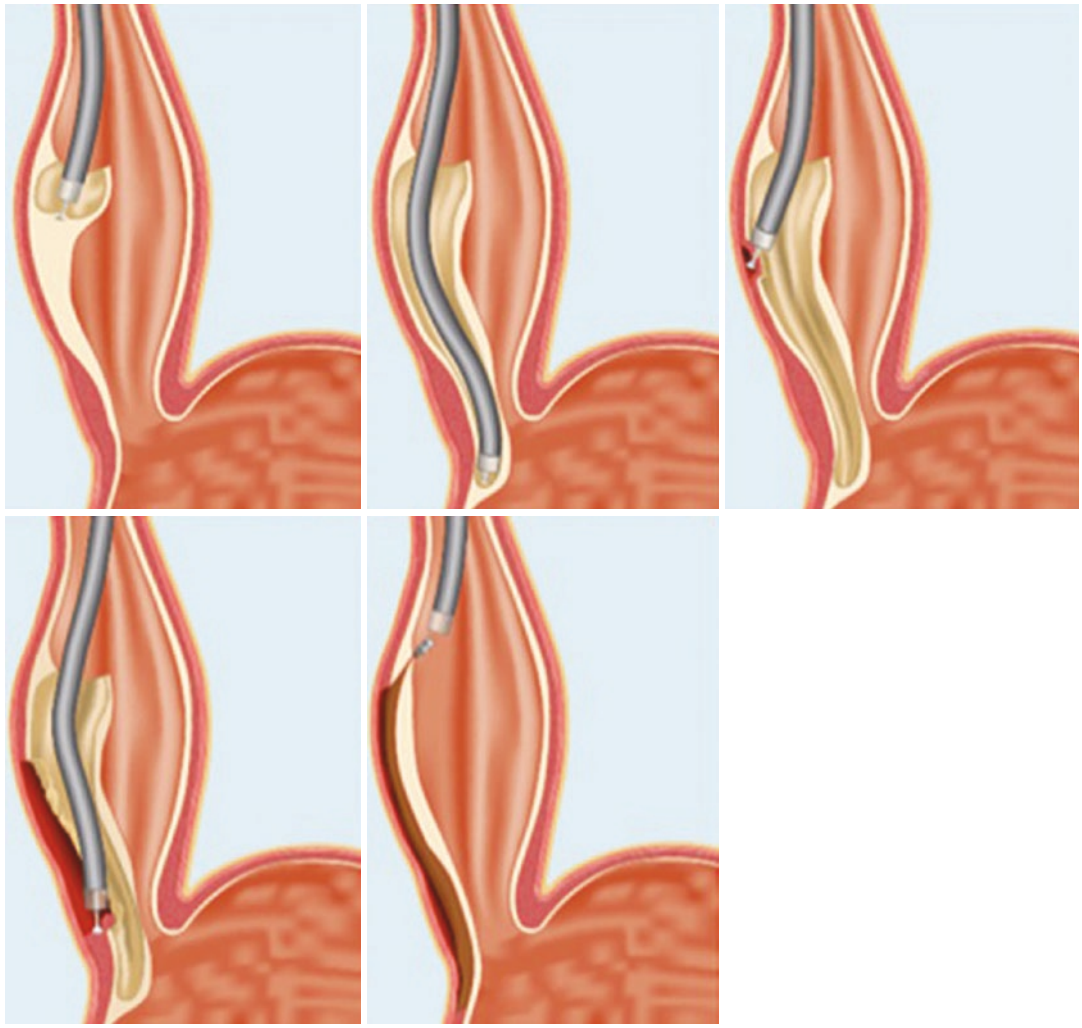


Fig. 1.11 POEM technique. (Reprinted with permission ©Georg Thieme Verlag KG [24])

the other hand, a multicenter retrospective analysis of a large administrative database including 2116 laparoscopic myotomies and 149 robotic myotomies showed comparable results between both groups, but increased costs in the robotic cohort [22].

Already described by Ortega in 1980 [23], per-oral endoscopic myotomy (POEM) was rediscovered and fairly widespread by Inoue et al. in 2010 [24]. It is a procedure similar to that of Heller but performed according to precepts of the natural orifice transluminal endoscopic surgery (NOTES), with good immediate results (Fig.1.11).

With the current literature data, we observed again that although both LHM and POEM present good results in the resolution of dysphagia, reflux-disease incidence appears to be also significantly more frequent after POEM than after LHM with fundoplication [25].

Esophagectomy

In the same year of 1913 that Heller performed his first myotomy, two surgeons described different ways to perform an esophagectomy: Torek, a German surgeon, performed in New York a transthoracic esopha-

gectomy, and Von Arch, a German surgeon in Munich, a transmediastinal esophagectomy [26]. Pinotti (1977) [27] added the transection of the diaphragm for a better exposure of the mediastinum, a technique useful to treat the advanced megaesophagus.

Orringer (1982) [28, 29] proposed esophagectomy as definitive treatment for esophageal neuromotor dysfunction, with good results obtained in 22 patients operated mostly by transmediastinal route with a follow-up of 25 months [29].

Even today, an esophagectomy is still a complex procedure linked to high morbidity and mortality, as recently shown by a meta-analysis (27.1% morbidity rate and 2.1% mortality rate) [30]. Thus, an esophagectomy should be a last resort and should be reserved to patients who have been symptomatic for a long time and who have failed other treatment modalities such as PD, LHM, and POEM.

Pharmacological Treatment

Pharmacologic agents include smooth muscle relaxants, such as long-lasting nitrates and calcium channel blockers, and 5′-phosphodiesterase inhibitors. Since achalasia is a disease characterized by impaired release of nitric oxide (NO) from inhibitory neurons, the rationale for the use of these agents consists in the enhancement of the residual neural inhibitory function in the esophageal wall [31].

The first drug used to treat dysphagia by decreasing LES pressure in the 1940s was nitroglycerin. In the early 1980s, nifedipine, a calcium channel blocker, was used as well in the treatment of achalasia [32]. These drugs act by blocking the action of calcium that is necessary for the contraction of the esophageal smooth muscle cells. However, both types of drugs do not improve LES relaxation or esophageal motility.

More recently, the use of sildenafil, a 5′-phosphodiesterase inhibitor, has been proposed [33]. This agent has an inhibitory action on the 5′-phosphodiesterase that inactivates the NO-stimulated cGMP, thus increasing the intracellular levels of cGMP and therefore promoting the relaxation of the smooth muscular cells.

All these medications, however, are associated with poor clinical results and several side effects, and their use is currently reserved for patients with advanced age or significant comorbidities [34, 35].

Endoscopic Management

Pneumatic Dilatation

Although it has been used since the description of the disease, forced dilatation of the esophagus to treat achalasia showed great progress in the 1980s when it began to be guided by endoscopy.

Pneumatic dilatation (PD) using controlled pneumatic pressure devices (30, 35, and 40 mm in diameter) is the most effective non-surgical treatment for achalasia. The clinical response in terms of dysphagia relief to a single PD session is 85% at 1 month, 66% at 12 months, 50% at 5 years, and 25% at 10 years [36].

Literature data showed dysphagia relief with PD comparable to LHM. There is, however, a need for multiple PD sessions in a considerable number of cases. Boeckxstaens et al. [37] published the results of a European multicenter trial comparing the results of PD to the outcome of LHM and Dor fundoplication. After 2 years, therapeutic success was similar between the two groups, obtained in 86% of PD patients and 90% of LHM patients. In 2016, Moonen and colleagues [16] reported the results of the 5-year follow-up. In the full analysis, there was no significant difference in the success rate between PD (82%) and LHM (84%). Redilatation was performed in 25% of PD patients. Esophageal perforation is the most serious complication after PD, with an overall rate reported in the literature around 2%.Esophageal reflux occurs in a higher rate as compared to LHM [38].

Endoscopic Botulinum Toxin Injection

Described in 1993, endoscopic botulinum toxin injection (EBTI) has since been used to treat achalasia [39]. The toxin acts by decreasing LES pressure through the inhibition of the release of acetylcholine in the cholinergic synapses.

Table 1.1 Treatment algorithm for naïve achalasia based on Chicago Classification

Type I or II achalasia		Type III achalasia	
Pneumatic dilation	Heller myotomy	POEM	POEM
Less morbidity/cost	Equal to PD in RCT	Highly effective in short-term RCT	Only procedure to adequately cut the length of the spasms
Expect repeated dilations over year	Effective across all ages/genders	Minimal pain	Avoids chest operation
Equal to HM in RCT	Preferred with megaesophagus, diverticulum, or hiatal hernia	Lots of GERD (>50%)	Superior to PD and HM
Older women may do best	More GERD	Insurance issues	Insurance issues
Minimal GERD			

HM Heller myotom, *RCT* randomized controlled trial, *GERD* gastroesophageal reflux disease, *PD* pneumatic dilatation, *POEM* per-oral endoscopic myotomy

The effect of EBTI progressively diminishes over time, with more than 60% of patients experiencing recurrent symptoms after 1 year [40]. EBTI needs to be repeated in most patients to achieve some benefits that, however, are of short duration due to the regeneration of the axons and the development of antibodies. In a meta-analysis published in 2009, Campos et al. confirmed the decreasing efficacy overtime of the EBTI [38]. Among patients who were treated with EBTI, symptoms relief was present in 70% after 3 months, 53% after 6 months, and 41% after 12 months, and almost 50% of patients required a second EBTI.

Thus, currently EBTI should be only considered in patients with advanced age or significant comorbidities who are not candidates for LHM or POEM.

Current Situation

After all this historical evolution, it is currently accepted that all achalasia patients in good clinical condition should undergo PD, LHM or POEM (Table 1.1). Pharmacological therapy (smooth muscle relaxants, such as long-lasting nitrates and calcium channel blockers, and 5′-phosphodiesterase inhibitors) and/or endoscopic Botox injection (EBTI) should be considered only in patients with advanced age or significant comorbidities who are not candidates for LHM or POEM. Patients who have failed initial treatment should be referred for pneumatic dilatation. If symptoms persist, it is reasonable to consider POEM for those who underwent LHM initially and LHM for those who underwent POEM first. Esophagectomy should be reserved for patients who have failed all these previous interventions [41].

Conflict of Interest The authors have no conflicts of interest to declare.

References

1. Schlottmann F, et al. Esophageal achalasia: pathophysiology, clinical presentation, and diagnostic evaluation. Am Surg. 2018;84(4):467–72.
2. Ghoshal UC, Daschakraborty SB, Singh R. Pathogenesis of achalasia cardia. World J Gastroenterol. 2012;18(24):3050–7.
3. Brewer LA 3rd. History of surgery of the esophagus. Am J Surg. 1980;139(6):730–43.
4. Collis JL. The history of British oesophageal surgery. Thorax. 1982;37(11):795–802.
5. Deschamps C. History of esophageal surgery for benign disease. Chest Surg Clin N Am. 2000;10(1):135–44, ix–x.
6. de Rezende JM, Moreira H. Chagasic megaesophagus and megacolon. Historical review and present concepts. Arq Gastroenterol. 1988;25:32–43.
7. Serra-Doria OB, Serra-Doria OM, Silva-Doria OR. New surgical management for megaesophagus [in Portuguese: Nova conduta cirúrgica para o tratamento do megaesôfago]. An Paul Med Cir. 1970;97:115–21.
8. Dillard DH, Merendino KA. Experiences with the interposed jejunal segment operation combined with adjunct procedures in the prevention of esophagitis; an experimental study. Surg Forum. 1955;5:323–8.

9. Thomas GI, Merendino KA. Jejunal interposition operation; analysis of thirty-three clinical cases. J Am Med Assoc. 1958;168(13):1759–66.
10. Heller E. Extramuköse Cardioplastik beim chronischen Cardiospasmus mit Dilatation des Oesphagus. Mitt Grenzgeb Med Chir. 1913;27:141–9.
11. Pinotti HW, et al. New basis for the surgical treatment of megaesophagus: esophagocardiomyotomy with esophagus-fundus-gastropexy. AMB Rev Assoc Med Bras. 1974;20(9):331–4.
12. Shimi S, Nathanson LK, Cuschieri A. Laparoscopic cardiomyotomy for achalasia. J R Coll Surg Edinb. 1991;36(3):152–4.
13. Pellegrini C, et al. Thoracoscopic esophagomyotomy. Initial experience with a new approach for the treatment of achalasia. Ann Surg. 1992;216(3):291–6; discussion 296–9.
14. Patti MG, et al. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. Ann Surg. 1999;230(4):587–93; discussion 593–4.
15. Zaninotto G, et al. Four hundred laparoscopic myotomies for esophageal achalasia: a single centre experience. Ann Surg. 2008;248(6):986–93.
16. Moonen A, et al. Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. Gut. 2016;65(5):732–9.
17. Persson J, et al. Treatment of achalasia with laparoscopic myotomy or pneumatic dilatation: long-term results of a prospective, randomized study. World J Surg. 2015;39(3):713–20.
18. Melvin WS, et al. Computer-assisted robotic heller myotomy: initial case report. J Laparoendosc Adv Surg Tech A. 2001;11(4):251–3.
19. Horgan S, et al. Robotic-assisted Heller myotomy versus laparoscopic Heller myotomy for the treatment of esophageal achalasia: multicenter study. J Gastrointest Surg. 2005;9(8):1020–9; discussion 1029–30.
20. Huffmanm LC, et al. Robotic Heller myotomy: a safe operation with higher postoperative quality-of-life indices. Surgery. 2007;142(4):613–8; discussion 618–20.
21. Perry KA, et al. Efficacy and durability of robotic Heller myotomy for achalasia: patient symptoms and satisfaction at long-term follow-up. Surg Endosc. 2014;28(11):3162–7.
22. Shaligram A, et al. How does the robot affect outcomes? A retrospective review of open, laparoscopic, and robotic Heller myotomy for achalasia. Surg Endosc. 2012;26(4):1047–50.
23. Ortega JA, Madureri V, Perez L. Endoscopic myotomy in the treatment of achalasia. Gastrointest Endosc. 1980;26(1):8–10.
24. Inoue H, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71.
25. Schlottmann F, Patti MG. Laparoscopic Heller Myotomy versus per oral endoscopic myotomy: evidence-based approach to the treatment of esophageal achalasia. Am Surg. 2018;84(4):496–500.
26. Kun L, Herbella FA, Dubecz A. 1913: Annus mirabilis of esophageal surgery. Thorac Cardiovasc Surg. 2013;61(6):460–3.
27. Pinotti HW. Subtotal esophagectomy by transmediastinal tunnel without thoracotomy. AMB Rev Assoc Med Bras. 1977;23(11):395–8.
28. Orringer MB, Sloan H. Esophagectomy without thoracotomy. J Thorac Cardiovasc Surg. 1978;76(5):643–54.
29. Orringer MB, Orringer JS. Esophagectomy: definitive treatment for esophageal neuromotor dysfunction. Ann Thorac Surg. 1982;34(3):237–48.
30. Aiolfi A, et al. Esophageal resection for end-stage achalasia. Am Surg. 2018;84(4):506–11.
31. Schlottmann F, et al. Modern management of esophageal achalasia: from pathophysiology to treatment. Curr Probl Surg. 2018;55(1):10–37.
32. Bortolotti M, Labo G. Clinical and manometric effects of nifedipine in patients with esophageal achalasia. Gastroenterology. 1981;80(1):39–44.
33. Bortolotti M, et al. Effects of sildenafil on esophageal motility of patients with idiopathic achalasia. Gastroenterology. 2000;118(2):253–7.
34. Storr M, Allescher HD. Esophageal pharmacology and treatment of primary motility disorders. Dis Esophagus. 1999;12(4):241–57.
35. Hoogerwerf WA, Pasricha PJ. Pharmacologic therapy in treating achalasia. Gastrointest Endosc Clin N Am. 2001;11(2):311–24.. vii
36. Allaix ME, Patti MG. Toward a tailored treatment of achalasia: an evidence-based approach. J Laparoendosc Adv Surg Tech A. 2016;26(4):256–63.
37. Boeckxstaens GE, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. 2011;364(19):1807–16.
38. Campos GM, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249(1):45–57.
39. Pasricha PJ, et al. Intrasphincteric botulinum toxin for the treatment of achalasia. N Engl J Med. 1995;332(12):774–8.
40. Zaninotto G, et al. Randomized controlled trial of botulinum toxin versus laparoscopic heller myotomy for esophageal achalasia. Ann Surg. 2004;239(3):364–70.
41. Zaninotto G, et al. The 2018 ISDE achalasia guidelines. Dis Esophagus. 2018;31(9).

Achalasia: Clinical Presentation and Evaluation

2

Marco Di Corpo, Francisco Schlottmann, and Marco G. Patti

Introduction

Esophageal achalasia is a chronic and progressive disease characterized by lack of esophageal peristalsis and by partial or absent relaxation of the lower esophageal sphincter (LES) in response to swallowing [1]. With a peak incidence occurring between 30 and 60 years of age and an equal distribution across genders, it is a rare disease with an incidence of 1 per 100,000 people per year in the United States and a prevalence of 10.82 cases per 100,000 individuals [2]. Despite its low prevalence, achalasia represents the most common primary esophageal disorder after gastroesophageal reflux disease (GERD). Achalasia usually presents with symptoms of dysphagia, regurgitation of undigested food, respiratory symptoms (e.g., nocturnal cough or recurrent aspiration), chest pain, and weight loss. Similar clinical presentation, however, can occur in patients with pseudoachalasia (5% of patients with suspected achalasia) due to malignant obstruction or secondary to operations at the esophagogastric junction [3, 4]. Achalasia can also be secondary to a tropical disease called Chagas' disease, characterized by degeneration of the myenteric plexus due to *Trypanosoma cruzi* infection [5].

A proper work-up is necessary to establish the correct diagnosis of achalasia, and it should include symptomatic evaluation, esophagogastroduodenoscopy (EGD), barium esophagogram, esophageal manometry, and sometimes ambulatory 24-h pH monitoring. Despite the improvements in quality of life and prognosis achieved through the development of effective therapeutic protocols, treatment is not curative but palliative, as it aims to eliminate the outflow resistance at the level of the gastroesophageal junction caused by the non-relaxing LES.

This chapter reviews the clinical presentation and the diagnostic evaluation of achalasia.

Clinical Presentation of Achalasia

The diagnosis of achalasia can be challenging, as it is a rare disease and because symptoms are nonspecific. Dysphagia, heartburn, chest pain, regurgitation, and aspiration can be caused by diseases other than achalasia. As a consequence, there is often a long delay between the onset of symptoms and the diagnosis [6].

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

F. Schlottmann
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti (✉)
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA
e-mail: marco_patti@med.unc.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_2

Dysphagia

Dysphagia is the most frequently reported symptom, being present in about 95% of achalasia patients. Usually, it occurs for both solids and liquids. Of note, dysphagia for liquids represents a key clue for esophageal motility disorder as this symptom is uncommon in mechanical causes of esophageal obstruction (peptic stricture, cancer), except for advanced diseases. Patients with achalasia usually describe themselves as "slow eaters" and avoid certain solid foods that are difficult to swallow. By changing their diet, most are often able to maintain a stable weight, whereas others experience a progressive increase in dysphagia that eventually leads to weight loss [7].

Regurgitation and Aspiration

Regurgitation of indigested food occurring minutes to hours after a meal is the second most frequent symptom and is present in about 60–70% of patients. Regurgitation occurs more often in the supine position and may lead to aspiration with cough, hoarseness, wheezing, and episodes of pneumonia [7]. Dysphagia usually precedes respiratory symptoms by an average of 24 months, indicating the progressive nature of symptoms with lack of treatment [8].

Heartburn

Heartburn is present in about 50% of the patients. In the untreated patient, it is not due to abnormal gastroesophageal reflux, but rather to stasis and fermentation of undigested food in the esophagus (also known as "false reflux"). Unfortunately, a misdiagnosis of achalasia as gastroesophageal reflux disease can occur, particularly in early stages of achalasia, and patients are treated with proton-pump inhibitors with a consequent delay in diagnosis [9].

Chest Pain

Chest pain or retrosternal discomfort is experienced by nearly 40% of the patients with achalasia. It may mimic angina by location and character but differs as it is not aggravated by exercise, but rather it is exacerbated by eating. The cause of chest pain is still unknown, but it has been suggested that esophageal distention or esophageal contractions of abnormally high amplitude or long duration maybe responsible [10]. In untreated patients, chest pain frequency tends to diminish spontaneously with advancing age [11]. Perretta and colleagues [12] analyzed 211 achalasia patients of whom 117 (55%) experienced chest pain at the time of presentation. The pain was felt mostly in the retrosternal area, particularly during the day. No differences were observed in age, duration of symptoms or manometric profile between patients with or without chest pain. With a median follow-up of 24 months, chest pain resolved in 84% and improved in 11% of the patients after laparoscopic Heller myotomy (LHM). These data suggest that the relief or improvement of chest pain is due to elimination of the outflow obstruction at the gastroesophageal junction with improvement of esophageal emptying.

Symptom Scores

The Eckardt score is the most commonly score system used to assess patients before and after treatment. It is the sum of the scores for dysphagia, regurgitation, and chest pain (a score of 0 indicates absence of symptoms, 1 indicates occasional symptoms, 2 indicates daily symptoms, 3 indicates symptoms at each meal). For weight loss, 1 indicates a loss less than 5 kg, 2 indicates a loss between 5 and 10 kg, and 3 indicates more than 10 kg of weight loss (Table 2.1). The maximum score on the Eckardt scale is 12, and treatment is usually considered successful if it brings the Eckardt score to equal or less than 3 [13].

Table 2.1 Clinical scoring system for achalasia (Eckardt score)

Score	Weight loss (Kg)	Dysphagia	Retrosternal pain	Regurgitation
0	0	None	None	None
1	<5	Occasional	Occasional	Occasional
2	5–10	Daily	Daily	Daily
3	>10	Each meal	Each meal	Each meal

Diagnostic Evaluation

In order to establish a diagnosis of achalasia, it is important to have a comprehensive work-up which includes barium swallow, upper endoscopy, esophageal manometry [14], and sometimes ambulatory 24-h pH monitoring [15, 16]. An endoscopic ultrasound and a chest CT scan are useful when pseudoachalasia secondary to a tumor is suspected.

Esophagogastroduodenoscopy (EGD)

EGD with biopsies should be performed in patients who experience dysphagia, in order to rule out the presence of a mechanical obstruction secondary to a peptic stricture or cancer. An infiltrating tumor of the gastroesophageal junction can mimic the clinical, radiological, and manometric findings of achalasia, resulting in impaired LES relaxation and absence of peristalsis. In patients older than 60 years old with rapidly progressing dysphagia and severe weight loss, "secondary achalasia" or "pseudoachalasia" should be suspected [17].

Endoscopic features of achalasia include a dilated or tortuous esophagus, food and fluid pooling in the esophagus, and resistance to passage of the scope through the gastroesophageal junction. The esophageal mucosa can be normal or show signs of esophagitis usually secondary to food stasis or candida infection (Fig. 2.1) [18]. In about 30–40% of patients, the EGD can be normal.

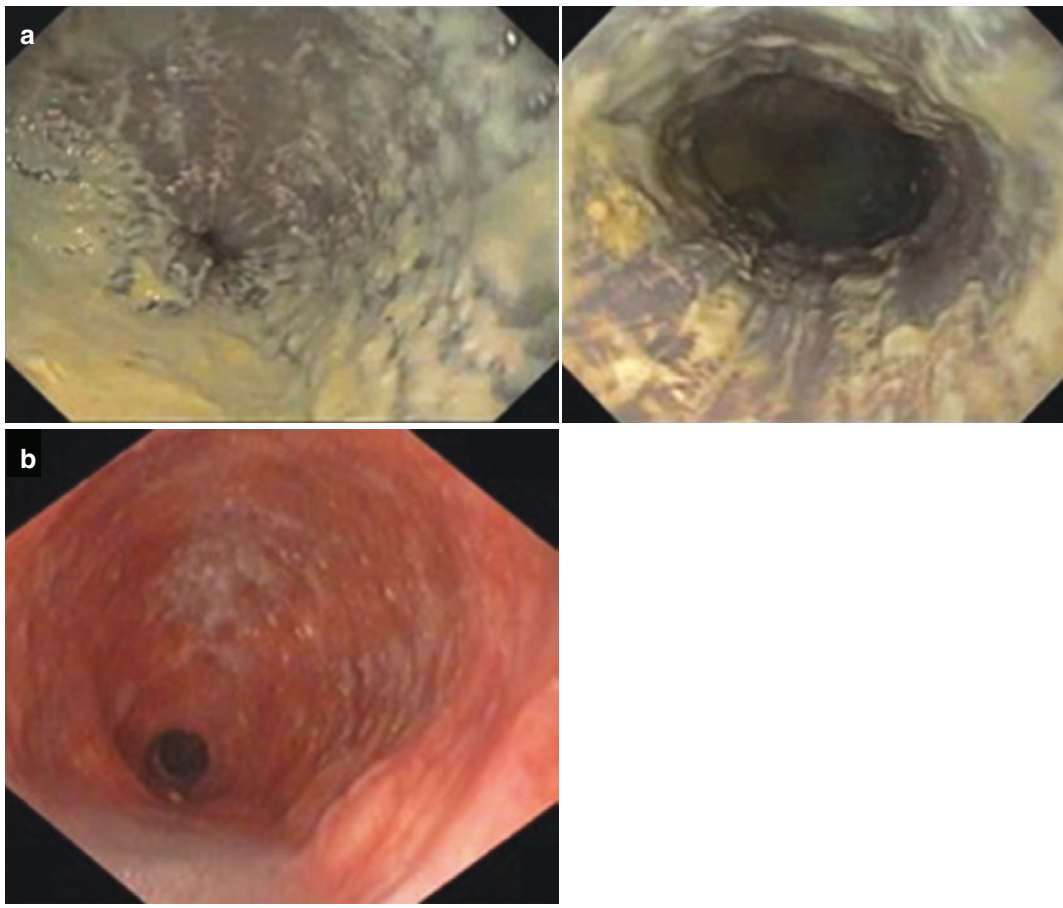


Fig. 2.1 Endoscopic findings in a patient with achalasia. (Courtesy of Rudolf Buxhoeveden, MD. Buenos Aires, Argentina). (**a**) Retained food; (**b**) dilated esophagus

Although endoscopy may suggest achalasia, other tests must be performed to confirm the diagnosis.

Barium Swallow

This test provides information about the anatomy (diameter and axis) and the emptying of the esophagus. The "bird-beak" appearance is pathognomonic of achalasia (Fig. 2.2). Other typical radiologic findings are slow emptying of the contrast from the esophagus into the stomach, an air-fluid level (Fig. 2.3), and tertiary contractions of the esophageal wall. In more advanced cases, severe dilatation and a sigmoid-like appearance can occur (Fig. 2.4). This information is particularly important to plan treatment. In the presence of a very dilated and sigmoid esophagus, pneumatic dilatation and POEM are less effective. In addition, a laparoscopic myotomy will require a more extensive dissection in the posterior mediastinum to straighten the esophageal axis. If performed as timed barium swallow, it can also quantify the efficacy of treatment [19].

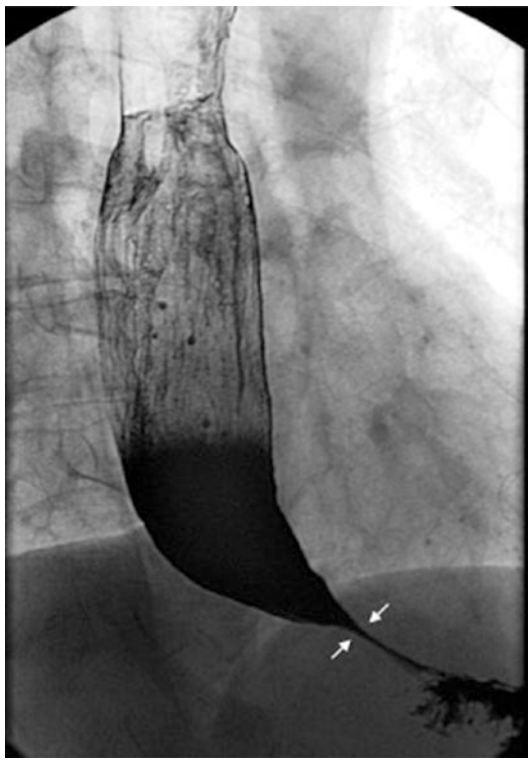


Fig. 2.2 Barium swallow: esophageal dilatation and a smooth tapering of the distal esophagus. (bird's beak sign – arrows)

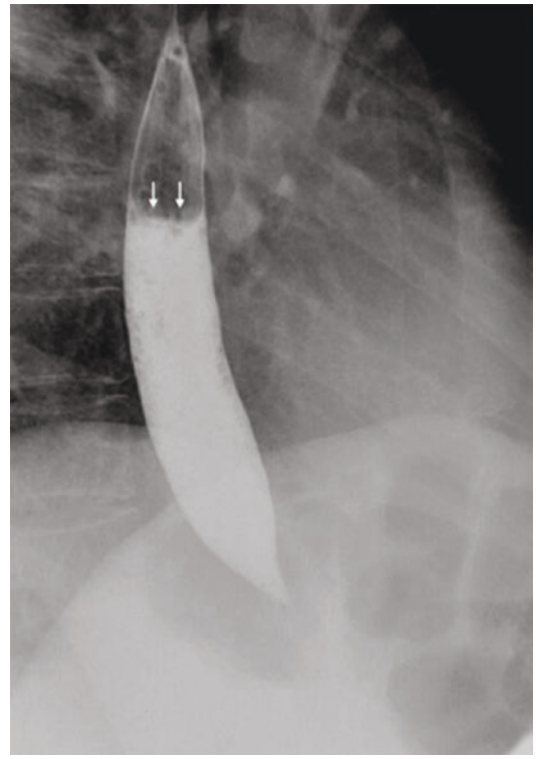


Fig. 2.3 Air-fluid level (arrows)

Although barium swallow is a key test in the work-up, it may show no abnormalities in about 30% of the patients. The expertise of the radiologist with this rare disease is key for a proper interpretation of the radiologic features [20].

Esophageal Manometry

Esophageal manometry has become the gold standard for diagnosing and classifying achalasia. The diagnosis is classically made by demonstrating impaired relaxation of the lower esophageal sphincter in response to swallowing and absent peristalsis. The LES is hypertensive in about 50% of patients [21].

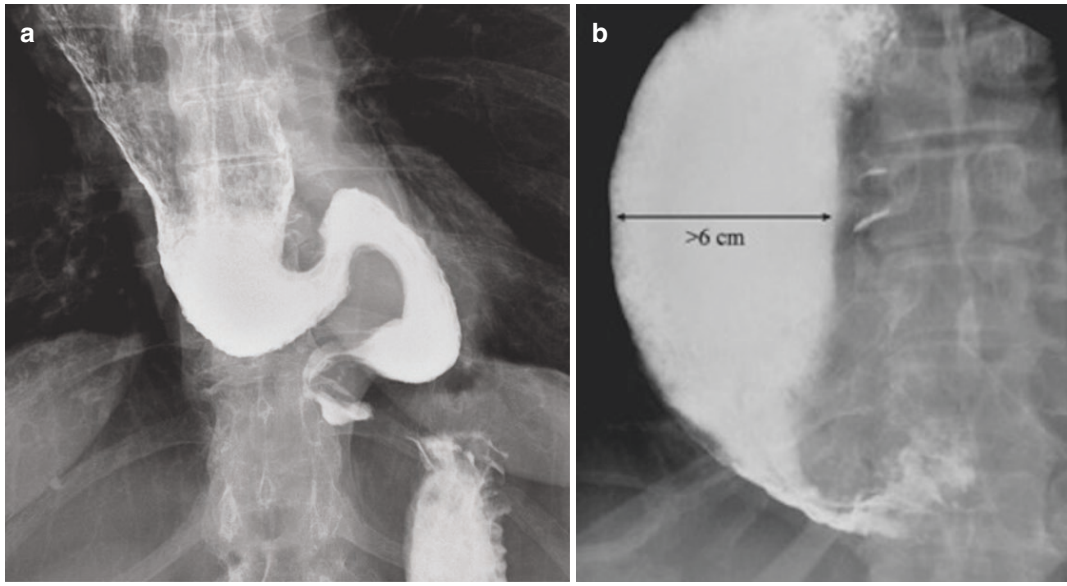


Fig. 2.4 (**a**) Sigmoid-shaped esophagus; (**b**) esophageal dilatation

The increased precision of the high-resolution manometry (HRM) has improved the ability to diagnose achalasia and identify different contractile patterns. As compared to conventional manometry, HRM determines more comfort and speediness to the test, easiness to teach, interobserver and intraobserver reproducibility, and compensation of movements artifacts [21, 22]. Pressure, length, and relaxation of the LES, as well as the pressure of the upper esophageal sphincter, are measured with more than 30 sensors spaced at 1 cm intervals, allowing for a precise pressure recording throughout the whole esophagus.

HRM included new manometric parameters, which were summarized in the so-called Chicago Classification [23, 24]. This new classification includes three distinct subtypes of achalasia that have both prognostic and therapeutic implications (Fig. 2.5):

- Type I: incomplete or absent LES relaxation, aperistalsis and absence of esophageal pressurization
- Type II: incomplete or absent LES relaxation, aperistalsis and pan-esophageal pressurization in at least 20% of swallows
- Type III: incomplete or absent LES relaxation and premature contractions in at least 20% of swallows ("spastic achalasia")

Subclassification of achalasia in types I, II, and III seems to be useful to predict the outcome and select treatment. Pandolfino and colleagues [25] reported that type II achalasia patients are more likely to respond to laparoscopic Heller myotomy (LHM) (100%), as compared to type I (56% overall) and type III (29% overall). Concordantly, Salvador et al. [26] evaluated 246 consecutive patients who underwent LHM and found that treatment failure rates were significantly different among the subtypes of achalasia: type I 14.6%, type II 4.7%, and type III 30.4% (p = 0.0007). A recent meta-analysis encompassing 9 studies and 727 patients also showed that type II achalasia was associated with the best prognosis after pneumatic dilatation and LHM, while type III achalasia had the worst prognosis [27].

The selection of the best initial approach for achalasia also appears to be influenced by the Chicago Classification. While in type I and II achalasia, pneumatic dilatation and LHM appear to be the best optimal treatment, type III achalasia

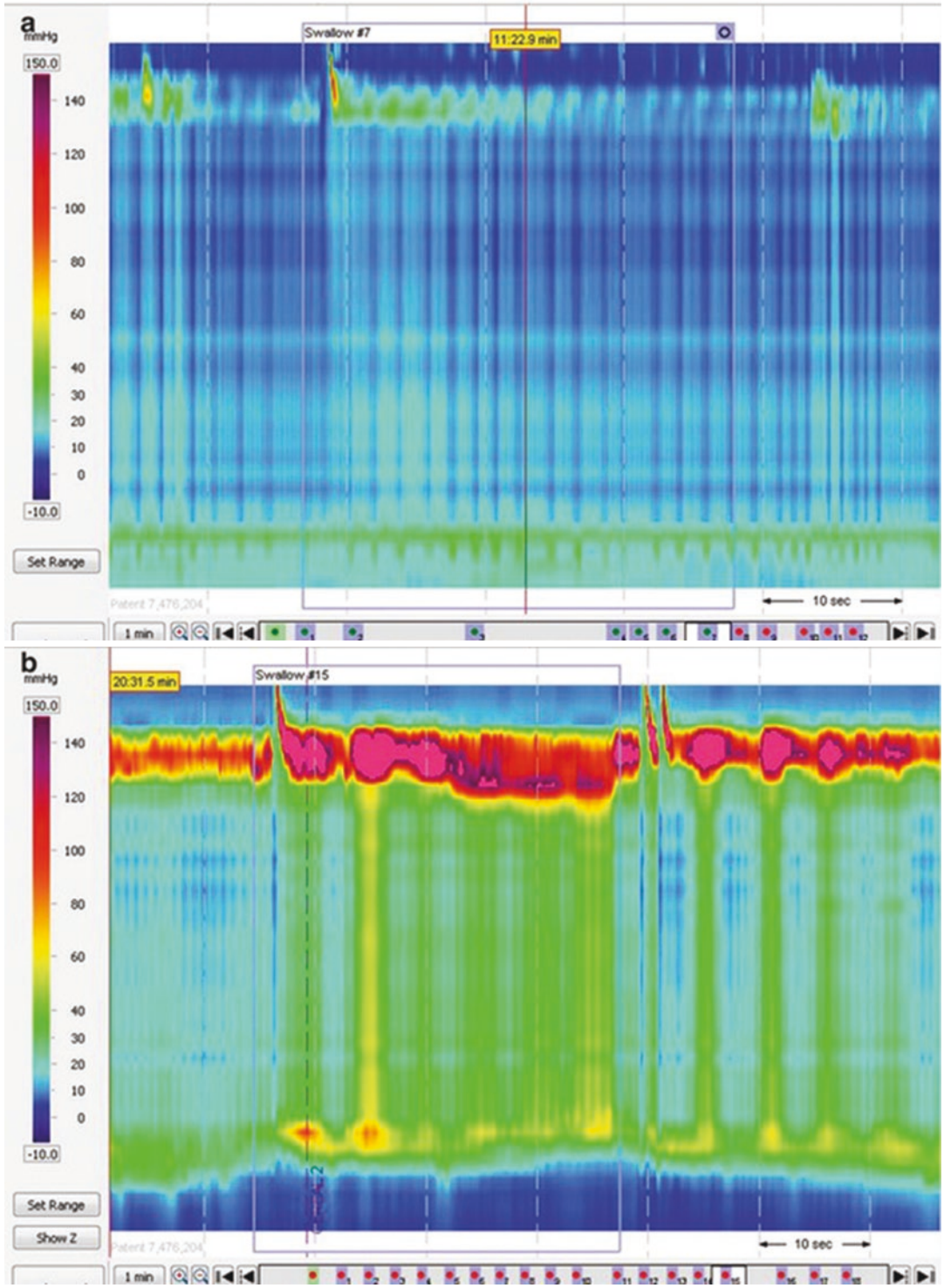


Fig. 2.5 High-resolution manometry. According to Chicago Classification: (**a**) Type I: incomplete or absent LES relaxation, aperistalsis, and absence of esophageal pressurization. (Reprinted with permission © Springer Nature [33]) (**b**) Type II: incomplete or absent LES relaxation, aperistalsis and pan-esophageal pressurization in at least 20% of swallows. (Reprinted with permission © Springer Nature [33]). (**c**) Type III: incomplete or absent LES relaxation and premature contractions in at least 20% of swallows ("spastic achalasia"). (Reprinted with permission © Springer Nature [33])

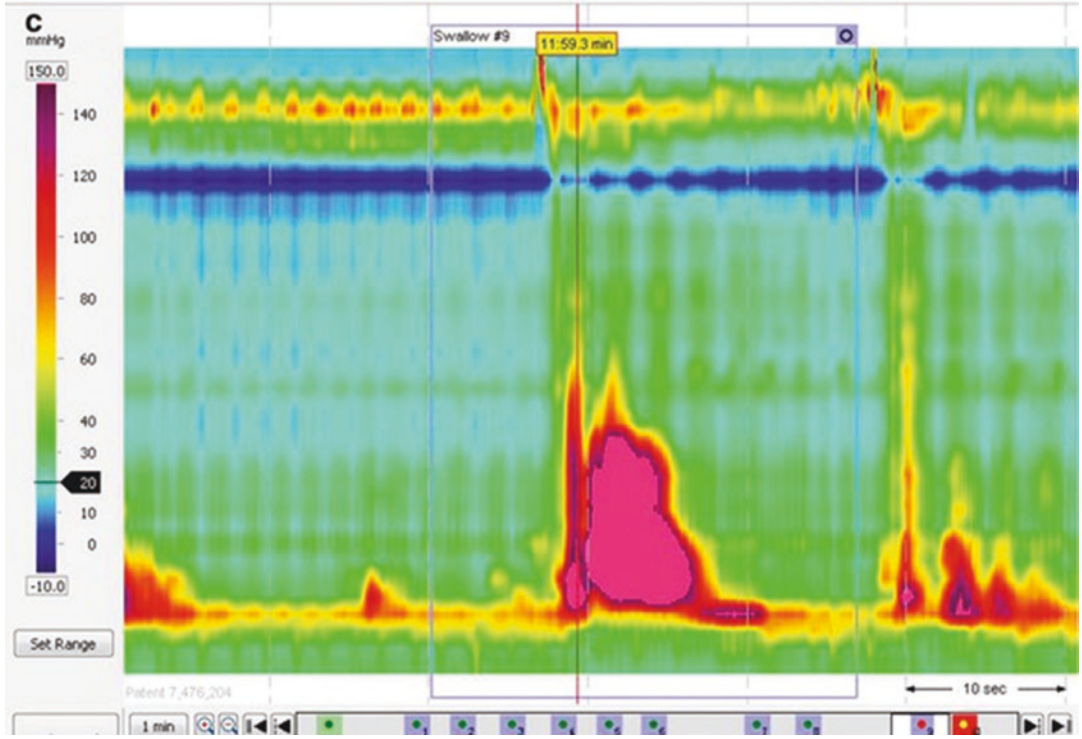


Fig. 2.5 (continued)

seems to be better managed with per-oral endoscopic myotomy, probably due to the ability to perform a longer myotomy of the thoracic esophagus [28, 29].

Ambulatory pH Monitoring

This test is recommended in selected patients when the diagnosis is uncertain, in order to distinguish between GERD (real reflux) and achalasia (false reflux) (Fig. 2.6). Unfortunately, many patients are treated with acid-reducing medications, or even with a fundoplication, on the assumption that the heartburn and the regurgitations are secondary to abnormal reflux. A multicenter study examined the records of 524 patients whose final diagnosis was achalasia, and found that 152 patients (29%) had been treated for an average of 29 months with proton-pump inhibitors with poor response (classified as having "refractory GERD"), and had been referred for antireflux surgery [30].

The examination of the pH monitoring tracing is mandatory. In both GERD and achalasia, the score can be abnormal, but the tracing is different. While in GERD patients the tracing is characterized by intermittent drops of pH below 4 with subsequent return of the pH values above 5, in achalasia patients, there is a slow and progressive drift of the pH below 4 with no return to higher values (pseudo-GERD due to food fermentation) [31].

Overall, the American College of Gastroenterology guidelines for the diagnosis of achalasia recommend endoscopy to rule out pseudoachalasia, barium swallow to delineate the esophageal emptying and anatomy, and esophageal manometry to confirm the diagnosis [32].

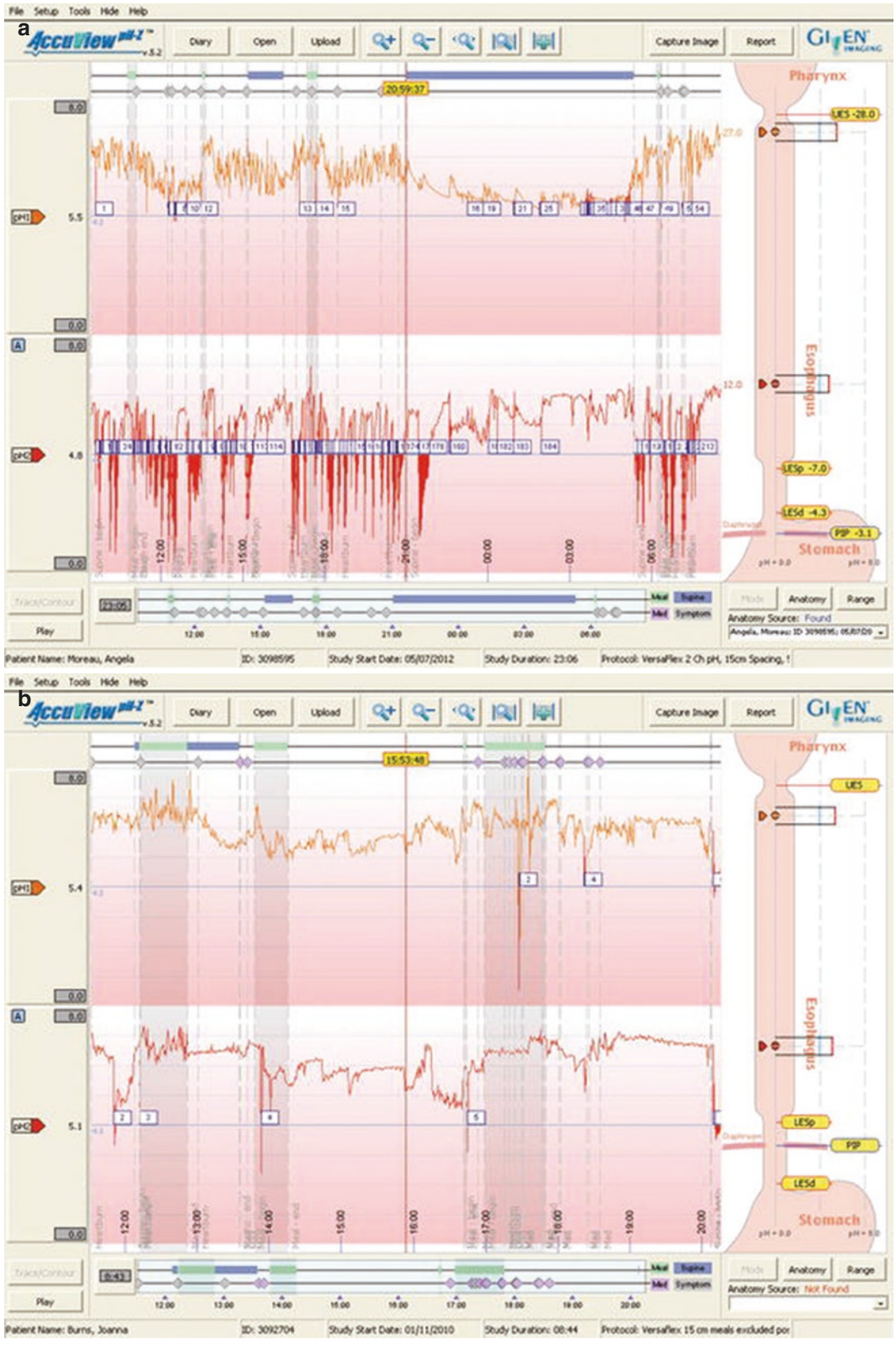


Fig. 2.6 pH monitoring showing the difference between real and false reflux tracings. (**a**) Real reflux; (**b**) False reflux. (Reprinted with permission © Springer Nature [34])

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Molena D, Yang SC. Surgical management of end-stage achalasia. SeminThoracCardiovasc Surg. 2012;24:19–26.
2. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet. 2014;383:83–93.
3. Ponds FA, van Raath MI, Mohamed SMM, Smout AJPM, Bredenoord AJ. Diagnostic features of malignancy-associated pseudoachalasia. Aliment PharmacolTher. 2017;45:1449–58.
4. Ravi K, Sweetser S, Katzka DA. Pseudoachalasia secondary to bariatric surgery. Dis Esophagus. 2016;29:992–5.
5. Herbella FA, Aquino JL, et al. Treatment of achalasia: lessons learned with Chagas' disease. Dis Esophagus. 2008;21:461–7.
6. Eckardt VF, Köhne U, Junginger T, Westermeier T. Risk factors for diagnostic delay in achalasia. Dig Dis Sci. 1997;42:580–5.
7. Fisichella PM, Raz D, Palazzo F, Niponmick I, Patti MG. Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. World J Surg. 2008;32:1974–9.
8. Gupta M, Ghoshal UC, Jindal S, Misra A, Nath A, Saraswat VA. Respiratory dysfunction is common in patients with achalasia and improves after pneumatic dilation. Dig Dis Sci. 2014;59:744–52.
9. Jung DH, Park H. Is Gastroesophageal Reflux Disease and Achalasia\Coincident or Not? J NeurogastroenterolMotil. 2017;23:5–8.
10. Ferguson MK, Little AG. Angina-like chest pain associated with high-amplitude peristaltic contractions of the esophagus. Surgery. 1988;104:713–9.
11. Eckardt VF, Stauf B, Bernhard G. Chest pain in achalasia: patient characteristics and clinical course. Gastroenterology. 1999;116:1300–4.
12. Perretta S, Fisichella PM, Galvani C, Gorodner MV, Way LW, Patti MG. Achalasia and chest pain: effect of laparoscopic Heller myotomy. J GastrointestSurg. 2003;7:595–8.
13. Gockel I, Junginger T. The value of scoring achalasia: a comparison of current systems and the impact on treatment – the surgeon's viewpoint. Am Surg. 2007;73:327–31.
14. Laurino-Neto RM, Herbella F, Schlottmann F, Patti M. Evaluation of esophageal achalasia: from symptoms to The Chicago Classification. Arq Bras Cir Dig. 2018;31:e1376.
15. Gockel I, Rabe SM, Niebisch S. Before and after esophageal surgery: which information is needed from the functional laboratory? Visc Med. 2018;34:116–21.
16. Andolfi C, Baffy G, Fisichella PM. Whose patient is it? The path to multidisciplinary management of achalasia. J Surg Res. 2018;228:8–13.
17. Sandler RS, Bozymski EM, Orlando RC. Failure of clinical criteria to distinguish between primary achalasia and achalasia secondary to tumor. Dig Dis Sci. 1982;27:209–13.
18. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. JAMA. 2015;313:1841–52.
19. de Oliveira JM, Birgisson S, Doinoff C, Einstein D, Herts B, Davros W, Obuchowski N, Koehler RE, Richter J, Baker ME. Timed barium swallow: a simple technique for evaluating esophageal emptying in patients with achalasia. AJR Am J Roentgenol. 1997;169:473–9.
20. Schlottmann F, Neto RML, Herbella FAM, Patti MG. Esophageal achalasia:pathophysiology, clinical presentation, and diagnostic evaluation. Am Surg. 2018;4(84):467–72.
21. Gorodner MV, Galvani C, Fisichella PM, Patti MG. Preoperative lower esophageal sphincter pressure has little influence on the outcome of laparoscopic Heller myotomy for achalasia. SurgEndosc. 2004;18(5):774–8.
22. Herbella FA, Patti MG. Can high-resolution manometry parameters for achalasia be obtained by conventional manometry? World J GastrointestPathophysiol. 2015;6(3):58–61.
23. Herbella FA, Armijo PR, Patti MG. A pictorial presentation of 3.0 Chicago Classification for esophageal motility disorders. Einstein (Sao Paulo). 2016;14(3):439–42.
24. Kahrilas PJ, Ghosh SK, Pandolfino JE. Esophageal motility disorders in terms of pressure topography: the Chicago Classification. J ClinGastroenterol. 2008;42(5):627–35.
25. Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology. 2008;135(5):1526–33.
26. Salvador R, Costantini M, Zaninotto G, et al. The preoperative manometric pattern predicts the outcome of surgical treatment for esophageal achalasia. J GastrointestSurg. 2010;14:1635–45.
27. Ou YH, Nie XM, Li LF, Wei ZJ, Jiang B. High-resolution manometric subtypes as a predictive factor for the treatment of achalasia: a meta-analysis and systematic review. J Dig Dis. 2016;17(4):222–35.
28. Kumbhari V, Tieu AH, Onimaru M, et al. Peroral endoscopic myotomy (POEM) vs laparoscopic Heller myotomy (LHM) for the treatment of Type III achalasia in 75 patients: a multicenter comparative study. EndoscInt Open. 2015;3(3):E195–201.
29. Khashab MA, Messallam AA, Onimaru M, et al. International multicenter experience with peroral endoscopic myotomy for the treatment of spastic esophageal disorders refractory to medical therapy (with video). GastrointestEndosc. 2015;81(5):1170–7.
30. Andolfi C, Bonavina L, Kavitt RT, Konda VJ, Asti E, Patti MG. Importance of Esophageal Manometry and pH Monitoring in the Evaluation of Patients with Refractory Gastroesophageal Reflux Disease: A Multicenter Study. J LaparoendoscAdvSurg Tech A. 2016;26(7):548–50.

31. Patti MG, Arcerito M, Tong J, De Pinto M, de Bellis M, Wang A, Feo CV, Mulvihill SJ, Way LW. Importance of preoperative and postoperative pH monitoring in patients with esophageal achalasia. J GastrointestSurg. 1997;1(6):505–10.
32. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108(8):1238–49.
33. Hungness ES, El Khoury R. Peroralendoscopic myotomy (POEM). In: Fisichella PM, Marco G, Patti MG, editors. Atlas of Esophageal Surgery. New York: Springer; 2015. p. 85–93.
34. Allaix ME, Borraez BA, Patti MG. Gastroesophageal reflux disease: diagnostic evaluation. In: Fisichella PM, Allaix ME, Ml M, Patti MG, editors. Esophageal diseases. New York: Springer; 2014. p. 53–67.

Achalasia and Chagas' Disease

3

Leonardo M. Del Grande
and Fernando A. M. Herbella

Introduction

Chagas' disease is a tropical infection caused by the protozoan *Trypanosoma cruzi* that is widespread in Latin America [1]. The prevalence of the disease has been decreasing due to investments in prevention. There are still, however, several endemic areas in America, such as parts of Bolivia and Brazil [2]. On the other side, several cases have been reported in non-endemic areas such as the US and Europe due to the immigration of infected individuals from Latin America [3]. Nevertheless, global incidence of the disease decreased from 18 million cases in 1991 to less than 6 million in 2010 with an estimated 400 thousand individuals infected outside Latin America [3, 4].

Trypanosoma cruzi is transmitted to humans through the feces of the insect that acts as vector, a *Triatominae* bug called kissing bug in North America or barber bug in South America (Fig. 3.1). It commonly inhabits holes in houses of thatched walls and roofs. The parasite is inoculated when the bug bites the host and defecates during the process. Other transmission mechanisms such as blood transfusion, organ transplantation, and vertical have been described [3, 4].

Fig. 3.1 Triatominae bug (Chagas disease vector)

Symptoms may not occur after infection (acute phase) or they may be nonspecific as flu symptoms (in 30% of the cases). Two-thirds of the infected individuals never develop complications (undetermined form). One-third will experience damage to target organs [5–7]. The heart is the target organ most affected among patients with chronic disease (60%). Chagasic cardiomyopathy is characterized by cardiac dilatation and conduction system abnormalities (typically right bundle branch block) [1, 5, 8]. The gastrointestinal system

L. M. Del Grande
Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, SP, Brazil

F. A. M. Herbella (✉)
Gastrointestinal Surgery – Esophagus and Stomach Division, Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, SP, Brazil
e-mail: herbella.dcir@epm.br

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_3

is affected in 20% of the cases, especially the esophagus or colon, with a 60% concomitance of cardiac manifestation [7, 9, 10].

There is no vaccine for prevention of Chagas' disease or specific treatment for the chronic stage [5].

Chagas' Disease Esophagopathy

Pathophysiology

Chagas' disease esophagopathy (CDE) is caused by immune destruction of the esophageal intramural ganglia. This process begins in anticipation of symptoms since the disease usually clinically manifests more than 15 years after contagion. Neural damage in idiopathic achalasia (IA) seems to be degenerative and leads to destruction of the Auerbach's myenteric plexus affecting only inhibitory neurons [9–12]. On the other side, inhibitory and excitatory neurons seem to be affected in CDE. This aganglionosis affects esophageal body contraction and lower esophageal sphincter relaxation.

Clinical Presentation

Clinical presentation for CDE and IA is similar. Dysphagia is the main symptom in almost all cases. Regurgitation, weight loss, and thoracic pain are also very frequent. A remarkable difference in presentation is, however, the time of complaint. It is common to find patients with two decades of dysphagia in CDE. This is probably caused by access to treatment in underdeveloped countries where the disease is endemic. Moreover, the vector insect inhabits rural areas, distant from large urban centers [11, 13].

Esophageal Motility

Esophageal achalasia is defined manometrically by aperistalsis and inadequate relaxation of the lower esophageal sphincter [12, 14, 15]. High-resolution manometry provides a more detailed evaluation of the disease including a classification based on esophageal pressurization. The same classification may be applied to CDE [12, 15] although type III was not present in patients with CDE probably due to the loss of inhibitory and excitatory ganglia in CDE, different from IA [11, 12]. CDE and IA are comparable in regard to manometric findings although higher pressures of the esophageal body are noticed in patients with IA and basal and residual pressures of the LES are lower in patients with CDE. This may be attributed to a more pronounced esophageal dilatation in patients with CDE [15]. It is still unclear if the Chicago Classification may predict prognosis in patients with CDE similarly to IA [15–19]. The higher prevalence of lower esophageal sphincter basal pressure in patients with CDE [15, 20] does not seem to affect outcomes even though some authors propose that better results are found in patients with hypertonic lower esophageal sphincter [21].

Interestingly, some authors recently questioned the need for complete aperistalsis to define achalasia [12]. Chagas' disease is a natural model for achalasia since patients without any clinical complain may be followed to evaluate deterioration or not of motility. Some studies did find some undetermined abnormalities in these patients, especially multipeaked waves, spontaneous activity, and repetitive waves [14, 15, 20].

Esophageal Dilatation

The degree of esophageal dilatation is an indicative of the disease severity and tailors therapy according to some authors. CDE is characteristically represented by esophageal dilatation, probably related to the delay in treatment as previously mentioned. Over 70% of the patients will present with >4 cm of esophageal caliber at first presentation in CDE series [22].

Esophageal dilatation may define end-stage disease. The threshold for advanced disease is variable. Some adopt the limit of 6 cm for maximum esophageal diameter [23], while others use 7 cm [24]. Most Brazilian surgeons adopt 10 cm as the upper limit [25]. Esophageal diameter > 10 cm can be found in up to 40% in CDE series [26].

Other Manifestations

Esophageal stasis is accentuated in dilated esophagi. This leads to secondary findings in the mucosa at the upper digestive endoscopy, especially esophagitis due to intrinsic production of acid during bacterial fermentation of retained food and leukoplakia, a premalignant finding [25, 26]. The risk for esophageal cancer is 10–50 times greater in patients with achalasia, and it is greater in patients with CDE probably due to the long-lasting time of symptoms [26, 27].

Epiphrenic diverticula are common in achalasia, but there is no evidence for a different incidence in patients with CDE as compared to IA [28, 29].

Evaluation

A complete work-up is necessary for the diagnosis and evaluation of patients with suspected CDE, not different from IA [30].

Barium esophagram is a simple test that may be diagnostic and classifies the disease according to the degree of dilatation (Table 3.1).

Upper digestive endoscopy is a mandatory test to exclude other diseases including pseudoachalasia due to an esophagogastric junction tumor, particularly because achalasia increases the risk for esophageal cancer.

Esophageal manometry is the gold standard test for the diagnosis of achalasia due to objective evaluation of peristalsis, detection of alterations even in incipient cases, and the possibility to define prognosis.

The heart and the colon may be other target organs of the Chagas' disease. Thus, a cardiologic evaluation is necessary in all patients. A colonic evaluation is necessary if this organ may be used to replace the esophagus after and esophagectomy.

Patients with massive dilatation of the esophagus must be carefully prepared for therapy. The risk for aspiration is great due to food stasis in the esophagus. Prolonged fasting and attention during intubation are mandatory. Pulmonary evaluation is welcome since subclinical aspiration may affect the lungs.

Table 3.1 Classification of Chagas' esophagopathy according to the degree of dilatation [18, 21]

Maximum esophageal diameter (cm)	Achalasia degree
<4	I
4–7	II
7–10	III
>10 or sigmoid-shaped	IV

Treatment (Table 3.2)

Pharmacological

Pharmacological treatment for achalasia aimed at decreasing the lower esophageal sphincter tonus has limited usage [30]. Results are precarious and side effects of the drugs are frequent. This therapy is seldom used for CDE.

Table 3.2 Treatment options for Chagas' disease esophagopathy

Treatment	Observations
Pharmacological	Limited use
Endoscopic – cardia dilatation	Frequent use in initial cases as primary therapy (dilatation <4 cm). Excellent/good results in over 80%
Endoscopic – botulinum toxin injection	Low level of evidence for outcomes in patients with Chagas' disease Different pathophysiology as compared to idiopathic disease may bring inferior outcomes
Endoscopic – peroral myotomy	Few studies in Chagas' disease Questionable value and feasibility in end-stage disease
Surgical – Heller myotomy	Frequently used Excellent/good results in over 80%
Surgical – esophagectomy	Frequently used for end-stage disease (dilatation >10 cm)
Surgical – other	Low level of evidence for outcomes in patients with Chagas' disease Laparoscopic Heller myotomy may be a better alternative in end-stage cases

Endoscopic

Endoscopic Forceful Cardia Dilatation

Endoscopic dilatation is probably the most used primary therapy in achalasia patients [30, 31]. It has, however, decreased efficacy in cases of massive esophageal dilatation. This fact limits the use of this procedure in patients with CDE. It is used in initial cases or as a palliative procedure to improve nutrition before an operation [30, 32, 33].

Botulinum Toxin Injection and Peroral Endoscopic Myotomy (POEM)

Intrasphincteric botulinum toxin injection experience in patients with CDE is very limited [34].

Experience with POEM is also limited. The high incidence of a dilated esophagus may make the procedure more challenging [35].

Surgery

Laparoscopic Heller Myotomy

Laparoscopic Heller myotomy and fundoplication are the most common procedures used to treat IA and CDE [30]. These are associated with long-lasting and excellent outcomes with CDE, similar to IA [32].

Esophagectomy

Esophagectomy is advocated by different authors to treat end-stage achalasia. The pronounced dilatation in CDE made esophagectomy a popular treatment in Latin America [36]. The operation is, however, more challenging than an operation for cancer [37], associated with significant morbidity (up to 70%) and mortality (up to 4%) for a benign disease [38, 39]. Moreover, the surgical risk is increased with larger degrees of dilatation [40]. For these reasons, the number of esophagectomies for achalasia has been decreasing in Brazil [41], and some authors advocate a laparoscopic Heller myotomy even with dilated esophagi [42, 43]. Others opt for esophageal mucosectomy and endomuscular pull-through [44].

Other Techniques

CDE is characterized by frequent esophageal dilatation as previously mentioned. Some Latin American surgeons use alternatives of an esophagectomy in cases of end-stage disease.

Gröndahl cardioplasty, later modified and added to a gastrectomy by Holt and Large [45], has been used by Latin American surgeons as an alternative to esophagectomy in advanced cases of CDE [13]. It has a lower morbidity as compared to an esophagectomy (up to 25%) and lower mortality (up to 2%) [13, 46].

Conclusions

Chagas' disease may affect the esophagus and create a motility disorder very similar to IA. The most significant difference between these two diseases is probably the higher proportion of esophageal dilatation found in Chagas' disease esophagopathy. Treatment is similar to IA, with Heller myotomy and fundoplication or endoscopic dilatation for initial cases and Heller myotomy and fundoplication or esophagectomy for more advanced cases.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Bern C. Antitrypanosomal therapy for chronic Chagas' disease. N Engl J Med. 2011;364:2527–34.
2. Samuels AM, Clark EH, Galdos-Cardenas G, et al. Epidemiology of andimpact of insecticide spraying on Chagasdisease in communities in the BolivianChaco. PLoSNegl Trop Dis. 2013;7(8):e2358.
3. Bonney KM. Chagas disease in the 21st century: a public health success or an emerging threat? Parasite. 2014;21:11.
4. Chagas disease in Latin America: an epidemiological update based on 2010 estimates. WklyEpidemiol Rec. 2015;90:33–43.
5. Bern C. Chagas' disease. N Engl J Med. 2015;373:456–66.
6. Rassi A Jr, Rassi A, Marcondes de Rezende J. American trypanosomiasis (Chagas disease). Infect Dis Clin N Am. 2012;26:275–91.
7. Pinotti HW, Felix WN, Zilberstein B, Cecconello I. Surgical complications of Chagas' disease; megaesophagus, achalasia of the pylorus and cholelithiasis. World J Surg. 1991;15:198–204.

8. Sabino EC, Ribeiro AL, Salemi VM, et al. Ten-year incidence of Chagas cardiomyopathy among asymptomatic Trypanosoma cruzi-seropositive former blood donors. Circulation. 2013;127:1105–15.
9. De Oliveira RB, Troncon LE, Dantas RO, Menghelli UG. Gastrointestinal manifestations of Chagas' disease. Am J Gastroenterol. 1998;93:884–9.
10. Pinazo MJ, Cañas E, Elizalde JI, et al. Diagnosis, management and treatment of chronic Chagas' gastrointestinal disease in areas where Trypanosoma cruzi infection is not endemic. GastroenterolHepatol. 2010;33:191–200.
11. Herbella FAM, Oliveira DRC, Del Grande JC. Are idiopathic and Chagasicachalasia two different diseases? Dig Dis Sci. 2004;49(3):353–60.
12. Vicentine FP, Herbella FAM, Allaix ME, Silva LC, Patti MG. High-resolution manometry classifications for idiopathic achalasia in patients with Chagas' disease Esophagopathy. J GastrointestSurg. 2014;18:221–5.
13. Stefani-Nakano SM, Faintuch J, Cecconello I, Rocha JM, Gama-Rodrigues JJ. Quality of life of patients operated for advanced Chagas' megaesophagus. ABCD Arq Bras Cir Dig. 2005;18:129–32.
14. de Oliveira RB, Rezende Filho J, Dantas RO, Iazigi N. The spectrum of esophageal motor disorders in Chagas' disease. Am J Gastroenterol. 1995;90:1119–24.
15. Vicentine FP, Herbella FAM, Allaix ME, Silva LC, Patti MG. Comparison of idiophathicacalasia and Chagas' disease esophagopathy at the light of high-resolution manometry. Dis Esophagus. 2014;27:128–33.
16. Rohof WO, Salvador R, Annese V, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology. 2013;144:e18.
17. Menezes MA, Andolfi C, Herbella FA, Patti MG. High-resolution manometry findings in patients with achalasia and massive dilated megaesophagus. Dis Esophagus. 2017;30:1–4.
18. Silva LC, Vicentine FP, Herbella FAM. High-resolution manometric findings in patients with Chagas' disease esophagopathy. Asian Pac Trop Med. 2012;5:110–2.
19. Arain MA, Peters JH, Tamhankar AP, Portale G, Almogy G, DeMeester SR, et al. Preoperative lower esophageal sphincter pressure affects outcome of laparoscopic esophageal myotomy for achalasia. J GastrointestSurg. 2008;8:328–34.
20. Rezende JM, Oliveira R, Lauar KN. Aspectosclínicos e radiológicos da aperistalsis do esôfago. Rev Bras Gastroenterol. 1960;12:247–621.
21. Patti MG, Feo CV, Diener U, Tamburini A, Arcerito M, Safadi B, Way LW. Laparoscopic Heller myotomy relieves dysphagia in achalasia when the esophagus is dilated. SurgEndosc. 1999;13:843–7.
22. Onopriev VI, Durleshter VM, Ryabchun VV. Comparative pre and postoperative results analysis of functional state of the esophagus assessment in patients with various stages of achalasia. Eur J CardiothoracSurg. 2005;28:1–6.
23. Ferreira Santos R. Aperistalsis of the esophagus and colon (megaesophagus and megacolon) etiologically related to Chagas disease. Am J Dig Dis. 1961;6:700–26.
24. Pantanali CA, Herbella FA, Henry MA, Mattos Farah JF, Patti MG. Laparoscopic Heller myotomy and fundoplication in patients with Chagas' disease achalasia and massively dilated esophagus. Am Surg. 2013;79:72–5.
25. Chino O, Kijima H, Shimada H, et al. Clinicopathological studies of esophageal carcinoma in achalasia: analyses of carcinogenesis using histological and immunohistochemical procedures. Anticancer Res. 2000;20:3717–22.
26. Kim H, Park H, Choi H, Shin Y, Park H, Youn YH, Kim JH. Retention esophagitis as a significant clinical predictor of progression to esophageal cancer in achalasia. ClinEndosc. 2018;51:161–6.
27. Streitz JM Jr, Ellis FH Jr, Gibb SP, Heatley GM. Achalasia and squamous cell carcinoma of the esophagus: analysis of 241 patients. Ann ThoracSurg. 1995;59:1604–9.
28. Herbella FA, Patti MG. Achalasia and epiphrenicdiverticulum. World J Surg. 2015;39:1620–4. 27.
29. Vicentine FP, Herbella FA, Silva LC, Patti MG. High-resolution manometry findings in patients with esophagealepiphrenic diverticula. Am Surg. 2011;77:1661–4.
30. Zaninotto G, Bennett C, Boeckxstaens G, et al. The 2018 ISDE achalasia guidelines. Dis Esophagus. 2018;31(9).
31. Spechler SJ. Pneumatic dilation and laparoscopic Heller's myotomy equally effective for achalasia. N Engl J Med. 2011;364:1868–70.
32. Herbella FA, Aquino JL, Stefani-Nakano S, Artifon EL, Sakai P, Crema E, Andreollo NA, Lopes LR, de Castro Pochini C, Corsi PR, Gagliardi D, Del Grande JC. Treatment of achalasia: lessons learned with Chagas' disease. Dis Esophagus. 2008;21:461–7.
33. Felix VN, Sakai P, Cecconello I, Pinotti HW. Esophageal endoscopic aspects after forceful dilation of the gastric cardia in patients with achalasia of Chagas' disease. Dis Esophagus. 2000;13:91–5.
34. Brant C, Moraes-Filho JP, Siqueira E, Nasi A, Libera E, Morais M, Rohr M, Macedo EP, Alonso G, Ferrari AP. Intrasphincteric botulinum toxin injection in the treatment of chagasic achalasia. Dis Esophagus. 2003;16:33–8.
35. Hu JW, Li QL, Zhou PH, Yao LQ, Xu MD, Zhang YQ, Zhong YS, Chen WF, Ma LL, Qin WZ, Cai MY. Peroral endoscopic myotomy for advanced achalasia with sigmoid-shaped esophagus: long-term outcomes from a prospective, single-center study. SurgEndosc. 2015;29(9):2841–50.
36. Pinotti HW, Cecconello I, da Rocha JM, Zilberstein B. Resection for achalasia of the esophagus. Hepato-Gastroenterology. 1991;38:470–3.

37. Mormando J, Barbetta A, Molena D. Esophagectomy for benign disease. J Thorac Dis. 2018;10:2026–33.
38. Aiolfi A, Asti E, Bonitta G, Siboni S, Bonavina L. Esophageal resection for end-stage achalasia. Am Surg. 2018;84:506–11.
39. Felix VN. Esophagectomy forend-stageachalasia. Ann N Y Acad Sci. 2016;1381:92–7.
40. Neto JG, de Cleva R, Zilberstein B, Gama-Rodrigues JJ. Surgicalriskfor patients withChagasicachalasiaand its correlation with the degree ofesophagealdilation. World J Gastroenterol. 2005;11:5840–4.
41. Ceneviva R, Ferreira-Santos R, Santos JS, Mente ED, Sankarankutty AK. Chronological changes of patients profile and of surgical treatment modality of the chagasicmegaesophagus. Acta Cir Bras. 2002;17:125–8.
42. Herbella FA, Patti MG. Laparoscopic Heller myotomy and fundoplication in patients withend-stageachalasia. World J Surg. 2015;39:1631–3.
43. Del Grande LM, Herbella FAM, Patti MG, Schlottmann F. One size fits all: laparoscopic Heller myotomy for the treatment of achalasia irrespective of the degree of dilatation. Topic: Achalasia Management: the South American viewpoint. Mini-invasive Surg. 2017;1:121–5. https://doi.org/10.20517/2574-1225.2017.23.
44. Aquino JLB, Reis Neto JA, Muraro CLPM, Camargo JGT. Esophageal mucosectomy in the treatment of the advanced megaesophagus: analysis of 60 cases. Rev Col Bras Cir. 2000;27:109–16.
45. Holt CJ, Large AM. Surgical management of reflux esophagitis. Ann Surg. 1961;153:555–62.
46. Ponciano H, Cecconello I, Alves L, Ferreira BD, GamaRodrigues J. Cardioplasty and Roux-en-Y partial gastrectomy (Serra-Dória procedure) forreoperationofachalasia. ArqGastroenterol. 2004;41:155–61.

4 Pneumatic Dilation for Esophageal Achalasia

Wojciech Blonski and Joel E. Richter

Current American College of Gastroenterology (ACG) guidelines consider pneumatic dilation (PD) the most effective nonsurgical treatment for achalasia [1]. According to current ACG guidelines, all achalasia patients with low surgical risk should be presented with two equally effective treatment modalities for achalasia: PD and Heller myotomy [1]. Based on patients' preference and expertise of the local center, either procedure can be selected [2, 3]. This chapter will summarize the data over the last 50 years to support the ACG guidelines. The Rigiflex balloons have greatly simplified PD and finally good randomized studies prove the long-term efficacy of PD in treating achalasia. This has been a journey the senior author began in the days of the Brown-McHardy balloon, performed some of the pilot work with the Rigiflex balloon in the 1980s, and now has a series of nearly 1000 PDs over the last 35 years.

W. Blonski
Orlando VA Medical Center and University of Central Florida College of Medicine, Orlando, FL, USA

J. E. Richter (✉)
Joy McCann Culverhouse Center for Swallowing Disorders, Division of Digestive Diseases and Nutrition, University of South Florida Morsani College of Medicine, Tampa, FL, USA
e-mail: jrichte1@health.usf.edu

Historical Perspective

The aim of PD is to disrupt the lower esophageal sphincter (LES), resulting in relief of symptoms and improved esophageal emptying. In actuality, the muscle is infrequently torn, but rather circumferential stretching occurs [4]. The first reported case of achalasia was treated with self-bougienage using a whale bone attached to a sponge [5].

Early dilators were metal (Stark) and later modified with expanding bags or balloons which could be positioned across the LES. The first balloon was the Plummer hydrostatic dilator, which used water to expand the balloon [5]. Subsequent dilators replaced water with air and were called "pneumatic dilators." These included the Browne-McHardy, Hurst-Tucker, Mosher, and Rider-Mueller dilators. The latter was a dumbbell-shaped bag that could be positioned across the LES and came for the first time in variable sizes. These balloons required fluoroscopy for proper placement, and balloon size, when expanded, ranged from 2.5 to 4.5 cm [5]. The overall experience with these balloons was excellent with improvement noted in 61% to 100% of patients with a perforation rate from 2% to 15% [5]. The variable quality of the older balloon dilators and high perforation rate limited their wide utility. The last Browne-McHardy dilator, the most popular of these older balloons, was made in 1982.

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_4

Modern Balloons and Dilation Techniques

The introduction in 1987 of the Microvasive Rigiflex balloon system (Boston Scientific, Boston, MA) has allowed for standardization of pneumatic dilation. These balloons are 10 cm long and consist of polyethylene polymer mounted on a flexible catheter. There are three diameters of the Rigiflex balloons: 30, 35, and 40 mm (Fig. 4.1). Although the balloon itself is not visible under fluoroscopy, it has four radiopaque markers on the shaft that define the upper, lower, and middle (double markers) borders. Additional feature of the Rigiflex balloon is that it can be inflated maximally only to its designated diameter (noncompliance).

Although PD was initially performed in the hospital setting with an overnight stay, for the last 20 years, this procedure has been performed in outpatient ambulatory surgical centers [6]. Prior to performing PD in the practice of the senior author, all patients with suspected achalasia have their diagnosis confirmed by high-resolution manometry. The diagnosis of achalasia is based on the Chicago Classification (achalasia types I, II, and III) [7]. In addition, timed barium esophagram (TBE) is performed [8]. In this technique, after drinking 8 oz. of low-density barium in the standing position, two-on-one spot films are obtained at 1 and 5 min to assess liquid emptying [9]. Next, the esophagus is rinsed with water followed by ingestion of a 13 mm barium tablet. The passage of the tablet is evaluated 5 min after ingestion. TBE allows for assessment of the degree of esophageal dilation, megaesophagus, and the rate of esophageal emptying of liquid barium and barium tablet over 5 min. In patients with markedly dilated esophagus or slow esophageal emptying, we recommend 3 days of clear liquids prior to PD. In all other patients, we recommend nothing per mouth status after midnight on the day of procedure.

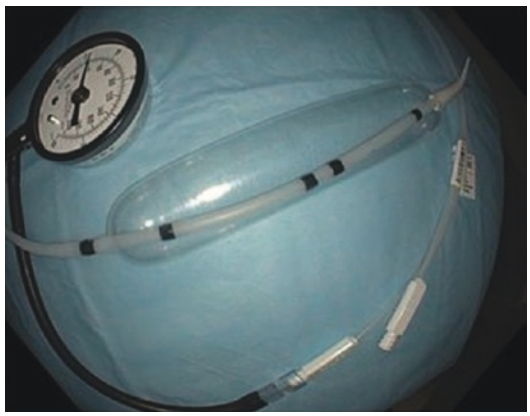


Fig. 4.1 Thirty millimeter Rigiflex balloon with radiopaque markers defining the upper, middle, and lower borders

Before PD is initiated, upper endoscopy under conscious sedation with propofol is performed. Initially, the patient is placed in the left lateral position with elevation of his/her head at least 30°. In our practice, intubation to protect the airway is required in less than 1% of patients. The esophagus (esophageal mucosa and LES) is carefully assessed with removal of any fluid and soft retained food with standard suction. In patients with large amounts of retained food, we perform water lavage with a large bore nasogastric tube.

All achalasia patients usually have mild to moderate dilation of the esophageal body with tortuosity of the distal third of the esophagus and some retention of clear secretions (saliva) and small amounts of soft food. Although the esophageal mucosa usually appears normal, some patients will show reddened, friable, thickened, cracked, desquamating mucosa with megaesophagus and chronic stasis. Endoscopic evidence of candidiasis with the classic white plaques may also be seen.

It is imperative to perform a careful inspection of the LES during upper endoscopy [6]. Patients with achalasia usually have a puckered appearance to the LES, which remains closed with air insufflation (Fig. 4.2). The gastroesophageal junction (Z-line) may not be easily seen due to its location 1–2 cm below the spastic area, which represents the proximal border of the LES. Upon applying gentle pressure, the endoscope should easily pass into the stomach, and about 25% will be associated with a popping release [6]. However, pseudoachalasia should be suspected if excessive pressure is required. We recommend a detailed evaluation of the gastric cardia in the ret-

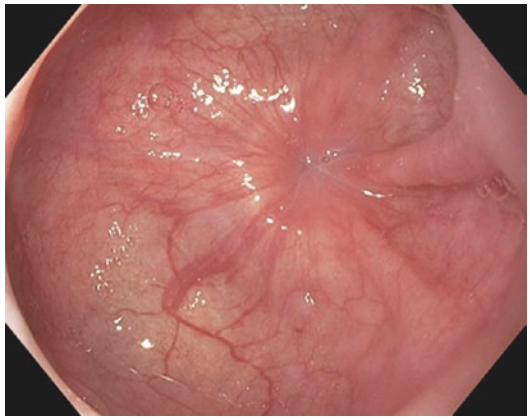


Fig. 4.2 Puckered appearance of the LES in patient with classic achalasia

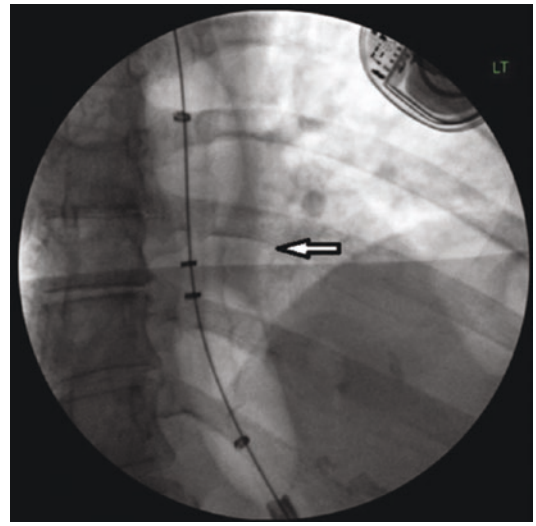


Fig. 4.3 Inflation of a 30 mm Rigiflex balloon revealing a "waist" at the EGJ. The waist is always on the left side of the balloon

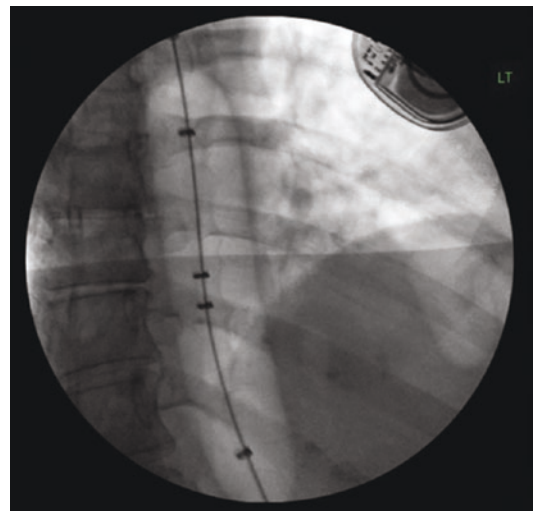


Fig. 4.4 Flattening of the "waist" following inflation of a 30 mm Rigiflex balloon

roflex view to ensure that there is no lesion suspicious for malignancy. In all instances of suspected cancer, multiple cold forceps biopsies should be performed within the distal esophagus and gastric cardia and consideration given to performing endoscopic ultrasound or chest CT scan.

After upper endoscopy is concluded, a Savary wire is placed into the stomach followed by blind passage of the Rigiflex balloon into the stomach. At that point, we change the patient's position from left lateral to supine and then initiate fluoroscopy for proper location and insufflation. It is our standard practice to start with the 30 mm balloon in the majority of our patients. In some patients, particularly younger healthy men, we may start with the 35 mm balloon because the LES is more difficult to disrupt in this population. Patients after Heller myotomy have scarring at the LES; therefore we always use a 35 mm balloon initially in this group of patients [6].

The most important part of the PD is accurate location of the balloon by fluoroscopy. We want to see the impingement on the waist caused by the non-relaxing LES on the middle portion of the balloon near the double opaque markers (Fig. 4.3). This usually occurs at the level of the diaphragm or 2–3 cm above with the exception of patients after Heller myotomy who may have the waist below the diaphragm. Once the accurate placement of balloon is confirmed fluoroscopically, the balloon is slowly distended to achieve flattening of the waist (Fig. 4.4). This usually occurs with 7–15 psi of air pressure which is held for 1 min while monitoring the balloon position fluoroscopically [6]. In other centers, the pneumatic balloon is kept distended for 15–120 seconds, and sometimes repeat dilation is performed before balloon removal. It is important for the endoscopist to secure the catheter snugly to the mouth guard as the esophagus will try to push the balloon distally into the stomach. After

completing the dilation, the air is removed with a 50 cc syringe and the balloon is removed. The presence of blood on the balloon indicates a mucosal tear but is not predictive of a successful dilation. We do not perform a repeat endoscopy immediately after PD. In our center, PD itself lasts approximately 5 min. The main elements of PD are illustrated in Fig. 4.5. Following the PD, patients are monitored for 30–60 min. We routinely obtain an upright barium esophagram before discharge to assess for esophageal perforation but not the degree of esophageal emptying. The rationale for the use of barium over the gastrografin is that the former allows for better visualization of small leaks without the fear of respiratory problems in cases of aspiration. Following the barium esophagrams, the patient receives liquids and is discharged with our cell phone number, in case other problems arise. Patients may travel distances if required; however, we advise them to stay locally for one night to ensure that they can be transferred to our hospital if they develop any complications. We evaluate all our patients in 4–6 weeks after pneumatic dilation with assessment of symptoms and esophageal emptying by TBE. Repeat high-resolution esophageal manometry is rarely performed. In patients with persistent symptoms, especially in conjunction with poor esophageal emptying on TBE, we recommend repeat PD with the next larger balloon. We repeat PD until either satisfactory symptom relief or failure to respond to the largest 40 mm balloon occurs. All patients without response to PD with the 40 mm balloon are referred for Heller myotomy.

Complications After Pneumatic Dilation

Contraindications to PD are poor cardiopulmonary status or other comorbid illnesses that would prevent surgery should an esophageal perforation occur. For these sicker patients, botulinum toxin injections might be the better treatment. Up to 33% of patients have complications during or after PD, although most are minor including chest pain, aspiration pneumonia, fever, painful mucosal tears without perforation, and hematoma [10]. Esophageal perforation is the most serious complication with an overall rate in experienced hands of 1.9% (range 0–16%) of which 50% require surgery. Small perforations and deep, painful tears may be treated conservatively with antibiotics and sometimes esophageal stents. However, surgical repair through a thoracotomy is best for large perforations with extensive soilage of the mediastinum. Most perforations occur

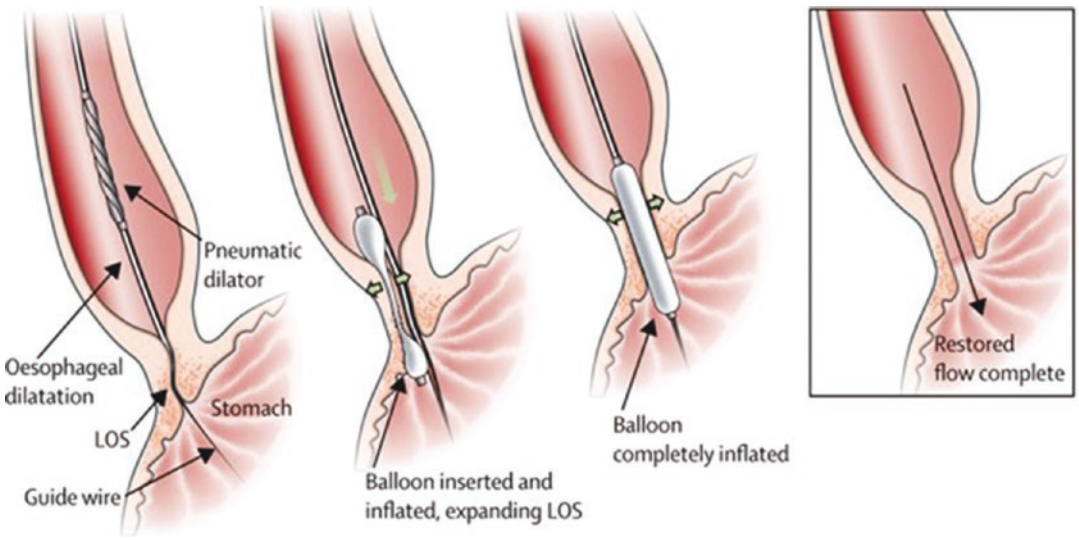


Fig. 4.5 Pneumatic dilatation with the Rigiflex system. (Reprinted with permission © Lancet Publishing Group [2])

during the initial dilation; difficulty keeping the balloon in position is a potential risk factor [2]. Although no other predictors for perforation have been identified, the European Achalasia Trial did report four perforations, mostly in older patients, when the first PD was done with a 35 mm compared with a 30 mm balloon [2]. Severe GERD is infrequent after PD, but 15–35% of patients have heartburn, which improves with proton-pump inhibitors [11].

Long-Term Success of Pneumatic Dilation

Repeated series from throughout the world confirm the effectiveness of PD for the treatment of achalasia. In a review of more than 1100 patients (24 studies) with an average follow-up of 37 months [11], Rigiflex pneumatic dilation resulted in good to excellent symptom relief in 74%, 86%, and 90% of patients treated with 30, 35, and 40 mm balloons, respectively. Consistent across these studies after 4–6 years, approximately 30 to 40% have symptom relapses (Fig. 4.6) [12, 13]; however, long-term remission can be achieved in nearly all these patients by repeat dilation by an on-demand strategy based on symptom relapse [14]. This approach is particularly popular in Europe and Australia with centers very experienced in PD and the lack of monetary incentives to pursue surgical myotomy [12, 14, 15]. In the senior author's experience, a single PD has been successful in several women up to 15 years and one young man for 22 years.

With the widespread use of Rigiflex balloons, we are beginning to identify risk factors for relapse after PD. These are mainly young age (<40 years), male gender, single dilation with a 3.0 cm balloon, posttreatment LES pressure > 10–15 mmHg, poor esophageal emptying on an upright barium esophagram, and type III achalasia pattern on high-resolution manometry [13, 16–21]. PD is the most cost-effective treatment for achalasia over a time period of 5 to 10 years [22, 23].

Pneumatic Dilation vs. Surgical Myotomy

Until recently, addressing the question of whether to choose PD or surgical myotomy was difficult because large prospective randomized trials were not available. The best data was from a large retrospective longitudinal study from the province of Ontario, Canada [24]. From 1991 to 2002, nearly 1500 patients were treated for

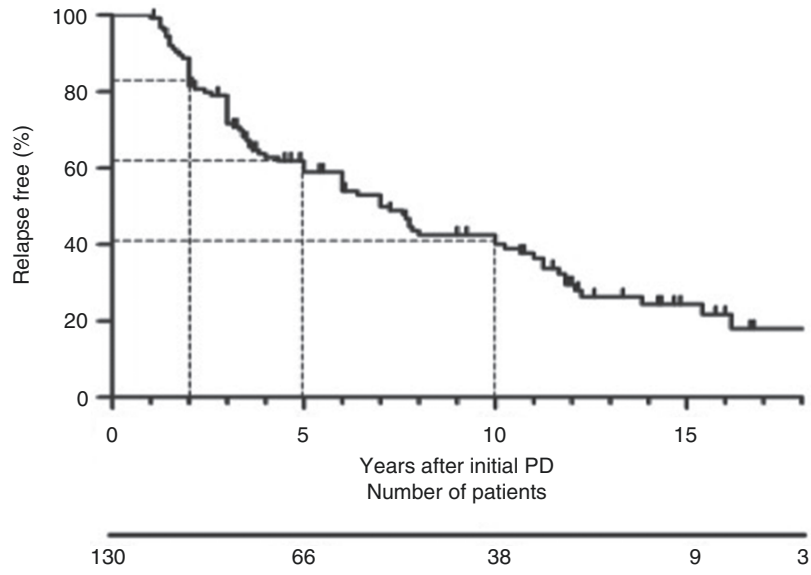


Fig. 4.6 Long-term outcome for pneumatic dilation for achalasia. 18-year experience from a single Australian center. Cumulative relapse rates for a cohort of 130 patients. Relapse rates were 18% by 2 years, 41% by 5 years, and 60% by 10 years. (Reprinted with permission © Blackwell Publishing Ltd. [15])

achalasia: 81% had PD and 19% had surgical myotomy as their first treatment. The cumulative risk of any subsequent treatment after 1, 5, and 10 years was 37%, 56%, and 64% after pneumatic dilation as compared to 16%, 30%, and 38% after surgical myotomy, respectively. In this scenario, repeat PD was recorded as a subsequent treatment.

In 2011, a prospective randomized comparative study was published comparing PD and laparoscopic myotomy performed by physicians highly skilled in both procedures. In the European Achalasia Trial [25], patients from five countries were randomized to Rigiflex PD (N = 94, 30, and 35 mm with up to three repeat dilations allowed) or surgical myotomy with Dor fundoplication. Both treatments had comparable success at 2 years as assessed by symptoms, LES pressure, and barium emptying: 86% for PD and 90% for myotomy. Preexisting daily chest pain, esophageal width less than 4 cm before treatment, and poor esophageal emptying posttreatment were identified as predictors of PD treatment failure. Twenty-three patients had a recurrence of symptoms requiring redilation, which was not successful in five patients. Later re-analysis of this study found PD and myotomy equivalent treatments for type I and II achalasia, while surgery was superior in type III achalasia [26].

This study continues to follow both groups with a recent report of the 5-year data (Fig. 4.7) [27]. In the full analysis set, there was no significant difference in success rates with 84% for surgical myotomy and 82% for PD. Redilation was performed in 24 (25%) of the PD patients. Younger age (<40 years), a width < 4 cm of the esophagus, and type III achalasia were identified as independent risk factors for redilation.

In contrast, a preliminary report of a European randomized trial of peroral endoscopic myotomy vs. PD found marked superiority of this new surgical procedure over 2 years [28]. A total of 130 patients were randomly assigned to POEM (64) or PD (66). Intention-to-treat analysis revealed a significantly higher

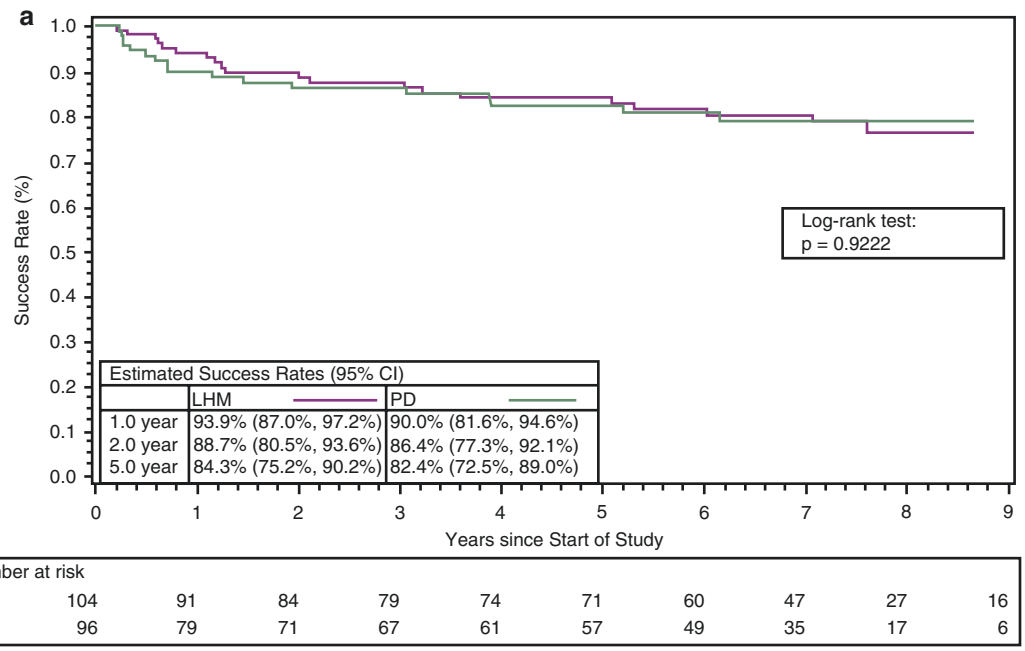


Fig. 4.7 Kaplan-Meir curves for the rate of treatment success over 5 years in the European Achalasia Trial. The survival curves show the rate of treatment success with pneumatic dilation (PD) compared with laparoscopic Heller myotomy (LHM) in the fall analysis set. (Reprinted with permission © British Medical Association [27])

Table 4.1 Treatment algorithm for naïve achalasia based on Chicago Classification

Type I or II achalasia			Type III achalasia
Pneumatic dilation	*Heller myotomy*	*POEM*	*POEM*
Less morbidity/cost	Equal to PD in RCT	Highly effective in short-term RCT	Only procedure to adequately cut the length of the spasms
Expect repeated dilations over years	Effective across all ages/genders	Minimal pain	Avoids chest operation
Equal to HM in RCT	Preferred with megaesophagus, diverticulum, or hiatal hernia	Lots of GERD (>50%)	Superior to PD and HM
Older women may do best	More GERD	Insurance issues	Insurance issues
Minimal GERD			

HM Heller myotomy
RCT Randomized controlled trial
GERD Gastroesophageal reflux disease

success rate for POEM (92%) compared to PD (54%) ($p < 0.001$). However, this study was very restrictive on the use of repeat PD defining failures if symptoms did not improve after 30 and 35 mm balloons.

Role of Pneumatic Dilation in Management of Achalasia

In accordance with societal guidelines [1, 2], healthy patients with achalasia should be given the option of pneumatic dilation or surgical myotomy (laparoscopic Heller myotomy or POEM). The advantages of PD to surgery includes an outpatient procedure, minimal pain, return to work next day, mild, if any GERD, and can be performed in any age group and during pregnancy. PD does not hinder future myotomy and all cost analyses find it less expensive than surgical myotomy. The major barrier for PD, at least in the United States, is fewer and fewer gastroenterologists are performing this relatively simple procedure. Fear of having a perforation may be one factor and increased availability of surgical myotomy is likely another. Most PDs now are being done in esophageal centers of excellence in a multidisciplinary team approach. In this setting, we perform 50–60 procedures a year primarily in achalasia patients but more recently have expanded indication to esophagogastric junction (EGJ) outflow obstruction, distal esophageal spasm, and tight Nissen fundoplication.

Refer to Table 4.1 for a general consensus shared by most esophagologists for the treatment of the three types of achalasia. Type I and II respond well to both PD and surgical myotomy. I personally prefer PD in my older patients and women where my results are very similar to myotomy. Young patients (<40 years) and men seem to do better with surgery. Both options are reviewed with the patients and they take an active part in selecting their initial treatment. For Type III achalasia, we all perform POEM, but insurance coverage is a major issue in many areas of the country.

About 15% of our PDs are performed in patients with incomplete myotomy as the cause of failure after surgical Heller myotomy or POEM. In this setting, we begin with the 35 mm balloon progressing then to the 40 mm size with an overall success rate of about 50% [29]. For the elderly frail patients, botulinum toxin injections are the preferred initial treatment in the United States. However, Europeans are very comfortable going directly to PD in high-volume centers with surgical expertise should the rare complication occur [3]. My oldest patient undergoing PD was 91, did well, and was very grateful. Therefore, PD has wide application for the treatment of achalasia when performed by gastroenterologists and surgeons skilled and comfortable with the procedure.

Conflict of Interest The authors have no conflicts of interest to declare.

References

1. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108:1238–49; quiz 1250.
2. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet. 2014;383:83–93.
3. Richter JE, Boeckxstaens GE. Management of achalasia: surgery or pneumatic dilation. Gut. 2011;60:869–76.
4. Borhan-Manesh KMJ, Taghavi AR. The efficacy of ballooon dilation in achalasia is the result of stretching of the lower esophagal sphincter, not muscular disruption. Dis Esophagus. 2016;29:262–6.
5. Richter JE. Achalasia. In: Castell DO, Richter JE, editors. The Esophagus. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. p. 220–61.
6. Jacobs J, Richter JE. Opening the bird's beak: tips and tricks for effective pneumatic dilation for achalasia. Am J Gastroenterol. 2016;111:157–8.
7. Kahrilas PJ, Bredenoord AJ, Fox M, et al. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015;27:160–74.
8. de Oliveira JM, Birgisson S, Doinoff C, et al. Timed barium swallow: a simple technique for evaluating esophageal emptying in patients with achalasia. AJR Am J Roentgenol. 1997;169:473–9.
9. Blonski W, Kumar A, Feldman J, et al. Timed barium swallow: diagnostic role and predictive value in untreated achalasia, esophagogastric junction outflow obstruction, and non-achalasia dysphagia. Am J Gastroenterol. 2018;113:196–203.
10. Katzka DA, Castell DO. Review article: An analysis of the efficacy, perforation rates and methods used for pneumatic dilation of the esophagus. Aliment Pharmacol Ther. 2011;34:832–9.
11. Richter JE. Update on the management of achalasia: balloons, surgery and drugs. Expert Rev Gastroenterol Hepatol. 2008;2:435–45.
12. Hulselmans M, Vanuytsel T, Degreef T, et al. Long-term outcome of pneumatic dilation in the treatment of achalasia. Clin Gastroenterol Hepatol. 2010;8:30–5.
13. Vela MF, Richter JE, Khandwala F, et al. The long-term efficacy of pneumatic dilation and Heller myotomy for the treatment of achalasia. Clin Gastroenterol Hepatol. 2006;4:580–7.
14. Zerbid F, Thetiot V, Richey F, et al. Repeated pneumatic dilations as long-term maintenance therapy for esophageal achalasia. Am J Gastroenterol. 2006;101:692–7.
15. Elliot TR, Wu PI, Fuentalba S, et al. Long-term outcome following pneumatic dilation as initial therapy for idiopathic achalasia: An 18 year single center experience. Aliment Pharmacol Ther. 2013;37:1210–9.
16. Vantrappen G, Hellemans J, Deloof W, et al. Treatment of achalasia with pneumatic dilatations. Gut. 1971;12:268–75.
17. Eckardt VF, Aignherr C, Bernhard G. Predictors of outcome in patients with achalasia treated by pneumatic dilation. Gastroenterology. 1992;103:1732–8.
18. Eckardt VF, Kanzler G, Westermeier T. Complications and their impact after pneumatic dilation for achalasia: prospective long-term follow-up study. Gastrointest Endosc. 1997;45:349–53.
19. Vaezi MF, Baker ME, Achkar E, et al. Timed barium oesophagram: better predictor of long term success after pneumatic dilation in achalasia than symptom assessment. Gut. 2002;50:765–70.
20. Ghoshal UC, Kumar S, Saraswat VA, et al. Long-term follow-up after pneumatic dilation for achalasia cardia: factors associated with treatment failure and recurrence. Am J Gastroenterol. 2004;99:2304–10.
21. Pandolfino JE, Kwiatek MA, Nealis T, et al. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology. 2008;135:1526–33.
22. O'Connor JB, Singer ME, Imperiale TF, et al. The cost-effectiveness of treatment strategies for achalasia. Dig Dis Sci. 2002;47:1516–25.
23. Karanicolas PJ, Smith SE, Inculet RI, et al. The cost of laparoscopic myotomy vs pneumatic dilation for esophageal achalasia. Surg Endosc. 2007;21:1198–206.
24. Lopushinsky SR, Urbach DR. Pneumatic dilation and surgical myotomy for achalasia. JAMA. 2006;296:2227–33.
25. Boeckxstaens GE, Annese V, Bruley des Varannes S, et al. Pneumatic dilation vs laparscopic Heller myotomy for idiopathic achalasia. NEJM. 2011;364:1807–16.
26. Rohof WO, Salvador R, Annese V, et al. Outcome of treatment achalasia depends on manometric subtype. Gastroenterology. 2013;144:718–25.
27. Moonen A, Annese V, Belmaus A, et al. Long-term results of the European achalasia trial: A multicenter randomized controlled trial comparing pneumatic dilation vs laparoscopic Heller myotomy. Gut. 2016;65:732–9.
28. Ponds F, Fochens P, Lei A, et al. Effect of peroral endoscopic myotomy versus pneumatic dilation on symptom severity and treatment of naïve patients with achalasia: A randomized controlled trial. JAMA. 2019;322:134–44.
29. Guardino J, Vela M, Conner J, et al. Pneumatic dilation for the treatment of achalasia in untreated achalasia and after failed Heller myotomy. J Clin Gastroenterol. 2004;38:855–60.

Per-oral Endoscopic Myotomy

5

Amy L. Holmstrom and Eric S. Hungness

Abbreviations

EGD	esophagogastroduodenoscopy
EGJ	esophagogastric junction
ESD	endoscopic submucosal dissection
GERD	gastroesophageal reflux disease
HRM	high-resolution manometry
POEM	per-oral endoscopic myotomy
TBE	time barium esophagram

Introduction

Minimally invasive surgery has evolved over the past four decades with the advancement of video, fluoroscopic, and fiber-optic technologies allowing for performance of intraluminal procedures of the gastrointestinal, vascular, respiratory, and genitourinary systems. Over the same period, the development and refinement of laparoscopic and thoracoscopic techniques have allowed for safe and less invasive alternatives to traditional open surgical procedures. These technologies have allowed interventions to be performed with significantly less morbidity to the patient without sacrificing outcomes. Interventions in the submucosal space or so-called third space are the latest in the innovation and advancements of minimally invasive techniques [1].

The submucosal space is the area between the mucosa and muscularis of the alimentary tract. This space can be accessed by using a common interventional endoscopic technique known as the saline lift. Endoscopists frequently use this technique to separate the mucosa from the underlying muscular layer in order to remove mucosal-based polyps or lesions. Pasricha and colleagues were the first to utilize the space created by the injection of fluid as an entry point into the submucosal space in 2007 when they performed a submucosal myotomy in an animal model [2]. The first clinical application in humans was published by Inoue and colleagues in 2010 with their results after per-oral endoscopic myotomy (POEM) for the treatment of achalasia [3]. Third space endoscopy is now used for the treatment of a variety of gastrointestinal pathologies; however, it was the refinement of the POEM procedure that realized the potential for successful endoscopic interventions in this space.

This chapter will be a review of the POEM procedure, including a discussion of perioperative workup and care, technical aspects of the procedure, and outcomes data.

A. L. Holmstrom · E. S. Hungness (✉)
Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL, USA
e-mail: Eric.hungness@nm.org

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_5

Indications and Alternative Therapies

Per-oral endoscopic myotomy is an accepted procedure used most commonly to treat achalasia and a subset of similar esophageal motility disorders such as distal esophageal spasm, jackhammer esophagus, and esophagogastric junction outflow obstruction. Achalasia is a rare disease of esophageal motility resulting from neuron loss in the esophageal myenteric plexus [4]. This leads to failure of both esophageal body peristalsis and relaxation of the lower esophageal sphincter during a swallow that normally allows passage of a food bolus. This pathology is thought to be due to an irreversible, immune-mediated process. This disease causes afflicted patients' symptoms of chest pain, weight loss, regurgitation, and progressive dysphagia. A high index of suspicion is necessary for diagnosis of achalasia as its prevalence of 1–2 cases per 100,000 people means the average primary care practitioner will rarely encounter this disease in their practice, which may result in significant delays in diagnosis [5, 6]. There are multiple treatment modalities available for patients with achalasia. These treatments aim to either relax, stretch, or disrupt the lower esophageal sphincter muscles in order to allow for easier passage of esophageal contents into the stomach. Botox injection has been used to decrease the pressure of the lower esophageal sphincter, though symptomatic relief is only temporary and repeated injections increase risk of scar tissue making future interventions more challenging. Endoscopic pneumatic dilation is another incisionless and short-lived therapy that involves inflation of a balloon across the esophagogastric junction (EGJ) which stretches the sphincter muscles [7, 8]. Similar to Botox injections, balloon dilations are able to be repeated once the symptomatic relief wears off. The more invasive and effective option is a Heller myotomy, a surgical procedure that is typically performed laparoscopically and involves controlled longitudinal division of the lower esophageal sphincter muscular complex [9, 10]. With the advances in submucosal surgery, POEM became an option that combines the advantages of the previous two interventions, as it is an endoscopic approach to permanent division of the lower esophageal sphincter muscle.

Preoperative Evaluation

Given the rarity of achalasia and similar esophageal disorders, it is important that a thorough and complete workup is performed to ensure accurate diagnosis. This is best performed at a tertiary or quaternary care center with significant achalasia experience and volume, at which a multidisciplinary team will review the various diagnostic tests and discuss appropriate management.

Symptom Evaluation

As with any preoperative encounter, a complete history and physical exam should be performed focusing on symptomatology commonly associated with achalasia. A scoring system, the Eckardt symptom score, was developed to assist with diagnosis of achalasia (see Table 5.1) [11]. This is a validated symptom assessment tool that uses a three-point rating scale across four symptom domains: weight loss, chest pain, regurgitation, and dysphagia. The sum of each domain score results in an overall score of 0–12, with higher scores representing more severe disease. This tool can be used postoperatively to assess symptom outcomes; however, significant variability within the chest pain and weight loss domains have recently led to questions about the reliability of this system [12]. Patients who have undergone

Table 5.1 Eckardt symptom score composed of four domains with summative scores ranging from 0–12

Symptom		Weight Loss (kg)	Dysphagia	Regurgitation	Chest Pain
Score	0	None	None	None	None
	1	<5	Occasional	Occasional	Occasional
	2	5–10	Daily	Daily	Daily
	3	>10	With every meal	With every meal	Several times/day

prior Botox injections and/or dilations will have increased procedural risk as they are more likely to have scar tissue making submucosal tunneling more challenging. In those patients who have undergone a prior myotomy, it is especially important to obtain the operative report for review if the procedure was performed by another endoscopist or at a different institution. Tunneling and myotomy should be performed at a different location than the prior intervention.

Imaging and Diagnostic Testing

Diagnostic tests and imaging are vitally important for establishing the diagnosis and ruling out alternative causes of presenting symptoms such as severe gastroesophageal reflux, peptic stricture, an obstructing mass, or pseudo-achalasia. The first step in ruling out many of these alternative etiologies is performance of flexible endoscopy. Patients with a negative endoscopy should then undergo a high-resolution manometry (HRM) to diagnose achalasia or other esophageal motility disorders. The Chicago Classification v3.0 stratifies the types of achalasia based on results from HRM [13, 14]. Finally, a timed barium esophagram (TBE) is useful for anatomical evaluation preoperatively [15]. Significant dilation, tortuosity, and gastroesophageal junction angulation contribute to increased technical challenge of POEM. Additionally, detection of a hiatal hernia on endoscopy or esophagram would lead to reconsideration of the operative approach to a myotomy as this condition would predispose patients to increased risk of post-POEM reflux. A laparoscopic approach would allow for simultaneous hiatal hernia repair, myotomy, and antireflux procedure and would therefore be the preferred intervention for those patients found to have a concurrent hiatal hernia.

Operative Technique

POEM is an intervention in the submucosal space that uses a submucosal lift technique followed by endoscopic submucosal dissection (ESD) to create a submucosal flap or tunnel. The tunnel allows for the mucosal layer to remain intact over the area of muscular disruption, protecting the mediastinum and peritoneum from contact with gastrointestinal luminal contents. Following completion of the endoscopic submucosal myotomy, the tunnel entry point is closed, and the procedure is completed with no external incisions on the patient. Several technical variants to the performance of this procedure have been described, and this chapter will discuss our institutional practice, which is similar to Inoue and colleagues [3]. Complications are best avoided when practitioners employ methods most familiar to their practice in addition to strict adherence to the fundamental principles of surgery.

Preparation for POEM

In preparation for the procedure, the patient receives a 7-day course of oral fluconazole leading up to the procedure. Patients with achalasia are at a higher risk of having esophageal candidiasis, the presence of which would result in cancellation of the procedure. The patient is also instructed to maintain a clear liquid diet for the 2 days immediately preceding his/her myotomy in addition to the standard nil per os status the night prior to avoid extensive retained food which could also cause procedural delay. POEM should be performed by a specialized team of care providers in an operating room or advanced endoscopy suite. Endoscopic equipment in addition to instruments necessary for rapid decompression of the chest or abdomen should be readily available at the time of the procedure. In our practice, the patient is positioned supine on the operating room table. The anesthesia team performs rapid sequence endotracheal intubation for all of these patients because their pathology places them at high risk for retained esophageal contents and, therefore, aspiration at the time of induction of anesthesia. In the case of a known or presumed difficult airway, fiber-optic intubation is performed.

Endoscopy

Following successful intubation, a flexible endoscopy is performed using a standard high-definition endoscope with carbon dioxide insufflation. Occasionally, an esophageal overtube is used for assistance with the extremely dilated esophagus. In order to prevent hemodynamic compromise in the event of accidental entrance into the mediastinal or peritoneal cavity, air insufflation must be turned off. A diagnostic endoscopy allows for irrigation and suctioning of the esophagus and stomach as needed, and evaluation for Candida esophagitis or significant solid food burden, which, when encountered, results in abortion of the procedure. If the esophagus is adequately clear, the scope shaft is then used to take measurements from the incisors at the mouth to the squamocolumnar junction of the EGJ. These measurements are used during the operation to maintain awareness of scope location and also assess progress during the myotomy to ensure adequate dissection. Some centers inject blue dye into the submucosa of the anterior lesser curvature of the stomach, 2–3 cm distal to the EGJ, in an effort to assist with identification of the endpoint of the submucosal dissection. This provides an additional visual cue to the endoscopist to ensure that the myotomy will extend across the entirety of the lower esophageal sphincter and onto the gastric wall but may predispose to distal mucosal injury.

Submucosal Injection and Mucosotomy

The initial site for mucosotomy and tunneling is chosen based on the patient's prior interventions. Our institution prefers to perform an anterior myotomy and reserves the posterior approach for those patients who have had a prior anterior myotomy. The position for initial submucosal dissection is therefore typically chosen on the anterior esophagus at a 12 to 1 o'clock position approximately 4–6 cm proximal to the planned starting point of the myotomy. An endoscopic injection needle is used to create a submucosal lift or bleb. This technique allows for hydrodissection of the submucosal space by lifting the mucosa off of the underlying muscular layer. The solution used for injection is typically saline based but can also be a solution that is less easily absorbed such as hydroxypropyl methylcellulose or sodium hyaluronate. Next, a longitudinal mucosotomy is performed through the lifted mucosa with an endoscopic cautery knife on cut mode in order to reduce thermal spread (Fig. 5.1a**).** The endoscope is fitted with an angled, transparent dissecting cap and is then used to bluntly enter the submucosal space through the mucosotomy.

Submucosal Dissection and Tunneling

Once the endoscope is in the submucosal tunnel, the dissecting cap places the fibers between the layers on stretch, which facilitates dissection (Fig. 5.1b).The endoscopist proceeds with electrocautery dissection caudally utilizing a specialized ESD electrosurgical knife. Most centers use either the Olympus triangle tip knife, or the Erbe hybrid knife. Additional saline injections along the path of the tunnel are performed to assist with endoscopic dissection. To prevent spiraling and maintain orientation while in the confined space of the submucosal tunnel, it is important to maintain the circular muscle layer in the anterior position at all times during dissection. This also helps to prevent injury to the mucosa by allowing the mucosal flap to remain posterior while dissecting anteriorly close to the muscle fibers. Dissection in the submucosal tunnel should proceed until about 3 cm onto the gastric wall. The EGJ can be identified during the submucosal dissection in several ways, narrowing of the tunnel and mucosa/muscle interface, visualization of palisading or large caliber blood vessels and the disorganized, oblique muscular fibers of the stomach, and comparison of scope position to pre-dissection endoscopic measurements, and a final confirmatory option is the use of a second endoscope to visualize positioning of the tunneled scope via retroflexion [16]. Extra care

should be taken during dissection at the EGJ as this is the most common location for inadvertent mucosal injury (Fig. 5.1c) [17].

Myotomy

Once the submucosal tunnel across the EGJ is completed, the myotomy is performed. The length of the myotomy depends on a number of factors including the indication, the degree of esophageal dilation, and the Chicago Classification in the case of patients diagnosed with achalasia. Patients with Type III achalasia may benefit from a longer tunnel in order to perform a tailored extended myotomy based on findings on preoperative HRM [18, 19]. Our institution performs a selective myotomy of the circular muscle fibers of the muscularis propria with preservation of the longitudinal fibers (Fig. 5.1d). The selective myotomy technique helps protect the mediastinal structures and is

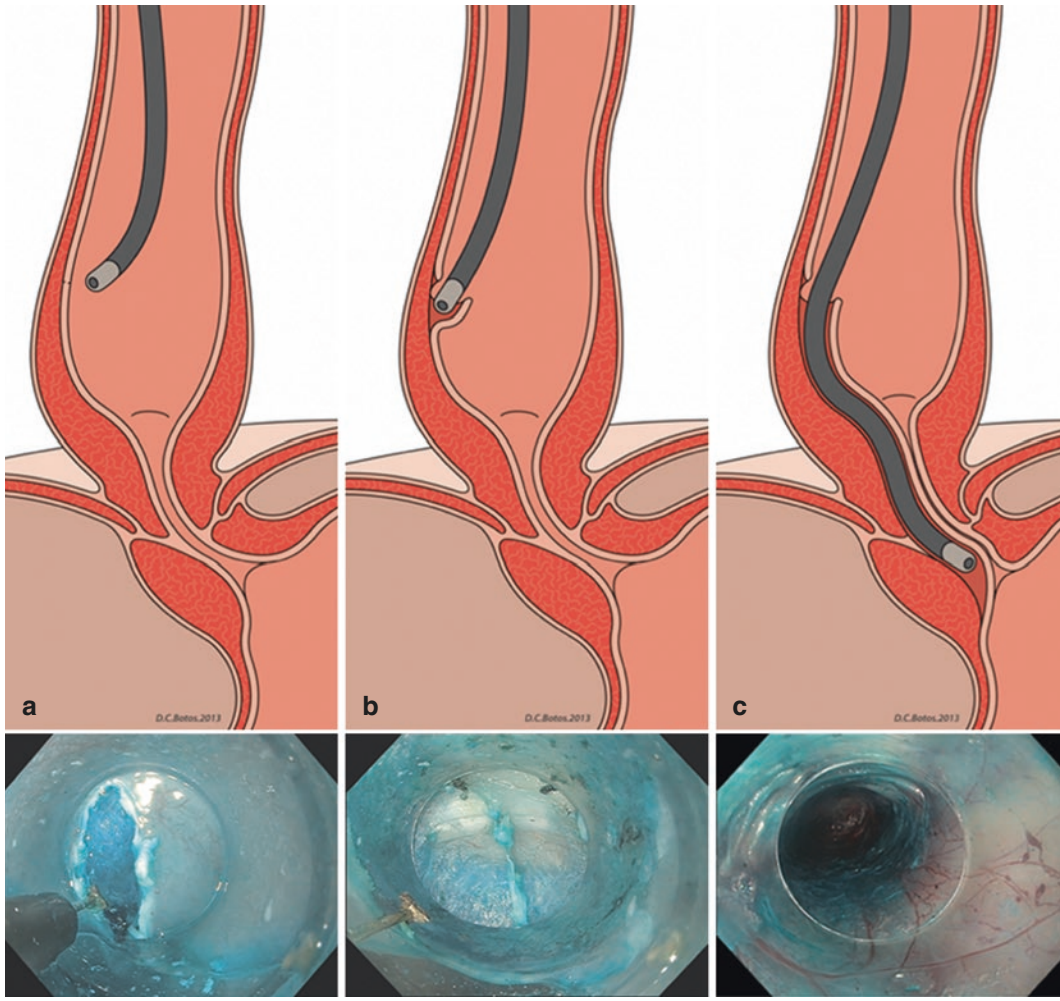


Fig. 5.1 Animated steps of per-oral endoscopic myotomy with representative endoscopic images (**a**) Mucosotomy. (**b**) Entry into the submucosal space with a clear dissecting cap. The muscle is oriented anteriorly or superior on the image and the mucosa is oriented posteriorly or inferior on the image. (**c**) Completion of endoscopic submucosal dissection and tunneling. (**d**) Beginning of myotomy of the circular muscle fibers. (**e**) Completed myotomy. (**f**) Closure of the mucosotomy with clips. (Animations reproduced with permission © Wolters Kluwer Health [20])

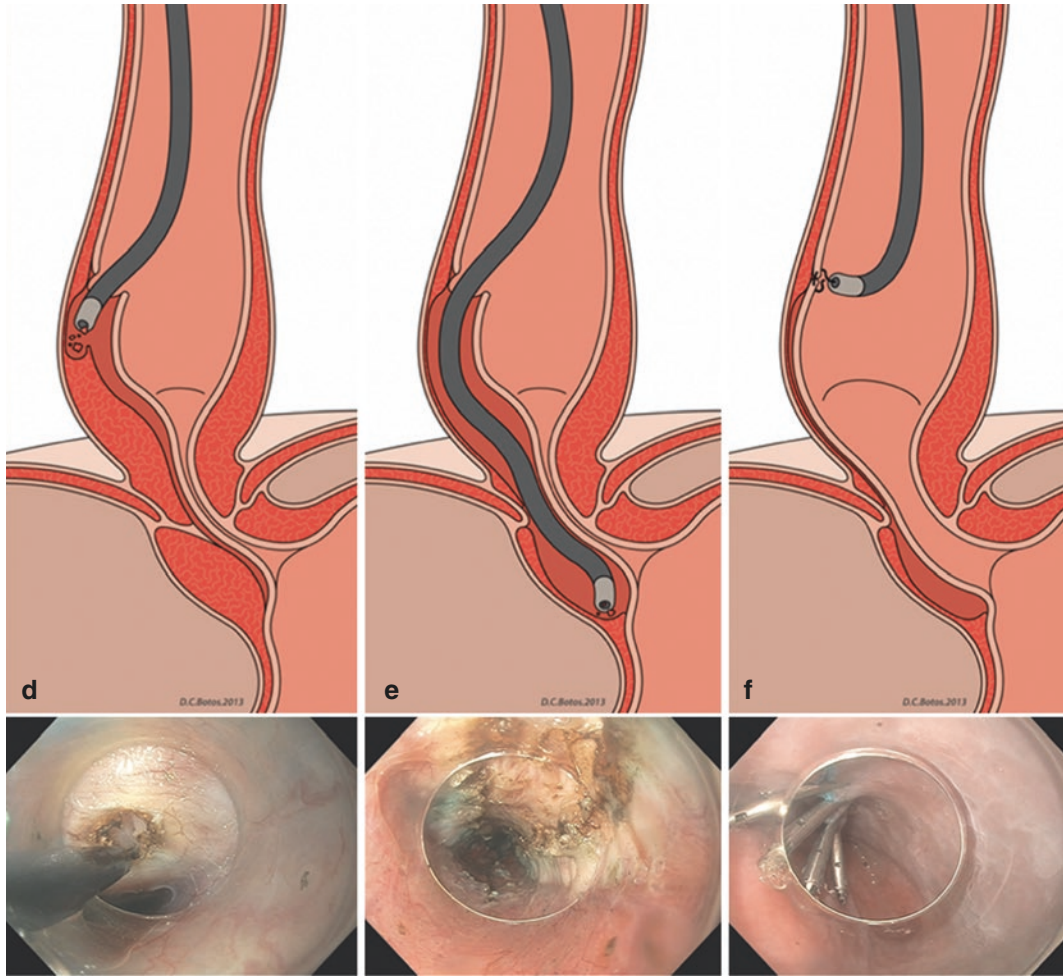


Fig. 5.1 (continued)

thought to potentially lower the rates of post-myotomy reflux. The myotomy should begin at a position 6 cm proximal to the squamocolumnar junction and extend across the EGJ, 2–3 cm onto the stomach. During division of the circular fibers, the longitudinal muscle fibers will be seen underneath, but are typically quite thin and often get splayed or divided (Fig. 5.1e).

Closure

Following completion of the myotomy, the endoscope is removed from the submucosal tunnel. The mucosotomy is closed with clips, which provide an efficient and secure closure (Fig. 5.1f). A sutured repair with an endoscopic suturing device is an alternative closure technique that some centers employ.

Complications

POEM, when performed by experienced practitioners, has low rates of associated complications [20]. However, there is a significant learning curve associated with performance of this procedure, even for advanced endoscopists, as operating in the submucosal space is still an emerging technique. Perioperative complications, such as mucosal perforations and increased operative time, have been shown to be associated with the

operator learning curve [17, 21]. It is therefore recommended that the POEM novice first spend time observing an experienced practitioner, followed by deliberate practice in simulation, cadaveric, and live animal models, in order to ensure proficiency with each step of the operation [22]. Finally, they may graduate to supervised performance and, ultimately, independent performance of the POEM procedure. Only experienced interventional endoscopists who will have significant volume of cases should perform POEMs.

Bleeding is a common intraoperative complication that can make visualization in the small working space of the submucosal tunnel challenging. When bleeding is encountered, the operator must exercise control and diligence to achieve hemostasis. Mild bleeding can often be controlled with electrocautery, but when larger vessels are encountered, a coagulation grasper should be utilized. Bleeding that obscures visualization requires the use of irrigation through either an external system or one of the dual ESD/irrigation tools. The use of dilute epinephrine solution within the tunnel has also been described [23]. External pressure may also be applied requiring withdrawal of the endoscope from the submucosal tunnel and direct pressure to the tunnel from the intraluminal side. The use of intraluminal balloons such as those used for bleeding varices should be absolutely avoided given the risk of esophageal perforation in the setting of a new myotomy. Significant bleeding requiring conversion to a laparoscopic or open operation, or the transfusion of blood products is exceedingly rare. Close communication with anesthesia to ensure that the patient's systolic blood pressure is maintained below 120 mmHg for the duration of the operation will help minimize engorgement of the delicate submucosal vessels.

Capnoperitoneum is a relatively common intraoperative event occurring in 20–40% of cases [21, 24]. However, it should not be considered a true complication unless it goes unrecognized and leads to abdominal compartment syndrome. Capnoperitoneum is diagnosed when progressive abdominal distension occurs despite adequate gastric decompression. A Veress needle should be used for abdominal decompression in these cases, which is a simple and effective treatment. Capnothorax is uncommon and when encountered, resulting hemodynamic compromise is extremely unlikely [25, 26]. However, we still recommend tools necessary for rapid decompression of the chest be readily available during performance of a POEM.

Postoperative Care

Routine postoperative care following POEM may vary slightly depending on institution. Our institutional practice following POEM is to allow a clear liquid diet on the evening of postoperative day zero as long as the patient is not affected by postoperative nausea. All patients are discharged on a proton-pump inhibitor that continues until six months postoperatively at which time, formal pH testing is performed. Patients are typically discharged on postoperative day one; however, some patients may feel well enough to leave on the day of surgery. Some centers are moving toward outpatient, same-day discharge for POEMs due to the brief recovery period. We allow advancement to a mechanical soft diet 1 week following surgery and solid foods 3 to 4 weeks postoperatively. Routine outpatient follow-up commences at two to four weeks and subsequently six months at which time, in addition to pH testing, patients undergo symptom assessment, endoscopy, HRM, and a TBE. Due to the low specificity for clinically relevant complications, our institution no longer obtains an immediate postoperative esophagram; however, we would recommend routine use in the early POEM experiences for the novice practitioner [27].

Outcomes

POEM has been refined over the past decade since it was first used clinically in 2008. The procedure has been shown to be safe and effective with a perioperative complication profile similar to standard of care interventions [20, 28–31]. As previously discussed, the vast majority of perioperative complications arise while

the endoscopist is in the early stages of the learning curve [17, 20, 23]. Major complications such as esophageal perforation, pneumothorax, or complications requiring reintervention occur in less than 1% of patients [32]. POEM has also been shown to have a significant reduction in convalescence period when compared to laparoscopic Heller myotomy that results in shorter hospital length of stay [20, 33–36]. As already mentioned, some centers have even transitioned to performing POEM as an outpatient procedure with same-day discharge.

Symptomatic improvement following POEM has been demonstrated as comparable to standard of care treatments with excellent improvement in dysphagia and regurgitation in the short- and moderate-term [30, 33, 37–39]. Follow-up at 1–2 years showed symptomatic success (Eckardt score ≤ 3) in 90–95% of patients. This success remained over 80% at five years, which is comparable to the five-year outcomes of laparoscopic Heller myotomy and pneumatic dilation [7, 24, 30, 40]. Several studies have shown that POEM may offer superior symptomatic outcomes for patients with Type III achalasia due to its ability to perform an extended proximal esophageal myotomy compared to LHM [18, 19].

Physiologic parameters have also been demonstrated to be improved following POEM. Basal EGJ pressure as measured on HRM was shown to be significantly reduced [40–42]. Postoperative impedance planimetry demonstrated sustained reductions in the EGJ distensibility index [43]. Timed barium esophagram revealed improvements in barium retention [44]. Monitoring of physiologic parameters by EGD, HRM, and TBE is encouraged at 2- to 3-year intervals postoperatively.

Post-myotomy gastroesophageal reflux disease (GERD) was an early concern for POEM. Heller myotomy employs a partial fundoplication following myotomy to minimize postoperative reflux, while POEM has no such anti-reflux component. However, a theorized advantage to POEM is the lack of surgical disruption of the body's natural anti-reflux anatomy, namely, the angle of His and the phrenoesophageal ligament. GERD has multiple clinical assessment tools including subjective symptom questionnaires and objective measurements such as pH monitors and endoscopic evaluation. There is no standardization among centers regarding which evaluative measures to use, which limits comparative studies across institutions. An additional complicating factor remains the challenge of patient compliance with postoperative physiologic studies [20, 34, 40]. The most robust long-term outcomes data have estimated rates of GERD symptoms post-POEM at 20–30% [23]. The rates of endoscopic esophagitis and positive pH studies were higher at 30–56% and 40–60%, respectively [23]. These values are slightly higher compared to rates of reflux after LHM with partial fundoplication, which are reported at 21–42% in well-controlled studies [8, 45]. Fortunately, post-myotomy reflux is readily controlled on an anti-secretory medication and in long-term follow-up rarely requires intervention [28, 40].

Conclusion

POEM is a procedure that evolved from advances in endoscopic interventions and the advent of submucosal surgery. Over the past decade, POEM has been shown to be a safe and effective procedure for the treatment of achalasia. Due to the rarity of achalasia, POEM should remain a procedure performed at high-volume tertiary and quaternary care centers by advanced interventional endoscopists. Novice proceduralists who wish to perform this procedure should undergo graduated introduction to POEM to minimize learning curve-associated complications. Robust short- and moderate-term outcomes data rival current standard of care therapies. Long-term data is emerging from several centers of excellence with encouraging results. Patients have already begun to seek out POEM over Heller myotomy due to the advantages of a shorter convalescence period with preserved effectiveness and durability. As more long-term data is published, POEM might become the preferred initial treatment of achalasia and similar esophageal motility disorders.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Teitelbaum EN, Swanstrom LL. Submucosal surgery: novel interventions in the third space. Lancet Gastroenterol Hepatol. 2018;3(2):134–40.
2. Pasricha PJ, Hawari R, Ahmed I, Chen J, Cotton PB, Hawes RH, et al. Submucosal endoscopic esophageal myotomy: a novel experimental approach for the treatment of achalasia. Endoscopy. 2007;39(9):761–4.
3. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71.
4. Goldblum JRWR, Orringer MB, Appelman HD. Achalasia. A morphologic study of 42 resected specimens. Am J Surg Pathol. 1994;4(18):327–37.
5. Sadowski DC, Ackah F, Jiang B, Svenson LW. Achalasia: incidence, prevalence and survival. A population-based study. Neurogastroenterol Motil. 2010;22(9):e256–61.
6. Pandolfino JE, Gawron AJ. Achalasia: a systematic review. JAMA. 2015;313(18):1841–52.
7. Moonen A, Annese V, Belmans A, Bredenoord AJ, Bruley des Varannes S, Costantini M, et al. Long-term results of the European achalasia trial: a multicentre randomised controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. Gut. 2016;65(5):732–9.
8. Boeckxstaens GE, Annese V, des Varannes SB, Chaussade S, Costantini M, Cuttitta A, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. N Engl J Med. 2011;364(19):1807–16.
9. Patti MG, Pellegrini CA, Horgan S, Arcerito M, Omelanczuk P, Tamburini A, et al. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. Ann Surg. 1999;230(4):587.
10. Zaninotto G, Costantini M, Molena D, Portale G, Costantino M, Nicoletti L, et al. Minimally invasive surgery for esophageal achalasia. JLaparoendoscAdv Surg Tech. 2001;11(6):351–9.
11. Eckardt VF. Clinical presentation and complications of achalasia. Gastrointest Endosc Clin N Am. 2001;11(2):281–92.
12. Taft TH, Carlson DA, Triggs J, Craft J, Starkey K, Yadlapati R, et al. Evaluating the reliability and construct validity of the Eckardt symptom score as a measure of achalasia severity. Neurogastroenterol Motil. 2018;30(6):e13287.
13. Bredenoord AJ, Fox M, Kahrilas PJ, Pandolfino JE, Schwizer W, Smout AJPM. Chicago classification criteria of esophageal motility disorders defined in high resolution esophageal pressure topography1. NeurogastroenterolMotil. 2012;24(s1):57–65.
14. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJPM, et al. The Chicago classification of esophageal motility disorders, v3.0. NeurogastroenterolMotil. 2014;27(2):160–74.
15. Kachala SS, Rice TW, Baker ME, Rajeswaran J, Thota PN, Murthy SC, et al. Value of routine timed barium esophagram follow-up in achalasia after myotomy. J Thorac Cardiovasc Surg. 2018;156:871.
16. Stavropoulos SN, Modayil RJ, Friedel D, Savides T. The International Per Oral Endoscopic Myotomy Survey (IPOEMS): a snapshot of the global POEM experience. Surg Endosc. 2013;27(9):3322–38.
17. Teitelbaum EN, Soper NJ, Arafat FO, Santos BF, Kahrilas PJ, Pandolfino JE, et al. Analysis of a learning curve and predictors of intraoperative difficulty for peroral esophageal myotomy (POEM). J Gastrointest Surg. 2014;18(1):92–9.
18. Kumbhari V, Tieu AH, Onimaru M, El Zein MH, Teitelbaum EN, Ujiki MB, et al. Peroral endoscopic myotomy (POEM) vs laparoscopic Heller myotomy (LHM) for the treatment of type III achalasia in 75 patients: a multicenter comparative study. Endosc Int Open. 2015;3(03):E195–201.
19. Rohof WO, Salvador R, Annese V, Bruley des Varannes S, Chaussade S, Costantini M, et al. Outcomes of treatment for achalasia depend on manometric subtype. Gastroenterology. 2013;144(4):718–25.
20. Hungness ES, Sternbach JM, Teitelbaum EN, Kahrilas PJ, Pandolfino JE, Soper NJ. Per-oral endoscopic myotomy (POEM) after the learning curve: durable long-term results with a low complication rate. Ann Surg. 2016;264(3):508–17.
21. Kurian AA, Dunst CM, Sharata A, Bhayani NH, Reavis KM, Swanström LL. Peroral endoscopic esophageal myotomy: defining the learning curve. Gastrointest Endosc. 2013;77(5):719–25.
22. Swanstrom LL, Rieder E, Dunst CM. A stepwise approach and early clinical experience in peroral endoscopic myotomy for the treatment of achalasia and esophageal motility disorders. J Am Coll Surg. 2011;213(6):751–6.
23. Hungness ES, Jorge JM. Per-oral esophageal myotomy: is it a safe and durable procedure for achalasia? Adv Surg. 2017;51(1):193–205.
24. Hungness ES, Teitelbaum EN, Santos BF, Arafat FO, Pandolfino JE, Kahrilas PJ, et al. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. 2013;17(2):228–35.
25. von Renteln D, Inoue H, Minami H, Werner YB, Pace A, Kersten JF, et al. Peroral endoscopic myotomy for the treatment of achalasia: aprospective single center study. Am J Gastroenterol. 2011;107:411.
26. Von Renteln D, Fuchs KH, Fockens P, Bauerfeind P, Vassiliou MC, Werner YB, et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. Gastroenterology. 2013;145(2):309–11.e3.
27. El Khoury R, Teitelbaum EN, Sternbach JM, Soper NJ, Harmath CB, Pandolfino JE, et al. Evaluation

of the need for routine esophagram after per-oral endoscopic myotomy (POEM). Surg Endosc. 2016;30(7):2969–74.
28. Inoue H, Sato H, Ikeda H, Onimaru M, Sato C, Minami H, et al. Per-oral endoscopic myotomy: a series of 500 patients. J Am Coll Surg. 2015;221(2):256–64.
29. Werner YB, Costamagna G, Swanström LL, von Renteln D, Familiari P, Sharata AM, et al. Clinical response to peroral endoscopic myotomy in patients with idiopathic achalasia at a minimum follow-up of 2 years. Gut. 2016;65(6):899–906.
30. Bhayani NH, Kurian AA, Dunst CM, Sharata AM, Rieder E, Swanstrom LL. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Ann Surg. 2014;259(6):1098–103.
31. Crespin OM, Liu LWC, Parmar A, Jackson TD, Hamid J, Shlomovitz E, et al. Safety and efficacy of POEM for treatment of achalasia: a systematic review of the literature. Surg Endosc. 2017;31(5):2187–201.
32. Barbieri LA, Hassan C, Rosati R, Romario UF, Correale L, Repici A. Systematic review and meta-analysis: efficacy and safety of POEM for achalasia. United European Gastroenterol J. 2015;3(4):325–34.
33. Marano L, Pallabazzer G, Solito B, Santi S, Pigazzi A, De Luca R, et al. Surgery or peroral esophageal myotomy for achalasia: a systematic review and meta-analysis. Medicine (Baltimore). 2016;95(10):e3001.
34. Talukdar R, Inoue H, Reddy DN. Efficacy of per-oral endoscopic myotomy (POEM) in the treatment of achalasia: a systematic review and meta-analysis. Surg Endosc. 2015;29(11):3030–46.
35. Sharata AM, Dunst CM, Pescarus R, Shlomovitz E, Wille AJ, Reavis KM, et al. Peroral endoscopic myotomy (POEM) for esophageal primary motility disorders: analysis of 100 consecutive patients. J Gastrointest Surg. 2015;19(1):161–70; discussion 70.
36. Ward MA, Gitelis M, Patel L, Vigneswaran Y, Carbray J, Ujiki MB. Outcomes in patients with over 1-year follow-up after peroral endoscopic myotomy (POEM). Surg Endosc. 2017;31(4):1550–7.
37. Teitelbaum EN, Soper NJ, Santos BF, Arafat FO, Pandolfino JE, Kahrilas PJ, et al. Symptomatic and physiologic outcomes one year after peroral esophageal myotomy (POEM) for treatment of achalasia. Surg Endosc. 2014;28(12):3359–65.
38. von Renteln D, Inoue H, Minami H, Werner YB, Pace A, Kersten JF, et al. Peroral endoscopic myotomy for the treatment of achalasia: a prospective single center study. Am J Gastroenterol. 2012;107(3):411–7.
39. Chen X, Li Q-p, Ji G-z, Ge X-x, Zhang X-h, X-y Z, et al. Two-year follow-up for 45 patients with achalasia who underwent peroral endoscopic myotomy. Eur J Cardiothorac Surg. 2015;47(5):890–6.
40. Teitelbaum EN, Dunst CM, Reavis KM, Sharata AM, Ward MA, DeMeester SR, et al. Clinical outcomes five years after POEM for treatment of primary esophageal motility disorders. Surg Endosc. 2018;32(1):421–7.
41. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256(4):659–67.
42. Costamagna G, Marchese M, Familiari P, Tringali A, Inoue H, Perri V. Peroral endoscopic myotomy (POEM) for oesophageal achalasia: preliminary results in humans. Dig Liver Dis. 2012;44(10):827–32.
43. Rohof WO, Hirsch DP, Kessing BF, Boeckxstaens GE. Efficacy of treatment for patients with achalasia depends on the distensibility of the esophagogastric junction. Gastroenterology. 2012;143(2):328–35.
44. Akintoye E, Kumar N, Obaitan I, Alayo QA, Thompson CC. Peroral endoscopic myotomy: a meta-analysis. Endoscopy. 2016;48(12):1059–68.
45. Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26(1):18–26.

6 Laparoscopic Heller Myotomy with Partial (Dor) Fundoplication

Francisco Schlottmann, Marco Di Corpo, and Marco G. Patti

Introduction

Esophageal achalasia is a primary esophageal motility disorder characterized by the absence of esophageal peristalsis and failure of the lower esophageal sphincter to relax in response to swallowing. Achalasia is rare disease, with an incidence of about 1 in 100,000 individuals that occurs with equal frequency in men and women [1].

The pathophysiology of the disease involves the selective degeneration of inhibitory neurons of the esophageal myenteric plexus, which are needed for the peristalsis of the smooth muscle of the esophageal body, as well as for the relaxation of the tonic lower esophageal sphincter (LES) [2]. Dysphagia, regurgitation, heartburn, and chest pain are the most frequent symptoms in achalasia patients.

There are no curative therapies for achalasia. Treatment is palliative and is directed toward decreasing the outflow resistance at the level of the gastroesophageal junction caused by a nonrelaxing and often hypertensive LES. Currently, a laparoscopic Heller myotomy (LHM) with a partial fundoplication is considered the best treatment modality.

A properly executed operation is key for the success of LHM.

Laparoscopic Heller Myotomy Technique

Position of the Patient

After induction of general endotracheal anesthesia, the patient is positioned supine in low lithotomy position with the lower extremities extended on stirrups, with knees flexed 20°–30°. To avoid sliding due to the steep reverse Trendelenburg position used during the entire procedure, a beanbag is inflated to create a "saddle" under the perineum. Pneumatic compression stockings are always used as prophylaxis against deep vein thrombosis (particularly important as the increased abdominal pressure secondary to the pneumoperitoneum and the steep Trendelenburg position decrease venous

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_6

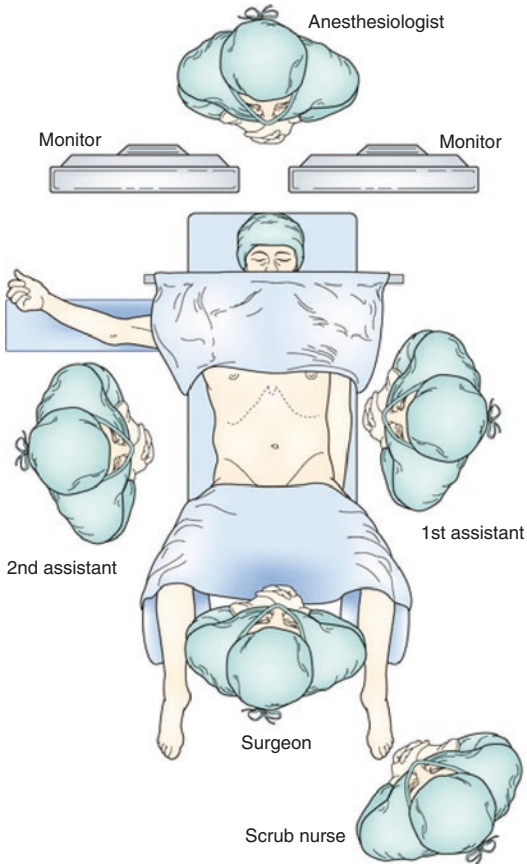


Fig. 6.1 Position of the patient. (Reprinted with permission © Springer Nature [6])

return). Subcutaneous heparin is also used. The surgeon stands between the patient's legs, and the first and second assistants on the right and left side of the operating table, respectively (Fig. 6.1).

Trocar Placement

Five 10-mm ports are used for the procedure. The first port is placed about 14 cm below the xiphoid process; it can be also placed slightly to the left of the midline to be in line with the hiatus. This port is used for insertion of the scope. The second port is placed in the left midclavicular line at the same level of port 1, and it is used for the insertion of a Babcock clamp for traction and the instrument used to take down the short gastric vessels. The third port is placed in the right midclavicular line at the same level of the other two ports, and it is

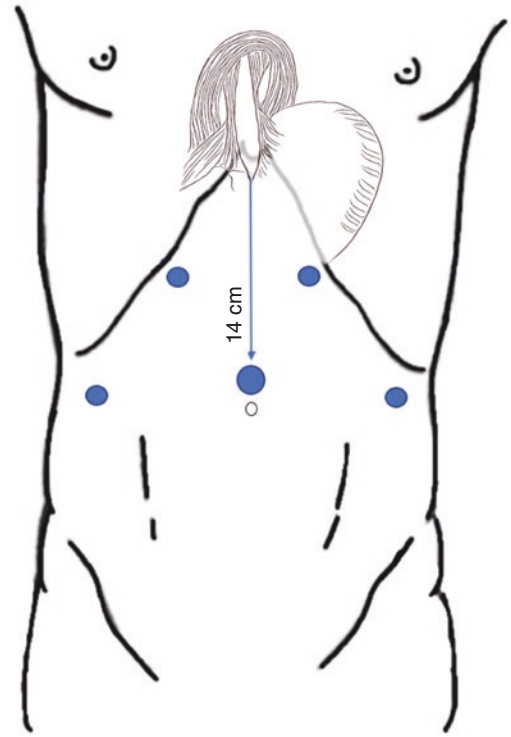


Fig. 6.2 Position of trocars for laparoscopic Heller myotomy

used for the liver retractor. The fourth and fifth ports are placed under the right and left costal margins so that their axes and the camera form an angle of about 120°. These ports are used for the insertion of graspers, scissors, and dissecting and suturing instruments (Fig. 6.2).

Key Note Care must be taken not to place the trocars too low. This can make the operation more challenging (e.g., difficult to take down the more proximal short gastric vessels or inability to reach the gastroesophageal junction with the Babcock).

Division of Gastrohepatic Ligament and Identification of Right Crus of the Diaphragm and Posterior Vagus Nerve

After the left segment of the liver is retracted and the gastroesophageal junction is exposed, the gastrohepatic ligament is divided. We begin the dissection above the caudate lobe of the liver and

continue proximally until the right crus is identified. The crus is then separated from the esophagus by blunt dissection and the posterior vagus nerve is identified.

Key Note An accessory left hepatic artery originating from the left gastric artery can be encountered, which can be usually safely divided. The electrocautery should be used with caution next to the right pillar of the crus because the lateral spread of the current may injure the posterior vagus nerve.

Division of Peritoneum and Phrenoesophageal Membrane Above the Esophagus and Identification of the Left Crus of the Diaphragm and Anterior Vagus Nerve

The peritoneum and the phrenoesophageal membrane above the esophagus are divided and the anterior vagus nerve is identified. The left pillar of the crus is separated from the esophagus. Dissection is limited to the anterior and lateral aspects of the esophagus, and no posterior dissection is needed if a Dor fundoplication will be performed.

Key Note Care must be taken not to damage the anterior vagus nerve or the esophageal wall. For this reason, the nerve should be left attached to the esophageal wall, and the peritoneum and the phrenoesophageal membranes should be lifted from the esophageal wall by blunt dissection before they are divided.

Division of Short Gastric Vessels

The short gastric vessels are taken down all the way to the left pillar of the crus, starting from a point midway along the greater curvature of the stomach (Fig. 6.3).

Key Note Bleeding from the gastric vessels or the spleen is usually caused by excessive traction or by transection of a vessel not completely sealed. In addition, damage of the gastric wall can be caused by the grasping instruments or by burn from the electrocautery.

Esophageal Myotomy

First, the fat pad over the esophageal and gastric walls should be removed in order to expose the gastroesophageal junction. A Babcock clamp is then applied over the junction, and the esophagus is pulled downward and to the left in order to expose the right side of the esophagus. The myotomy is performed at the 11 o' clock position and is started about 3 cm above the gastroesophageal junction by reaching the proper submucosal plane. The myotomy is then extended proximally for about 6 cm above the esophagogastric junction, and distally for about

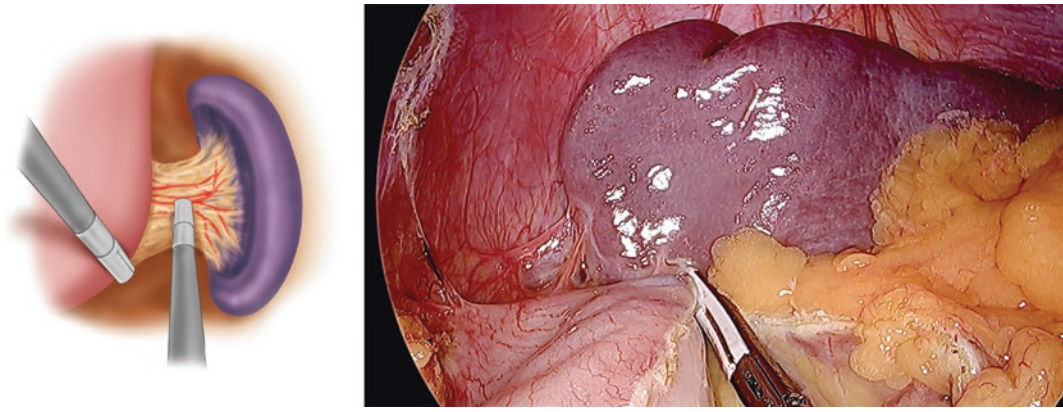


Fig. 6.3 Division of short gastric vessels

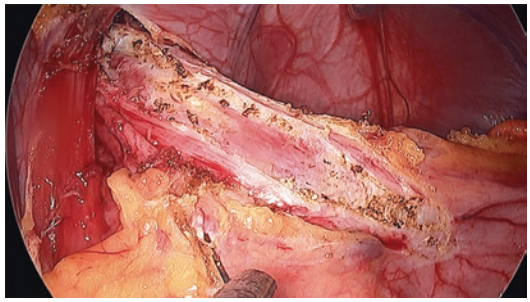


Fig. 6.4 Heller myotomy

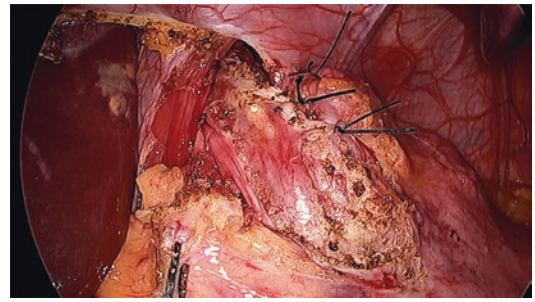


Fig. 6.5 First (left) row of stitches of Dor fundoplication

2.5 cm onto the gastric wall. Thus, the total length of the myotomy is typically about 8.5 cm (Fig. 6.4). Extending the myotomy downward on the gastric wall is key to deal thoroughly with the non-relaxing LES [3].

Key Note The myotomy should not be started close to the esophagogastric junction, because at this level, the layers are often poorly defined, particularly if prior dilations or botulinum toxin injections have been performed. Once the submucosal plane is reached above the esophagogastric junction, it is easier to extend the myotomy proximally and distally. There are many instruments that can be used to perform the myotomy. We prefer an electrocautery with a 90° hook, as it allows careful lifting and division of the circular fibers. If bleeding occurs from the cut muscle fibers, gentle compression is preferable to electrocautery. Any perforation should be repaired using a fine absorbable suture material (4-0 or 5-0).

Dor Fundoplication

The Dor fundoplication (180° anterior) has two rows of sutures, one left and one right. The left row comprises three stitches: the uppermost stitch incorporates the fundus of the stomach, the esophageal wall, and the left pillar of the crus; the other two incorporate the stomach and the esophageal wall (Fig. 6.5). The gastric fundus is then folded over the exposed mucosa, so that the greater curvature is next to the right pillar of the crus. The second row of stitches comprises three stitches between the fundus and the right pillar of the crus, and two additional stitches between the superior aspect of the fundoplication and the rim of the esophageal hiatus (Fig. 6.6). These last stitches remove any tension from the second row of sutures.

The decision between a Dor fundoplication (180° anterior) and a Toupet fundoplication (270° posterior) is usually based on the surgeon's preference. The advantages of a Dor fundoplication are that it does not require posterior dissection (avoiding a possible injury to the posterior vagus nerve) and covers the exposed esophageal mucosa. The advantages of a Toupet fundoplication are that it keeps the edges of the myotomy separated and theoretically may provide better reflux control. Two randomized controlled trials tried to identify which fundoplication was most beneficial for patients and found no significant difference in control of symptoms and similar postoperative reflux profiles with both types of fundoplication [4, 5].

Key Note It is important to take down the short gastric vessels to obtain a fundoplication without tension.

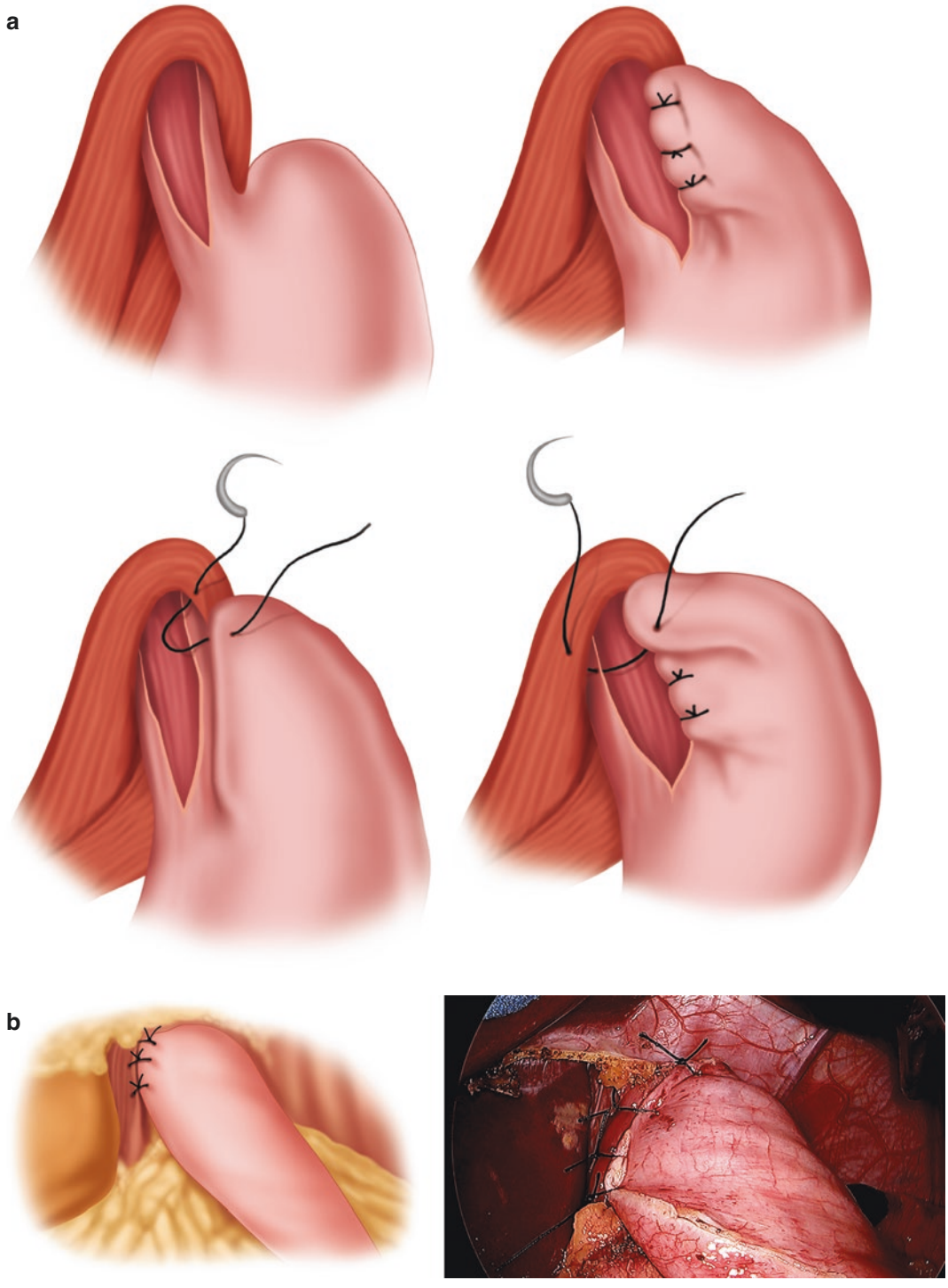


Fig. 6.6 (**a**, **b**) Dor fundoplication

Conclusion

A properly executed laparoscopic Heller myotomy is an effective and long-lasting treatment for patients with achalasia. Technical elements of the procedure should be carefully respected to obtain symptomatic relief and avoid postoperative complications.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Schlottmann F, Patti MG. Esophageal achalasia: current diagnosis and treatment. Expert Rev Gastroenterol Hepatol. 2018;12(7):711–21.
2. Schlottmann F, Neto RML, Herbella FAM, Patti MG. Esophageal achalasia: pathophysiology, clinical presentation, and diagnostic evaluation. Am Surg. 2018;84(4):467–72.
3. Oelschlager BK, Chang L, Pellegrini CA. Improved outcome after extended gastric myotomy for achalasia. Arch Surg. 2003;138(5):490–5.
4. Rawlings A, Soper NJ, Oelschlager B, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26(1):18–26.
5. Kumagai K, Kjellin A, Tsai JA, et al. Toupet versus Dor as a procedure to prevent reflux after cardiomyotomy for achalasia: results of a randomised clinical trial. Int J Surg. 2014;12(7):673–80.
6. Borraez B, Ramirez M, Patti MG. Patient positioning. In: Fisichella PM, Patti MG, editors. Atlas of esophageal surgery. New York: Springer; 2015. p. 39–44.

7 Laparoscopic Heller Myotomy and Posterior Partial Fundoplication

Timothy M. Farrell, Marco Di Corpo, and Marco G. Patti

Introduction

Achalasia is a rare disease with a prevalence traditionally assumed to be 1 in 100,000 individuals [1]. Recent data, however, have shown that the prevalence is at least two- to threefold greater than previous estimates [2]. The incidence increases with age and has an equal distribution across gender and race [1, 3, 4].

Achalasia is a chronic and progressive disease characterized by lack of esophageal peristalsis and partial or absent relaxation of the lower esophageal sphincter (LES) in response to swallowing [5, 6]. The most common form of achalasia is idiopathic [7, 8]. The pathophysiology of achalasia involves the selective degeneration of inhibitory neurons of the esophageal myenteric plexus, which are needed for peristalsis of the smooth muscle of the esophageal body, as well as relaxation of the tonic LES [9]. Regardless of the cause, the lack of peristalsis and the non-relaxing LES affect the emptying of food from the esophagus into the stomach and eventually cause dilatation and tortuosity of the esophageal body [10]. Consequently, the transit of the food into the stomach is impaired, and patients typically experience dysphagia, regurgitation, and respiratory symptoms (cough, wheezing, aspiration, pneumonia) [1]. Additionally, an increased risk of squamous esophageal cancer has been identified, albeit very low [11]. Treated patients who develop GER also have an increased risk of developing Barrett's esophagus and adenocarcinoma [12].

Therapy is palliative, and it is directed toward decreasing outflow resistance caused by the dysfunctional LES. Smooth muscle relaxants such as calcium blockers and long-acting nitrates [13] or endoscopic injection of botulinum toxin into the LES have limited effect [14]. Endoscopic dilatation, per-oral endoscopic myotomy (POEM), and laparoscopic myotomy are the treatment modalities most commonly used [3, 15].

Previous studies have reported better long-term outcomes with surgical myotomy than with medical therapy or pneumatic dilatation (PD) [16, 17], and the superiority of LHM over PD was confirmed by three meta-analyses [18–20]. Patti and colleagues also demonstrated the supe-

T. M. Farrell (✉) · M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA
e-mail: tfarrell@med.unc.edu

M. G. Patti
Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_7

riority of LHM, describing it as the gold standard treatment for most of achalasia patients [6, 21], and LHM is proposed on SAGES guidelines as a safe and low-risk procedure for controlling dysphagia and improving quality of life in the majority of the patients (recommendation ++++, strong evidence) [13].

Although LHM has been previously demonstrated to have positive long-term outcomes for achalasia patients (>90% long-term dysphagia relief [22]) [3, 13, 17, 23], it is recognized that a fundoplication is needed after LHM to prevent GERD [24, 25]; this lesson was learned during the evolution of minimally invasive procedures for achalasia from thoracoscopic to laparoscopic approach [26, 27]. For example, Richards and colleagues reported 47.6% pathologic reflux at 6-month follow-up after LHM alone but 9.1% only when a Dor fundoplication was added [28]. The value of a fundoplication has been confirmed by other studies [29–31].

This chapter reviews the pros and cons of the different types of fundoplication after LHM and the technical recommendations for posterior partial fundoplication.

Fundoplication: Yes or No

In 1956, Rudolph Nissen popularized a 360° fundoplication for the treatment of GER [32], but it was not until 1962 that J. Dor from Marseille, France, proposed the "technique de Heller-Nissen modifiee" for the prevention of reflux after a Heller cardiomyotomy [33]. This operation was performed through a transabdominal approach, and the left side of the myotomy was sutured to the anterior wall of the stomach, which was then folded anteriorly and secured to the right edge of the myotomy with another row of sutures. In 1963, a posterior partial fundoplication after Heller myotomy was devised by André Toupet [34]. These techniques were proposed as a means to limit gastroesophageal reflux while still allowing relief of dysphagia.

As minimally invasive techniques were developing for Heller myotomy, the value of adding a fundoplication was still uncertain. On one side of the debate, several authors argued that a fundoplication was not needed after Heller myotomy as it would cause recurrence of dysphagia due to lack of peristalsis [35, 36]. Others were proponents of routine fundoplication after LHM.

In 2003, Falkenback and colleagues reported a prospective randomized trial in 20 open Heller myotomy patients comparing those with and without floppy Nissen fundoplication [37]. At >3-year follow-up, the authors found pathologic GER by pH testing in 13.1% of the no-fundoplication group and only in 0.15% of the fundoplication group.

In 2004, Richards and colleagues, in a prospective randomized double-blind clinical trial, demonstrated that LHM with Dor fundoplication was superior to Heller alone for incidence of postoperative GER evaluated by 24-hour pH monitoring after surgery [28]. In addition, a large-scale meta-analysis including more than 3000 patients after LHM found the incidence of postoperative GER was notably higher when no fundoplication was performed (32% vs. 9%) [18]. On the basis of these high-level data, LHM with fundoplication is considered in most centers worldwide as the gold standard for the surgical treatment of patients with esophageal achalasia.

LHM and Fundoplications: Total or Partial?

Among those who were proponents of a fundoplication after LHM for achalasia, there was disagreement over the type of fundoplication. Since a floppy total fundoplication has been shown to be effective in cases of weak esophageal peristalsis [38], some authors initially tried to apply total fundoplication after LHM [37, 39]. However, since achalasia is a state of aperistalsis, others argued that total fundoplication would create too much resistance, impeding esophageal emptying and causing persistent or recurrent dysphagia [31, 40]; they pointed out

that partial fundoplication compares favorably with total fundoplication for GER control with less postoperative dysphagia [41]. In the literature, there are a few case series and retrospective comparative studies, and one randomized trial comparing partial and total fundoplication after LHM.

Case series are conflicting. Topart and colleagues [42] found recurrent dysphagia in 82% of patients 10 years after LHM and total fundoplication, while Rossetti et al. [43] reported excellent dysphagia relief in >90% and no GER at mean follow-up of 83 months. Di Martino and colleagues [44] performed a retrospective comparative study between well-matched patients who had anterior versus posterior fundoplication after LHM. After 2-year follow-up, they reported similar GER and dysphagia symptom scores, with lower GEJ pressures and higher distal esophageal acid after partial fundoplication.

Rebecchi and colleagues ran a prospective, randomized trial comparing Dor to Nissen fundoplication after Heller myotomy [41]. They enrolled 144 patients: 72 had a partial anterior fundoplication and 72 underwent a total fundoplication. At a 5-year follow-up, the incidence of GER was low and similar in the two groups, but 15% of patients after Nissen fundoplication had dysphagia compared to only 2.8% after Dor fundoplication.

Similar findings have been recently confirmed by several groups, which show LHM with fundoplication results in relief of dysphagia symptoms with a low incidence of postoperative GER, resulting in an improved quality of life. Moreover, they highlight that the relief of dysphagia is not hampered by the addition of a partial fundoplication [17, 30, 45]. In addition, a recent review paper details how several early proponents of total fundoplication have altered their recommendations after recognizing late esophageal decompensation may cause recurrence of dysphagia [40].

Therefore, today there is a general consensus that a 360° wrap after LHM can lead to an increased rate of postoperative dysphagia [3, 13]. As stated by the 2018 International Society for Diseases of the Esophagus (ISDE) guidelines [3], laparoscopic Heller myotomy with partial fundoplication should be considered the procedure of choice for esophageal achalasia, as it attains the best balance between relief of dysphagia and prevention of reflux.

LHM and Fundoplications: Anterior or Posterior?

What type of partial fundoplication to use is still unclear. To date, two randomized controlled trials and a meta-analysis have addressed this question. Rawlings and colleagues [30] randomized 60 patients having LHM to either Dor fundoplication ($n = 36$) or Toupet fundoplication ($n = 24$). After 1-year follow up, they concluded that there was no significant difference in control of symptoms between the two groups, and although there was a higher percentage of patients with abnormal 24-h pH test results in the Dor group, the difference was not statistically significant.

Kumagai and colleagues [46] randomized 42 patients to either a Dor fundoplication ($n = 20$) or a Toupet fundoplication ($n = 22$) after LHM and looked at outcomes over the first year. There was no significant difference in the incidence of postoperative gastroesophageal reflux by pH testing, and at 1 year, Eckardt scores dramatically improved after both procedures, but certain functional scores and emptying as assessed by timed barium esophagram were relatively better after Toupet.

Results from a meta-analysis that studied partial anterior vs. partial posterior fundoplication after LHM encompassed almost 3000 patients [47]. The authors concluded that the addition of fundoplication reduced postoperative GER rates in both groups with no significant difference and that the partial posterior fundoplication may be associated with significantly lower reintervention rates for postoperative dysphagia.

Notably, some surgeons prefer the partial posterior Toupet (~270°) fundoplication because

it keeps the edges of the myotomy separated, thus reducing the risk of recurrent dysphagia [48, 49]. Other experts suggest that the use of a partial anterior Dor (~180°) fundoplication allows limited hiatal dissection avoiding disruption of anatomic structures that help control GER and allows coverage of the exposed esophageal mucosa [31, 50].

Technical Recommendations

Laparoscopic Heller Myotomy with Posterior Partial Fundoplication

Pneumoperitoneum is established, and a five-port technique is used. Reverse Trendelenburg position is helpful. The left liver is elevated with a table-mounted retractor. The gastrohepatic omentum is opened (Fig. 7.1) and the phrenoesophageal membrane is divided (Fig. 7.2), taking care to avoid the anterior vagus nerve and

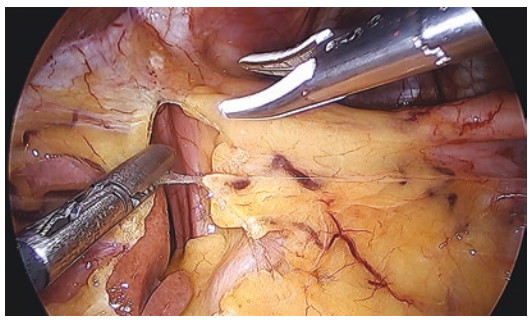


Fig. 7.1 Division of gastrohepatic ligament

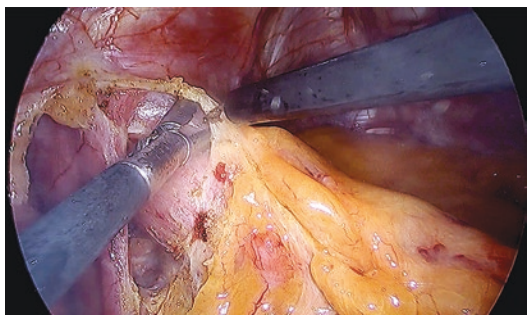


Fig. 7.2 Division of phrenoesophageal membrane

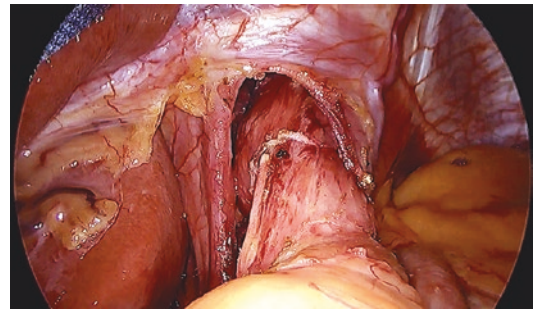


Fig. 7.3 Circumferential exposure of the esophagus

esophagus. The diaphragmatic crura are circumferentially dissected away from the gastroesophageal junction (Fig. 7.3). The greater curvature of the stomach is mobilized, and the esophagus and both vagus nerves are encircled with a Penrose drain (Fig. 7.4).

Before creating the fundic wrap, the GEJ fat pad is reflected or resected (Fig. 7.5), and then a longitudinal seromuscular incision is made starting either just below or just above the GE junction. Longitudinal and circumferential muscle fibers are divided until mucosa is visualized. The myotomy is extended 6 cm above the GEJ and 2–3 cm distally onto the stomach (Fig. 7.6a, b), taking precautions to avoid the anterior vagus nerve. One possible risk of Heller myotomy is mucosal perforation. Patients previously treated for achalasia, by either pneumatic dilation or botulinum toxin, are at greater risk. Intraoperative injuries are repaired immediately with absorbable sutures, usually without additional morbidity. Many surgeons routinely assess mucosal integrity at the completion of the myotomy by instillation of methylene blue or air. If a perforation is repaired, usually a Dor fundoplication is chosen as the stomach will cover the area of repair.

The diaphragmatic crura are then reapproximated posterior to the esophagus. Then, the gastric fundus is passed through the retroesophageal window, and a ~240-degree partial posterior hemifundoplication is fashioned with the fundus anchored to the cut edges of the esophageal muscle to help maintain their separation.

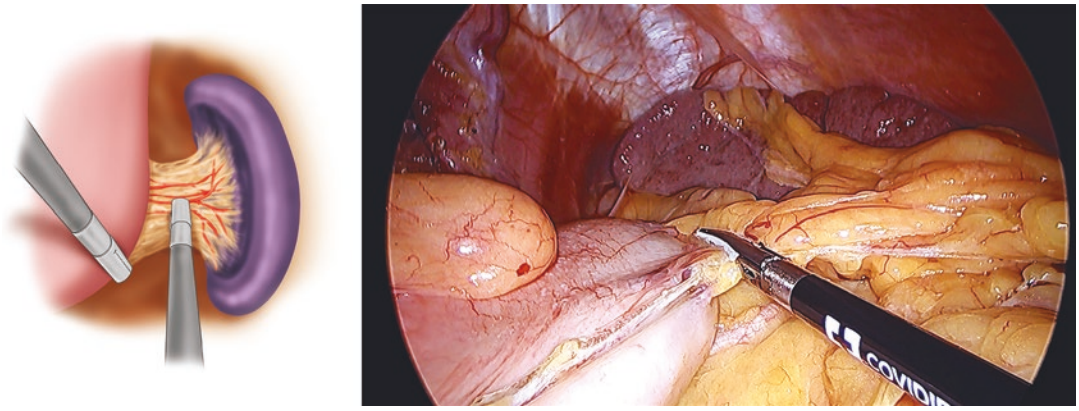


Fig. 7.4 Division of short-gastric vessels

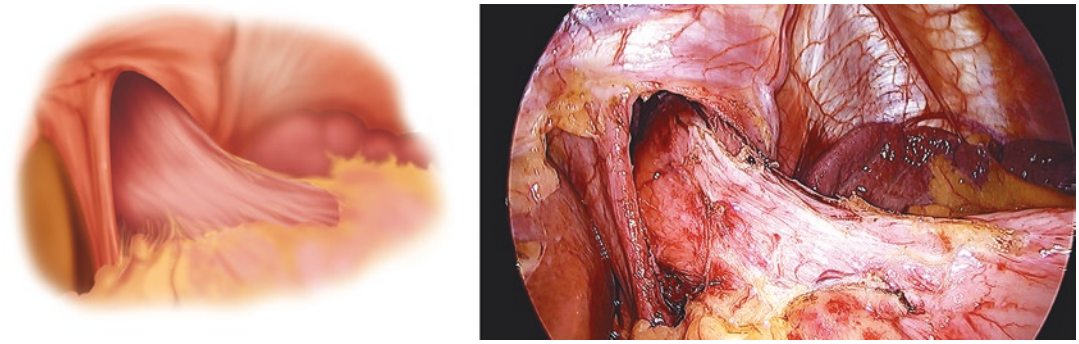


Fig. 7.5 Exposure of the gastroesophageal junction

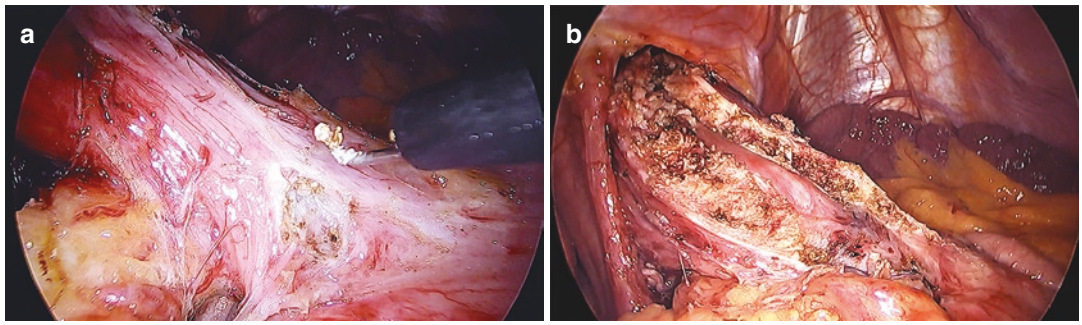


Fig. 7.6 (**a**) Starting the myotomy; (**b**) 6 cm myotomy

Conclusions

The body of scientific evidence supports use of a partial fundoplication after Heller myotomy for patients with achalasia. The literature fails to show any significant difference between partial anterior and posterior fundoplication. In the absence of further large randomized controlled trials, the decision of performing an anterior or a posterior wrap is based on the surgeon's experience and preference [29].

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet. 2014;383(9911):83–93. https://doi.org/10.1016/S0140-6736(13)60651-0.
2. Samo S, Carlson DA, Gregory DL, Gawel SH, Pandolfino JE, Kahrilas PJ. Incidence and prevalence of achalasia in Central Chicago, 2004–2014, since the widespread use of high-resolution manometry. Clin Gastroenterol Hepatol. 2014;15(1):34–48. https://doi.org/10.1016/j.cgh.2016.08.030.
3. Zaninotto G, Bennett C, Boeckxstaens G, et al. The 2018 ISDE achalasia guidelines. Dis Esophagus. 2018;31(9):1–29. https://doi.org/10.1093/dote/doy071.
4. Enestvedt BK, Lucas Williams J, Sonnenberg A. Epidemiology and practice patterns of achalasia in a large multi-center database. Aliment Pharmacol Ther. 2013;33(11):1–9. https://doi.org/10.1111/j.1365-2036.2011.04655.x.Epidemiology.
5. Molena D, Yang SC. Surgical management of end-stage achalasia. Semin Thorac Cardiovasc Surg. 2012;24(1):19–26. https://doi.org/10.1053/j.semtcvs.2012.01.015.
6. Schlottmann F, Patti MG. Esophageal achalasia: current diagnosis and treatment. Expert Rev Gastroenterol Hepatol. 2018;12(7):711–21. https://doi.org/10.1080/17474124.2018.1481748.
7. Pressman A, Behar J. Etiology and pathogenesis of idiopathic achalasia. J Clin Gastroenterol. 2017;51(3):195–202. https://doi.org/10.1097/MCG.0000000000000780.
8. Gockel I, Bohl JRE, Doostkam S, Eckardt VF, Junginger T. Spectrum of histopathologic findings in patients with achalasia reflects different etiologies. J Gastroenterol Hepatol. 2006;21(4):727–33. https://doi.org/10.1111/j.1440-1746.2006.04250.x.
9. Goyal RK, Chaudhury A. Pathogenesis of achalasia: lessons from mutant mice. Gastroenterology. 2010;139(4):1086–90. https://doi.org/10.1053/j.gastro.2010.08.013.
10. Schlottmann F, Herbella F, Allaix ME, Patti MG. Modern management of esophageal achalasia: from pathophysiology to treatment. Curr Probl Surg. 2018;55(1):10–37. https://doi.org/10.1067/j.cpsurg.2018.01.001.
11. Leeuwenburgh I, Scholten P, Alderliesten J, et al. Long-term esophageal cancer risk in patients with primary achalasia: a prospective study. Am J Gastroenterol. 2010;105(10):2144–9. https://doi.org/10.1038/ajg.2010.263.
12. Tustumi F, Bernardo WM, da Rocha JRM, et al. Esophageal achalasia: a risk factor for carcinoma. A systematic review and meta-analysis. Dis Esophagus. 2017;30(10):1–8. https://doi.org/10.1093/dote/dox072.
13. Stefanidis D, Richardson W, Farrell TM, Kohn GP, Augenstein V, Fanelli RD. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc Other Interv Tech. 2012;26(2):296–311. https://doi.org/10.1007/s00464-011-2017-2.
14. Yamaguchi D, Tsuruoka N, Sakata Y, Shimoda R, Fujimoto K, Iwakiri R. Safety and efficacy of botulinum toxin injection therapy for esophageal achalasia in Japan. J Clin Biochem Nutr. 2015;57(3):239–43. https://doi.org/10.3164/jcbn.15-47.
15. Inoue H, Sato H, Ikeda H, et al. Per-Oral endoscopic Myotomy: a series of 500 patients. J Am Coll Surg. 2015;221(2):256–64. https://doi.org/10.1016/j.jamcollsurg.2015.03.057.
16. Lopushinsky SR, Urbach DR. Pneumatic dilatation and surgical myotomy for achalasia. J Am Med Assoc. 2006;296(18):2227–33. https://doi.org/10.1001/jama.296.18.2227.
17. Weber CE, Davis CS, Kramer HJ, Gibbs JT, Robles L, Fisichella PM. Medium and long-term outcomes after pneumatic dilation or laparoscopic heller myotomy for achalasia: a meta-analysis. Surg Laparosc Endosc Percutaneous Tech. 2012;22(4):289–96. https://doi.org/10.1097/SLE.0b013e31825a2478.
18. Campos GM, Vittinghoff E, Rabl C, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249(1):45–57. https://doi.org/10.1097/SLA.0b013e31818e43ab.
19. Schoenberg MB, Marx S, Kersten JF, et al. Laparoscopic Heller myotomy versus endoscopic balloon dilatation for the treatment of achalasia: a network meta-analysis. Ann Surg. 2013;258(6):943–52. https://doi.org/10.1097/SLA.0000000000000212.
20. Yaghoobi M, Mayrand S, Martel M, Roshan-Afshar I, Bijarchi R, Barkun A. Laparoscopic Heller's myotomy versus pneumatic dilation in the treatment of idiopathic achalasia: a meta-analysis of randomized, controlled trials. Gastrointest Endosc. 2013;78(3):468–75. https://doi.org/10.1016/j.gie.2013.03.1335.
21. Patti MG, Andolfi C, Bowers SP, Soper NJ. POEM vs laparoscopic Heller Myotomy and fundoplication: which is now the gold standard for treatment of achalasia? J Gastrointest Surg. 2017;21(2):207–14. https://doi.org/10.1007/s11605-016-3310-0.
22. Zaninotto G, Costantini M, Rizzetto C, et al. Four hundred laparoscopic myotomies for esophageal achalasia a single centre experience. Ann Surg. 2008;248(6):986–93. https://doi.org/10.1097/SLA.0b013e3181907bdd.
23. SAGES. Quality of life outcomes after Heller Myotomy for achalasia comparing Dor and Toupet Fundoplications. https://www.sages.org/meetings/annual-meeting/abstracts-archive/quality-of-life-outcomes-after-heller-myotomy-for-achalasia-comparing-dor-and-toupet-fundoplications/.
24. Wei MT, He YZ, Deng XB, et al. Is Dor fundoplication optimum after laparoscopic Heller myotomy for achalasia? A meta-analysis. World J Gastroenterol. 2013;19(43):7804–12. https://doi.org/10.3748/wjg.v19.i43.7804.

25. Andolfi C, Baffy G, Fisichella PM. Whose patient is it? The path to multidisciplinary management of achalasia. J Surg Res. 2018;228:8–13. https://doi.org/10.1016/j.jss.2018.02.047.
26. Pellegrini C, Wetter LA, Patti M, et al. Thoracoscopic esophagomyotomy. Initial experience with a new approach for the treatment of achalasia. Ann Surg. 1992;216(3):291–6; discussion 296–9. http://www.ncbi.nlm.nih.gov/pubmed/1417178.
27. Patti MG, Pellegrini CA, Horgan S, et al. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. Ann Surg. 1999;230(4):587–93; discussion 593–4. https://doi.org/10.1097/MPG.0b013e318032062f.
28. Richards WO, Torquati A, Holzman MD, et al. Heller myotomy versus heller myotomy with dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. Ann Surg. 2004;240(3):405–15. https://doi.org/10.1097/01.sla.0000136940.32255.51.
29. Rebecchi F, Allaix ME, Schlottmann F, Patti MGMM. Laparoscopic Heller myotomy and fundoplication: what is the evidence ? Am Surg. 2018;84(4):481–9. http://libproxy.lib.unc.edu/login?url=https://search.proquest.com/docview/2042209620?accountid=14244.
30. Rawlings A, Soper NJ, Oelschlager B, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc Other Interv Tech. 2012;26(1):18–26. https://doi.org/10.1007/s00464-011-1822-y.
31. Tomasko JM, Augustin T, Tran TT, Haluck RS, Rogers AM, Lyn-Sue JR. Quality of life comparing Dor and Toupet after Heller Myotomy for achalasia. JSLS J Soc Laparoendosc Surg. 2014;18(3):e2014.00191. https://doi.org/10.4293/JSLS.2014.00191.
32. Nissen R. A simple operation for control of reflux esophagitis. Schweiz Med Wochenschr. 1956;86(Suppl 20):590–2. http://www.ncbi.nlm.nih.gov/pubmed/13337262.
33. Dor J, Humbert P, Dor V, Figarella J. L'interet de la technique de Nissen modifiee dans la prevention du reflux apres cardiomyotomie extramuqueuse de Heller. Mem Acad Chir. 1962;88:877–83.
34. Toupet A. Technique d'oesophago-gastroplastie avec phréno-gastropexie appliquée dans la cure radicale des hernies hiatales et comme complément de l'opération de Heller dans les cardiospasmes. Acad Chir. 1963;89:394–9.
35. Wang PC, Sharp KW, Holzman MD, Clements RH, Holcomb GW, Richards WO. The outcome of laparoscopic Heller myotomy without antireflux procedure in patients with achalasia. Am Surg. 1998;64(6):515–20; discussion 521. http://www.ncbi.nlm.nih.gov/pubmed/9619171.
36. Diamantis T, Pikoulis E, Felekouras E, et al. Laparoscopic esophagomyotomy for achalasia without a complementary antireflux procedure. J Laparoendosc Adv Surg Tech. 2006;16(4):345–9. https://doi.org/10.1089/lap.2006.16.345.
37. Falkenback D, Johansson J, Öberg S, et al. Heller's esophagomyotomy with or without a 360° floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. Dis Esophagus. 2003;16(4):284–90. https://doi.org/10.1111/j.1442-2050.2003.00348.x.
38. Patti MG, Robinson T, Galvani C, et al. Total fundoplication is superior to partial fundoplication even when esophageal peristalsis is weak. J Am Coll Surg. 2004;198(6):863–70. https://doi.org/10.1016/j.jamcollsurg.2004.01.029.
39. Donahue PE, Schlesinger PK, Sluss KF, et al. Esophagocardiomyotomy–floppy Nissen fundoplication effectively treats achalasia without causing esophageal obstruction. Surgery. 1994;116(4):719–24; discussion 724–5. http://www.ncbi.nlm.nih.gov/pubmed/7940171.
40. Patti MG, Herbella FA. Fundoplication after laparoscopic Heller Myotomy for esophageal achalasia: what type? J Gastrointest Surg. 2010;14(9):1453–8. https://doi.org/10.1007/s11605-010-1188-9.
41. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic heller myotomy plus dor fundoplication versus nissen fundoplication for achalasialong-term results. Ann Surg. 2008;248(6):1023–9. https://doi.org/10.1097/SLA.0b013e318190a776.
42. Topart P, Deschamps C, Taillefer R, Duranceau A. Long-term effect of total fundoplication on the myotomized esophagus. Ann Thorac Surg. 1992;54(6):1046–52. https://doi.org/10.1016/0003-4975(92)90068-F.
43. Rossetti G, Brusciano L, Amato G, et al. A total fundoplication is not an obstacle to esophageal emptying after heller myotomy for achalasia: results of a long-term follow up. Ann Surg. 2005;241(4):614–21. http://www.ncbi.nlm.nih.gov/pubmed/15798463.
44. di Martino N, Brillantino A, Monaco L, et al. Laparoscopic calibrated total vs partial fundoplication following heller myotomy for oesophageal achalasia. World J Gastroenterol. 2011;17(29):3431–40. https://doi.org/10.3748/wjg.v17.i29.3431.
45. Ortiz A, De Haro LFM, Parrilla P, et al. Very long-term objective evaluation of Heller myotomy plus posterior partial fundoplication in patients with achalasia of the cardia. Ann Surg. 2008;247(2):258–64. https://doi.org/10.1097/SLA.0b013e318159d7dd.
46. Kumagai K, Kjellin A, Tsai JA, et al. Toupet versus Dor as a procedure to prevent reflux after cardiomyotomy for achalasia: results of a randomised clinical trial. Int J Surg. 2014;12(7):673–80. https://doi.org/10.1016/j.ijsu.2014.05.077.
47. Kurian AA, Bhayani N, Sharata A, Reavis K, Dunst CM, Swanström LL. Partial anterior vs partial posterior fundoplication following transabdominal esophagocardiomyotomy for achalasia of the esophagus: meta-regression of objective postoperative gastroesophageal reflux and dysphagia. JAMA Surg. 2013;148(1):85–90. https://doi.org/10.1001/jamasurgery.2013.409.

48. Hunter JG, Trus TL, Branum GD, Waring JP. Laparoscopic Heller myotomy and fundoplication for achalasia. Ann Surg. 1997;225(6):655–64; discussion 664–5. http://www.ncbi.nlm.nih.gov/pubmed/9230806.
49. Tatum RP, Pellegrini CA. How i do it: laparoscopic heller myotomy with toupet fundoplication for achalasia. J Gastrointest Surg. 2009;13(6):1120–4. https://doi.org/10.1007/s11605-008-0585-9.
50. Patti MG, Fisichella PM. Laparoscopic heller myotomy and dor fundoplication for esophageal achalasia. How i do it. J Gastrointest Surg. 2008;12(4):764–6. https://doi.org/10.1007/s11605-007-0368-8.

Epiphrenic Diverticula: Diagnosis and Management

8

Jennifer A. Minneman and Andrew S. Wright

Background

Epiphrenic diverticula (ED) are mucosal outpouchings occurring in the distal 10 cm of the esophagus. Like Zenker's diverticula, epiphrenic diverticula are pulsion diverticula and do not include all layers of the esophageal wall. They are associated with esophageal motility disorders, and the diverticulum is considered secondary to the motility disorder. These diverticula are quite rare with less than 120 operations for this disease performed annually in the United States [1], and therefore evidence in the management of this disease is limited and primarily based on small case series and expert opinion.

Although achalasia is found in up to 57% of patients undergoing workup for ED [2–5], patients may also be diagnosed with distal esophageal spasm and hypercontractile peristalsis (nutcracker esophagus). Although Mondiere first proposed a link between diverticula and motility in 1833 [6], it was not until the 1960s that Belsey and Effler [7, 8] began addressing the motility disorder in the management of the diverticulum. Today, modern treatment of ED centers around management of the underlying motility disorder, typically through myotomy with or without resection of the diverticulum.

J. A. Minneman (✉) · A. S. Wright
Department of Surgery, University of Washington, Seattle, WA, USA
e-mail: awright2@uw.edu

Evaluation

If an ED is suspected based on symptoms or incidental imaging, the remainder of the workup proceeds with an upper GI (UGI) series, esophageal manometry, and esophagogastroduodenoscopy (EGD). An UGI series (Fig. 8.1) is often the first study to establish the diagnosis of ED and can offer crucial information for surgical planning, such as size of the diverticulum, width and location of the neck, and whether the diverticulum is

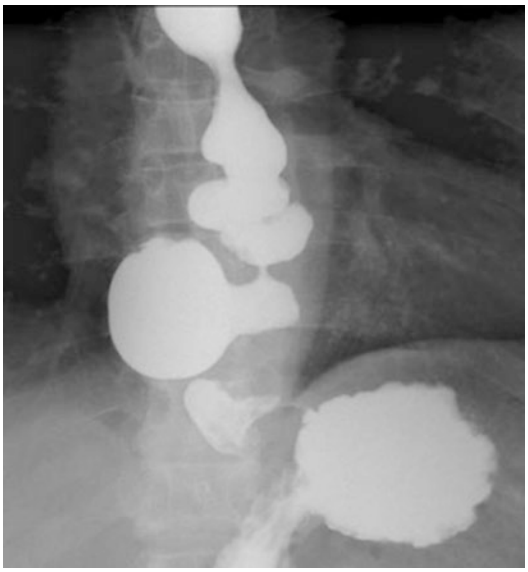


Fig. 8.1 Upper GI demonstrating epiphrenic diverticulum and esophageal dysmotility in a patient with type II achalasia

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_8

on the left or right side of the esophagus. UGI series can also demonstrate signs of esophageal dysmotility, including disordered contractions, a bird's beak or corkscrew esophagus, or other anatomic details such as hiatus hernia or intrinsic or extrinsic stricture of the esophagus.

It is often difficult to distinguish between symptoms of an ED and the underlying motility disorder. Dysphagia, regurgitation, chest pain, and aspiration can all be seen in both conditions, and in fact there does not seem to be a correlation between the size of an epiphrenic diverticulum and symptom severity [9]. All patients with ED should therefore undergo esophageal manometry in order to ascertain the extent of the disordered peristalsis and to guide treatment options and expectations. Conventional manometry fails to identify motility disorders in up to 40% of patients with epiphrenic diverticula [5, 10].

An extended 24-hour ambulatory manometry may reveal more subtle motility disorders missed in conventional manometry. In one small series, 6 of 21 patients (28%) needed 24-hr manometry to identify the underlying motility issue – 4 with diffuse esophageal spasm and 2 with a nonspecific motor disorder [11]. Some authors therefore recommend this extended 24-hr manometry in patients with normal initial motility studies [5, 11]. This may be obviated by the emergence of high-resolution manometry, which is more sensitive than conventional manometry. High-resolution manometry (Fig. 8.2) has been shown in one small series to detect abnormal motility in all patients studied, including subtle unnamed motility disorders that would have been missed in conventional manometry [12]. Some surgeons argue that a normal manometry does not preclude the need for the myotomy. Therefore, it is unclear if patients with "normal" manometry need any additional evaluation of their motility.

Rarely ED may be due to traction, typically from an extrinsic tumor, or pulsion against "pseudoachalasia" from an obstructing esophageal mass. There is at least one case report of diverticulum arising from pseudoachalasia due to laparoscopic adjustable gastric banding for obesity [13]. Upper endoscopy allows for detection of mucosal lesions, including premalignant lesions (Barrett's), ulcers, or malignancy in the esophagus, diverticulum, or stomach. Performing the UGI prior to the EGD allows the endoscopist to be aware of the epiphrenic diverticulum and therefore reduces the risks of blindly intubating and potentially perforating it. If there is any concern for possible traction diverticula, chest imaging is critical to evaluate for thoracic infection or malignancy. This is more common with mid-esophageal diverticula than with true epiphrenic diverticula.

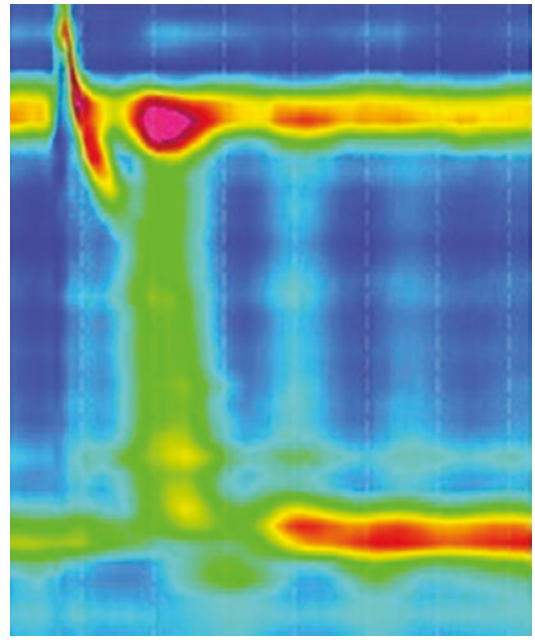


Fig. 8.2 High-resolution manometry from the same patient, with panesophageal pressurization consistent with type II achalasia

Watchful Waiting

Up to 40% of diverticula are asymptomatic or minimally symptomatic [14]. This is relevant as an asymptomatic diverticulum may be left in place without treatment. There are no surveillance recommendations for patients with known ED that are being observed with watchful waiting [14]. There have been rare case reports of spontaneous rupture [15], bleeding [16], and squamous cell carcinoma (SCC) in epiphrenic diverticula

[17]. The risk of SCC in ED has been estimated to be 0.6% and likely attributable to stasis and inflammation within the diverticulum [17]. Patients with a known ED presenting with worsening odynophagia, regurgitation, or hematemesis should be evaluated for malignant transformation.

Even if a patient is symptomatic, management of the motility disorder alone without diverticulectomy may be sufficient, if these symptoms are thought to be due to the underlying motility disorder and not the diverticulum. For example, Zaninotto et al. [5, 10] reported on 19 patients with ED for whom they either did not intervene [15] or performed only a pneumatic dilation [3]. The patients who underwent pneumatic dilation had improved symptom scores. Two of the non-intervention group eventually progressed on to need surgery. In the remaining 14 patients, however, symptoms were unchanged over the follow-up period (median 46 months).The authors concluded that surgery could be avoided in patients who were asymptomatic or minimally symptomatic with small diverticula. There are also case reports of botulinum toxin [18] or esophageal stents [19] used in symptomatic patients thought to be too high risk to undergo definitive surgical management.

Laparoscopic Management

The key element of surgical management of ED is myotomy of the esophagogastric junction with extension to at least to the base of the diverticulum. Although the historic management of esophageal diverticula was through the chest, with the advent of laparoscopy, most foregut surgeons now prefer a laparoscopic approach. The laparoscopic approach avoids single-lung ventilation, the morbidity of a thoracotomy or thoracoscopy, and the need for a chest tube. In addition to reduced trauma and faster recovery, the laparoscopic approach allows easier access to the GE junction and therefore an extended myotomy onto the cardia of the stomach, which in achalasia has been shown to reduce the risk of recurrent dysphagia [20]. A laparoscopic approach also allows for a more-easily performed partial fundoplication if desired.

There are a number of controversies in laparoscopic management of diverticula, including the extent of the myotomy, the need for diverticulectomy, and the need for antireflux procedure. Because this is a relatively rare disorder, most case series are small, and there is little evidence to guide these decisions.

Given the diversity of motility disorders that have been associated with epiphrenic diverticula, including disorders of the esophageal body with a normal lower esophageal sphincter, there has been disagreement among surgeons about the extent of the myotomy that is required. In particular, when a thoracic approach was favored, there was enthusiasm for sparing the lower esophageal sphincter (LES) in patients without achalasia or other disorders of the LES in the hopes of avoiding postoperative reflux. However, with the growing popularity of the laparoscopic approach with its easier extension onto the stomach and ability to add an antireflux procedure, complete myotomy of the LES even in non-achalasia patients has become well-established [5].

In our opinion, and based on the achalasia literature [20], the myotomy should extend distally for 3 cm on to the stomach. Proximally the myotomy should extend at least to and preferably beyond the base of the diverticulum. If the myotomy does not extend proximally past the base of the diverticulum, there is increased risk of recurrence [21]. There are some anecdotal reports of using intraoperative esophageal distensibility to guide the extent of myotomy using the Endoflip TM device (Medtronic Inc.); however to our knowledge, this has not yet been published in the literature or shown to improve outcomes. The myotomy itself should not go to the base of the diverticulum itself, as this risks perforation of the diverticulum. Instead, most surgeons will perform the myotomy at least 1–2 cm lateral to the base of the diverticulum.

The need for a diverticulectomy is also debated, as in many patients symptoms are not due to the diverticulum but instead to the underlying motility disorder. In some patients, diverticulectomy may not add any benefit and only

add risk due to the potential morbidity of a staple line leak. The actual rate of staple line leak is unclear but is reported to be 0–23% [3, 5, 22, 23]. On the other hand, a large diverticulum that does not drain well may cause trapping of food with fermentation, chest pressure and pain, and regurgitation. Patti's group reported a series of 13 patients undergoing myotomy for diverticulum, 6 with diverticulectomy and 7 without [24]. In the patients not undergoing resection, 3 were because the diverticulum was small and 4 were due to the diverticulum being too proximal or too adherent to fully dissect. Symptom control was excellent and equivalent in both groups, indicating that myotomy alone may be sufficient in selected patients.

In our practice, we carefully examine the preoperative dynamic cine films from the upper GI series. In a patient with a named motility disorder like achalasia, classic achalasia symptoms, and a small wide-mouthed diverticulum, we may plan to leave the diverticulum alone. We may also elect for myotomy alone if the patient is frail, and we judge that they could not tolerate a complication like a staple line leak. Intraoperatively we may decide on myotomy alone if operation is too technically challenging, for example, with a diverticulum higher in the chest. On the other hand, in patients where the primary symptoms seem to be from the diverticulum itself or if the diverticulum is large, is poorly draining, or has a narrow neck, we will be more aggressive in performing a diverticulectomy.

Because we routinely perform our myotomy across the GE junction onto the cardia of the stomach, we feel that a fundoplication is required to minimize the risk of postoperative reflux. A randomized trial of Dor vs. Toupet fundoplication in achalasia showed no difference in postoperative reflux, so either procedure may be performed based on the surgeon's preference [25]. Although that study showed no significant differences, there were non-significant trends in favor of posterior (Toupet) fundoplication. In our practice, we prefer a Toupet except in the rare circumstance of concern for possible mucosal injury, in which case we perform a Dor to help cover the mucosa.

Outcomes of laparoscopic management of ED are generally good. In one of the larger case series, Heniford's group at Carolinas reported on 27 patients over 20 years [5], all of whom underwent diverticulectomy, 90% with myotomy and 85% with antireflux procedure. There were no leaks, no mortality, and no recurrence with median follow-up of 36 months. Symptoms resolved in 89% of patients, with 11% having some residual dysphagia.

Technical Aspects of Laparoscopic Approach

We approach myotomy with or without resection exactly as we do a myotomy for achalasia as has been previously described by our group [26]. Briefly, preoperative preparation includes 3 days of clear liquid diet and an extended fasting period due to the risk of aspiration. Careful communication with anesthesia is required, and we recommend rapid sequence intubation. The patient is placed in either a split-leg or modified lithotomy position with pressure points well-padded and secured for at least 20 degrees of reverse Trendelenburg. We use a Veress needle at the costal margin in the left mid-clavicular line for insufflation, followed by optical access of the abdomen. The ports are placed in the usual configuration for hiatal surgery: camera port slightly to the left and superior to the umbilicus, operating ports superior to the camera ports below the costal margin on each side, a liver retractor in the epigastrium, and an assistant port near the left costal margin in the anterior axillary line (Fig. 8.3).

After the liver retractor is placed, the assistant retracts the stomach gently inferiorly and laterally. We incise the gastrophrenic ligament with cautery at the angle of His and the GE junction fat pad is mobilized off the diaphragm, and then the peritoneum attaching the fundus to the diaphragm is taken, creating space above the short gastric vessels. If a posterior fundoplication is planned, we then come approximately 6 cm down the greater curve and enter the lesser sac, taking the short gastric vessels and posterior attachments

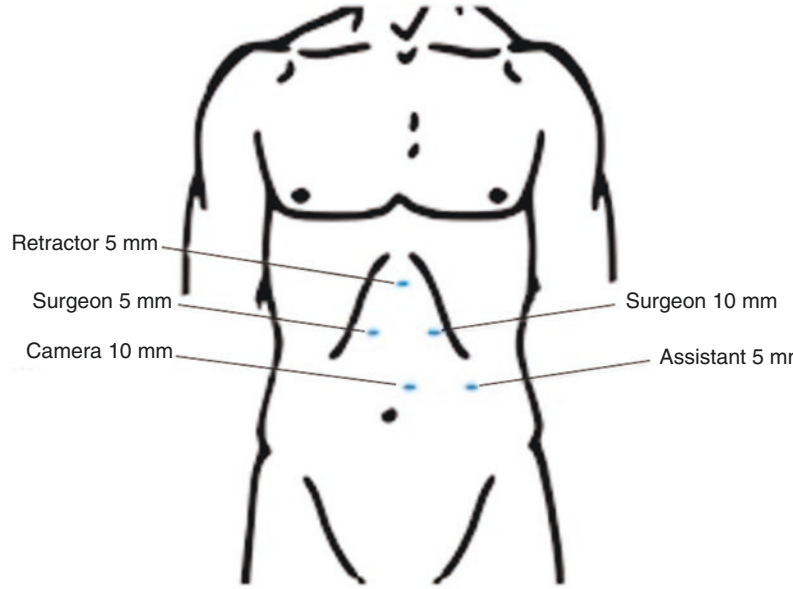


Fig. 8.3 Port placement for myotomy and epiphrenic diverticulectomy

with a bipolar device. The gastrohepatic membrane is incised and the dissection taken up to the right crus. The esophagus is exposed by incising the phrenoesophageal membrane, and the esophageal dissection continues into the mediastinum with special care taken to identify and preserve the anterior and posterior vagus nerves. A Penrose drain is placed around the esophagus for retraction. After the esophagus is dissected proximal to the base of the diverticulum, dissection of the diverticulum continues until the entire neck and pouch are free of adhesions. Flexible endoscopy to inflate and deflate the diverticulum may be of help in this dissection.

When the diverticulum is completely free, a lighted bougie (52Fr) is placed to prevent narrowing of the esophagus at the staple line. This can be a dangerous step of the procedure as the bougie can inadvertently perforate the diverticulum or esophagus. Careful communication with the anesthesia team is critical. If there is any doubt, the bougie should be placed by the surgeon or the bougie can be substituted with an endoscope to allow direct visualization during insertion. An Endo-GIA stapler is placed in the left subcostal operating port, advanced into the mediastinum and fired across the neck of the diverticulum. The resected diverticulum is placed off to the side. The pulsion diverticulum (and therefore the staple line) does not include the muscular layers. We therefore close the muscle over the staple line with a series of interrupted sutures.

With the lighted bougie or endoscope still in place, we then begin the myotomy. We first mobilize the anterior vagus nerve off of the GE junction, using the GE junction fat pad as a handle. We start the myotomy 3 cm distal to the gastroesophageal junction on the stomach in the submucosal plane. It is continued under the anterior vagus nerve up to the level of the diverticulum, staying at least a centimeter lateral from the staple line. The bougie is then removed.

If necessary, we then close the hiatus posteriorly with interrupted sutures, although to prevent narrowing and dysphagia, we will not usually be as aggressive in our hiatal closure as we might be in a similar operation for reflux or paraesophageal hernia. We then perform a Toupet fundoplication. The posterior fundus of the stomach is marked 3 cm from the GE junction and 2 cm from the greater curvature. We bring the posterior fundus under the esophagus and construct the fundoplication by suturing the marked posterior

stomach to the right crus and cut edge of the myotomy 3 cm from the GE junction. We then place 1–2 sutures from the wrap to the crura posteriorly as a gastropexy and complete the right side of the wrap with 2–3 additional sutures from the wrap to the cut edge of the myotomy, for a total length of 3 cm. We then create the left side of the wrap by taking the anterior fundus, again 3 cm from the GE junction and 2 cm from the greater curve, and securing it to the left crus and cut edge of the myotomy. We then perform flexible endoscopy to assure that there is no leak or obstruction. The diverticulum and the ports are removed under direct vision. We typically do not leave a drain.

Thoracic Myotomy and Diverticulectomy

Although the majority of these operations are now performed laparoscopically, a thoracic approach remains useful for diverticula high enough in the mediastinum to make a laparoscopic myotomy difficult or impossible and for those patients in whom an abdominal approach is contraindicated. Varghese et al. have reported the results of the largest series of patients undergoing thoracic approach to epiphrenic diverticulum, with 35 patients over 29 years at the University of Michigan. Most had resection of the diverticulum, long myotomy, and an antireflux procedure (Nissen, Collis-Nissen, or modified Belsey), although one patient had no antireflux procedure and one had plication rather than resection of the diverticulum. There was one death due to leak and one additional non-fatal leak. Symptoms completely resolved in 74% of patients, with 20% needing pneumatic dilation for dysphagia.

Although the thoracic approach can be either open or minimally invasive, the principles are the same. In an open approach, a posterolateral left thoracotomy is performed even though most diverticula project into the right chest because the left chest provides superior access to the gastroesophageal junction for the myotomy and partial fundoplication. Macke et al., who prefer a minimally invasive transthoracic approach, have published a case series of 33 patients undergoing VATS for esophageal diverticula, and they prefer to perform VATS from the right side [27].

In either approach, the inferior pulmonary ligament is divided and the lung is retracted anteriorly. The mediastinal pleura is divided and the esophagus is bluntly mobilized circumferentially. The anterior and posterior vagus nerves are identified and left on the esophagus. The diverticulum is identified and completely dissected off the surrounding structures, with the neck exposed so that the muscle layer is visible surrounding its entire circumference. As in the laparoscopic approach, a bougie is placed to prevent narrowing and a stapler is placed across the diverticulum, oriented in parallel to the esophagus.

The myotomy is then performed away from the diverticulectomy site, at least 1 cm and 180 degrees if feasible. This is extended superiorly to the inferior pulmonary vein and inferiorly to 2 cm beyond the gastroesophageal junction on the stomach. The esophagus and stomach are checked for leaks and the muscle layer is closed over the diverticulectomy site. Any leaks should be repaired with absorbable suture. An intercostal muscle flap may also be placed over the diverticulectomy site or over the site of a repaired mucosal injury.

Endoscopic Management

There are now a handful of reports of peroral endoscopic myotomy (POEM) for ED [28, 29], potentially including endoscopic division of the septum [30]. The long-term outcomes of this approach are unclear as are the indications, contraindications, and risks. Given that the role of resection is itself unclear, an endoscopic myotomy may be sufficient in selected patients but at this point POEM for epiphrenic diverticula has to be considered investigational. It may be best suited for patients who are quite symptomatic from their motility disorder and unwilling to undergo surgical myotomy and diverticulectomy. Further study is required to evaluate safety and long-term results of endoscopic therapy in the presence of a diverticulum.

Summary

Epiphrenic diverticula are rare. Most are thought to be associated with an underlying motility disorder. Workup includes upper GI series, manometry, and upper endoscopy. When asymptomatic or minimally symptomatic, they can be safely observed with a small rate of complications such as perforation, bleeding, or malignancy. Management of symptomatic diverticula should include myotomy, with diverticulectomy and fundoplication performed in most patients. Although there are no studies directly comparing thoracic and laparoscopic approaches, symptom resolution is similar between approaches and is generally good ranging from 80% to 100% [3, 14, 23]. In an analysis of the National Inpatient Sample database, morbidity was more than 7X higher in the thoracic approach than laparoscopic management of epiphrenic diverticula [1], and therefore we recommend the laparoscopic approach when feasible. The role of endoscopic myotomy is unclear and rapidly evolving, but at this time, it should be considered investigational. Because this is a rare disease (<120 cases/year in the US) with substantial risk of morbidity (up to 20% leak rate), it should be managed by experienced esophageal surgeons in high volume centers.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Onwugbufor MT, Obirieze AC, Ortega G, Allen D, Cornwell EE 3rd, Fullum TM. Surgical management of esophageal diverticulum: a review of the Nationwide inpatient sample database. J Surg Res. 2013;184(1):120–5.
2. D'Journo XB, Ferraro P, Martin J, Chen LQ, Duranceau A. Lower oesophageal sphincter dysfunction is part of the functional abnormality in epiphrenic diverticulum. Br J Surg. 2009;96(8):892–900.
3. Rossetti G, Fei L, del Genio G, et al. Epiphrenic diverticula mini-invasive surgery: a challenge for expert surgeons–personal experience and review of the literature. Scand J Surg. 2013;102(2):129–35.
4. Zaninotto G, Portale G, Costantini M, et al. Long-term outcome of operated and unoperated epiphrenic diverticula. J Gastrointest Surg. 2008;12(9):1485–90.
5. Kao AM, Arnold MR, Schlosser KA, et al. Epiphrenic diverticulum: 20-year single-institution experience. Am Surg. 2018;84(7):1159–63.
6. Mondiere J. Notes sur quelques maladies de l'oesophage. Arch Gen Med Paris. 1833;3:28–65.
7. Belsey R. Functional disease of the esophagus. J Thorac Cardiovasc Surg. 1966;52(2):164–88.
8. Effler DB, Barr D, Groves LK. Epiphrenic diverticulum of the esophagus: surgical treatment. Arch Surg. 1959;79:459–67.
9. Thomas ML, Anthony AA, Fosh BG, Finch JG, Maddern GJ. Oesophageal diverticula. Br J Surg. 2001;88(5):629–42.
10. Zaninotto G, Portale G, Constantini M, et al. Long-term outcome of operated and unoperated epiphrenic diverticulum. J Gastrointest Surg. 2008;12:1485–90.
11. Nehra D, Lord RV, DeMeester TR, et al. Physiologic basis for the treatment of epiphrenic diverticulum. Ann Surg. 2002;235(3):346–54.
12. Vicentine FP, Herbella FA, Silva LC, Patti MG. High resolution manometry findings in patients with esophageal epiphrenic diverticula. Am Surg. 2011;77(12):1661–4.
13. Stroh C, Hohmann U, Meyer F, Manger T. Epiphrenic esophageal diverticulum after laparoscopic placement of an adjustable gastric band. Obes Surg. 2006;16(3):372–4.
14. Fisichella PM, Jalilvand A, Dobrowolsky A. Achalasia and epiphrenic diverticulum. World J Surg. 2015;39(7):1614–9.
15. Stalheim AJ. Spontaneous perforation of diverticulum of distal esophagus. Minn Med. 1978;61(7):424–6.
16. Tse CS, Parikh ND. An uncommon source of upper gastrointestinal bleeding: epiphrenic esophageal diverticulum. Gastroenterol Rep (Oxf). 2017;5(4):313–5.
17. Herbella FA, Dubecz A, Patti MG. Esophageal diverticula and cancer. Dis Esophagus. 2012;25(2):153–8.
18. Katsinelos P, Chatzimavroudis G, Zavos C, Pilpilidis I, Paroutoglou G, Kountouras J. Long-term botulinum toxin treatment for dysphagia due to large epiphrenic diverticulum in elderly patients: a report of two cases. Dysphagia. 2009;24(1):109–13.
19. Aiolfi A, Bona D, Bonavina L. Endoscopic treatment of an epiphrenic diverticulum using a fully covered self-expanding metal stent. Endoscopy. 2013;45:E101.
20. Wright AS, Williams CW, Pellegrini CA, Oelschlager BK. Long-term outcomes confirm the superior efficacy of extended Heller myotomy with Toupet fundoplication for achalasia. Surg Endosc. 2007;21(5):6.
21. Valentini M, Pera M, Vidal O, Lacima G, Belda J, de Lacy AM. Incomplete esophageal myotomy and early recurrence of an epiphrenic diverticulum. Dis Esophagus. 2005;18(1):64–6.
22. Rosati R, Fumagalli U, Elmore U, de Pascale S, Massaron S, Peracchia A. Long-term results of minimally invasive surgery for symptomatic epiphrenic diverticulum. Am J Surg. 2011;201(1):132–5.
23. Herbella FA, Patti MG. Achalasia and epiphrenic diverticulum. World J Surg. 2015;39(7):1620–4.

24. Allaix ME, Borraez Segura BA, Herbella FA, Fisichella PM, Patti MG. Is resection of an esophageal epiphrenic diverticulum always necessary in the setting of achalasia? World J Surg. 2015;39(1):203–7.
25. Rawlings A, Soper NJ, Oelschlager B, et al. Laparoscopic dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26(1):18–26.
26. Tatum RP, Pellegrini CA. How I do it: laparoscopic Heller myotomy with Toupet fundoplication for achalasia. J Gastrointest Surg. 2009;13(6):1120–4.
27. Macke RA, Luketich JD, Pennathur A, et al. Thoracic esophageal diverticula: a 15-year experience of minimally invasive surgical management. Ann Thorac Surg. 2015;100(5):1795–802.
28. Yang J, Zeng X, Yuan X, et al. An international study on the use of peroral endoscopic myotomy (POEM) in the management of esophageal diverticula: the first multicenter D-POEM experience. Endoscopy. 2019;51(4):346–9.
29. Demeter M, Banovcin P Jr, Duricek M, Kunda R, Hyrdel R. Peroral endoscopic myotomy in achalasia and large epiphrenic diverticulum. Dig Endosc. 2018;30(2):260–2.
30. Nabi Z, Ramchandani M, Darisetty S, Kotla R, Reddy DN. Per-oral endoscopic myotomy with endoscopic septum division in a case of achalasia with large epiphrenic diverticulum. VideoGIE. 2019;4(1):14–6.

9 Persistent or Recurrent Symptoms After Heller Myotomy for Achalasia: Evaluation and Treatment

Marco G. Patti, Francisco Schlottmann, and Marco Di Corpo

A shift in the treatment algorithm of esophageal achalasia has slowly occurred in the last three decades due to the introduction of minimally invasive surgery. The technique has evolved over time, and today a laparoscopic Heller myotomy and partial fundoplication is considered in most Centers the treatment modality of choice [1–14].

In 1992, we reported our initial experience with a myotomy performed through a left thoracoscopic approach [15]. Using the guidance provided by intraoperative endoscopy, we performed a myotomy, which extended for only 5 mm onto the gastric wall, without an antireflux procedure. It became soon clear that, when compared to the classic approach by a left thoracotomy, the operation was associated with a shorter hospital stay, reduced postoperative discomfort, and a faster recovery [15]. Long-term follow-up showed that the operation achieved relief of dysphagia in almost 90% of patients, but that abnormal reflux occurred in 60% of patients when measured by ambulatory pH monitoring [1]. For this reason, the thoracoscopic approach was abandoned, and the laparoscopic approach was chosen as it provided a better exposure of the gastroesophageal junction (GEJ) and allowed the performance of a fundoplication [1]. Over time, the length of the myotomy onto the gastric wall was increased, as studies showed that a longer myotomy provided better relief of dysphagia [3, 6].

Overall, a major improvement in the swallowing status can be achieved today in about 90–95% of patients [4, 6, 7, 10]. However, some patients have recurrence of their symptoms over time (recurrent dysphagia). This chapter describes the technical elements that are important for a successful operation and our approach to the diagnosis and treatment of patients with persistent or recurrent dysphagia after a Heller myotomy.

Persistent Dysphagia

Persistent dysphagia is defined as dysphagia which is still present immediately or short after a Heller myotomy. Usually this is due to technical issues during the performance of the operation:

M. G. Patti (✉)
Departments of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA
e-mail: marco_patti@med.unc.edu

F. Schlottmann
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Di Corpo
Departments of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_9

Short Myotomy

The most common cause of persistent dysphagia is a short myotomy on the gastric side of the GEJ (Fig. 9.1). This became evident during our early experience, when the operation was performed through the chest and the ability to carry out the myotomy onto the gastric wall was limited. With the advent of the laparoscopic approach to the esophagus, we switched from the thoracoscopic to the laparoscopic approach. While this approach provided the opportunity to perform a longer myotomy in the gastric wall, we initially chose to extend it only 1–1.5 cm below the GEJ. Encouraged by what appeared to be a better resolution of dysphagia, a few years later we decided to extend the myotomy even further to 2.5–3.0 cm below the GEJ. In a landmark study, Oelschlager et al. compared the results of a conventional myotomy (1.5 cm onto the gastric wall) to those obtained with an "extended" myotomy (3.0 cm below the GEJ) [3]. Long-term relief of dysphagia was obtained in 83% and 97% of patients, respectively [6]. Today, an 8 cm myotomy, extending for 2.5 cm myotomy onto the gastric wall, is our standard technique for patients with achalasia. Intraoperative endoscopy is important to assess the distal extension in relationship to the endoscopic view of the squamocolumnar junction. With more experience, the endoscopy can be avoided and the first branch of the left gastric artery can be used as a landmark to gauge the extent of the myotomy onto the gastric wall.

Fig. 9.1 Short myotomy

Incomplete Myotomy

This may occur because of scar tissue at the level of the GEJ secondary to prior endoscopic treatment [2, 7, 16–18]. Both pneumatic dilatation and intrasphincteric injection of botulinum toxin can cause scarring at the level of the GEJ with fibrosis and loss of the normal anatomic planes. In these cases, the myotomy is more difficult, perforation of the mucosa is more common, and the results are less predictable [16].

Lack of Separation of the Muscle Edges

After completion of the myotomy, it is important to separate the edges of the muscle layers so that about 30–40% of the mucosa is uncovered [2]. This step decreases the chance of reapproximation of the muscle edges distally during healing and the formation of a new scar resulting in esophageal narrowing (Fig. 9.2).

Tight Closure of the Hiatus

We do not advocate hiatal closure in the average patient with achalasia because sutures that narrow the hiatal opening may impair esophageal emptying. Hiatal closure should be considered only for the rare patient who has an associated large hiatal hernia; and in those

Fig. 9.2 Lack of separation of the muscle edges

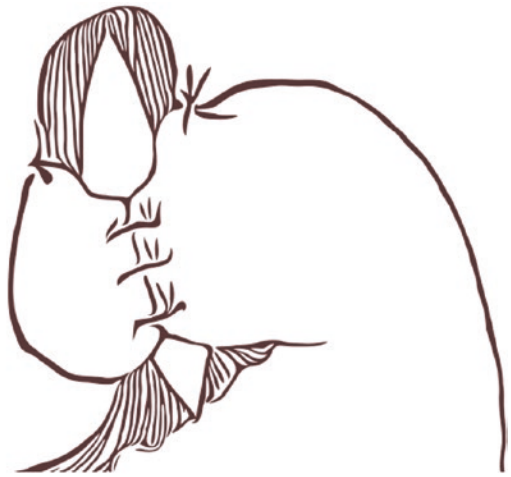


Fig. 9.3 Wrong type of fundoplication

patients, we recommend the hiatus be closed only partially to avoid persistence of dysphagia.

Wrong Type of Fundoplication

A 360° fundoplication may create a mechanical obstruction because of the lack of peristalsis in patients with achalasia (Fig. 9.3).

Wrong Configuration of the Fundoplication

Either an anterior or a posterior partial fundoplication may be a cause of persistent dysphagia. A Dor fundoplication (180° anterior) must be constructed with two rows of sutures only, one on the left and one on the right [9]. The left row should have three sutures, with the upper one incorporating the esophagus, the fundus of the stomach, and the left pillar of the crus. The second and the third stitches are placed between the fundus of the stomach and the left side of the esophageal wall (Fig. 9.4a, b). After folding the fundus over the exposed mucosa, three additional sutures are placed. The first one incorporates the fundus of the stomach, the esophagus, and the right pillar of the crus; the second and the third stitches should only incorporate the esophageal wall and the fundus. Apical stitches and transection of the short gastric vessels are also important as they avoid tension on the fundoplication.

Too many stitches at this level will cause constriction of the GEJ. Patti et al. showed that problems with the construction of a Dor fundoplication can be a cause of both persistent and recurrent dysphagia [2]. A Toupet fundoplication (240° posterior) may also cause angulation of the esophagus and problems with esophageal emptying [11].

Recurrent Dysphagia

These are patients who experience substantial relief for months or years after the initial Heller myotomy and then experience progressive dysphagia. The specific cause of recurrent dysphagia is not always easy to elucidate as progression of disease, scarring in the area of the previous Heller, or cancer may be causing it. Most common causes of recurrent dysphagia are:

Scarring of the Distal Edge of the Myotomy

When patients experience recurrent symptoms after a long symptom free interval, scarring at

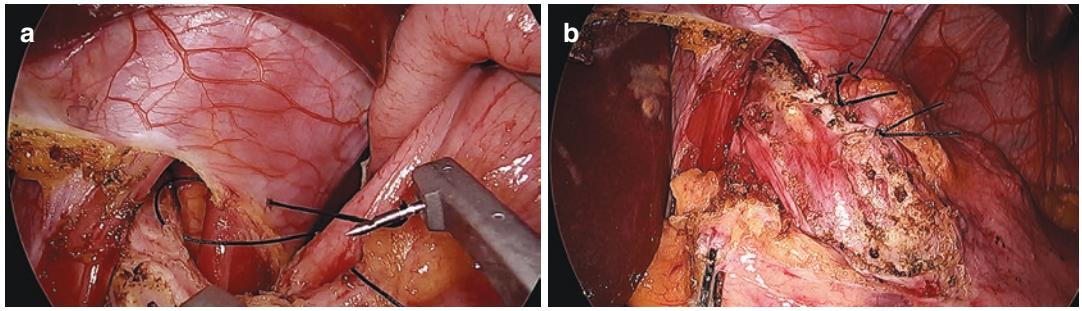


Fig. 9.4 First row of suture for Dor fundoplication. (**a**) First triangular stitch between gastric fundus, esophagus and left pillar. (**b**) First row for Dor fundoplication

the distal edge of the myotomy is the most common cause (Fig. 9.5) [2, 19, 20]. While studies to date have not identified specific factors that predict this problem, we believe that a longer myotomy and a wider separation of the muscular edges of the myotomy at the time of initial operation might decrease the frequency of this problem [3, 6].

Fig. 9.5 Scarring of the distal edge of the myotomy

360° Fundoplication

A partial fundoplication is the procedure of choice in conjunction with a Heller myotomy as it takes into consideration the lack of esophageal peristalsis. Because both a Dor and a Toupet fundoplication are effective in controlling reflux in only 80–90% of patients, some authors proposed the use of a Nissen fundoplication [21]. This approach, however, is associated with poor long-term results [22, 23]. For instance, Rebecchi et al. compared 71 patients who underwent a laparoscopic Heller myotomy and Dor fundoplication with 67 patients who had a Heller myotomy and a Nissen fundoplication [23]. After 10 years, dysphagia was present in 2.8% and 15% of patients, respectively. Similar problems have been reported by others [22].

Gastroesophageal Reflux Disease

Postoperative reflux is present in 50–60% of patients when a myotomy alone is performed and in 10–20% when a partial fundoplication is added. Abnormal reflux is considered a common cause of recurrent dysphagia. Csendes et al. showed that there is a progressive clinical deterioration of the initially good results over time and that this deterioration is mainly due to an increase in pathologic reflux and the development of short or long-segment Barrett's esophagus [24]. Unfortunately, most patients that develop pathologic reflux are asymptomatic [1]. It is therefore very important, particularly when operating on young patients, to perform an ambulatory pH monitoring after the operation [25]. If abnormal

reflux is present, acid-reducing medications should be prescribed and closer endoscopic follow-up performed.

Esophageal Cancer

Achalasia patients are at increased risk of developing squamous cell carcinoma. In addition, if pathologic reflux occurs after the myotomy, Barrett's esophagus and adenocarcinoma can develop causing recurrent dysphagia [26]. Although precise guidelines about endoscopic follow-up in achalasia patients have not been established, an upper endoscopy should be routinely performed every 3–5 years.

Diagnostic Evaluation

When a patient complains of recurrent dysphagia, it is important to perform a complete workup to try to identify the cause in order to formulate a tailored treatment plan [27].

The first step should always be to review the entire history – in particular that which existed before the first operation – and to review, when possible the diagnostic tests performed before the initial operation. It is at this time that we have found that some of these patients did not have achalasia to begin with. Once this process is complete, we like to review the report of the original operation. Often there are clues that explain the symptoms, such as the description of scar tissue due to prior treatment, failure of identifying the anatomic planes, or a short myotomy.

The symptomatic evaluation is the next step. It determines which symptoms are present and compares them to the symptoms present before the first operation. In addition, it distinguishes between persistent and recurrent dysphagia.

A *barium swallow* is very useful to determine the cause of the dysphagia. It identifies the area of obstruction, assesses the degree of esophageal dilatation, the emptying of the barium from the esophagus into the stomach, and shows the overall shape of the esophagus. It might help distinguish between a short myotomy, a tight closure of the hiatus, and a constricting or malpositioned fundoplication. Loviscek et al. reported a series of patients with recurrent dysphagia after Heller myotomy who underwent redo surgery and were able to correlate the preoperative radiologic findings on barium swallow to the postoperative improvement in symptoms. All patients with a straight esophagus (normal or dilated caliber) had improved dysphagia after revisional surgery, whereas dysphagia improvement was less consistent if the esophagus was sigmoid in shape [27].

An *upper endoscopy* should be carried out in every patient as it can show if there is mucosal damage due to reflux, candida esophagitis due to slow emptying, or cancer. Endoscopic evaluation can also reveal angulation of the distal esophagus due to a malpositioned or overly tight fundoplication.

Esophageal manometry is essential to confirm the diagnosis of achalasia and to measure the pressure and relaxation of the lower esophageal sphincter. When compared to the preoperative test, it can show if the myotomy has been extended appropriately onto the gastric wall or if a residual high-pressure zone is still present.

Ambulatory 24-hour pH monitoring should be performed in patients with recurrent dysphagia. It is important to look not only at the reflux score, but to review the pH tracing to distinguish between real reflux and false reflux due to stasis and fermentation. This test should be routinely done even in asymptomatic patients after a Heller myotomy as reflux can be often "silent" [1]. This is particularly important when operating on children as a life-long exposure to reflux can cause Barrett's esophagus or even esophageal cancer [24, 26, 28].

When pseudoachalasia secondary to the presence of cancer is suspected, endoscopic ultrasound and computed tomography can help establish the diagnosis [29].

Treatment

Pneumatic Balloon Dilatation

A balloon dilatation should always be considered in patients with recurrent dysphagia. Contrary to

common belief, the perforation rate is very low due to the fact that the myotomy is covered by the stomach if a Dor was performed or by the left lateral segment of the liver if a Toupet was added to the myotomy. Zaninotto et al. documented recurrent dysphagia in 9 of 113 patients (8%) after laparoscopic Heller myotomy and Dor fundoplication [19]. Seven of the nine patients were effectively treated by balloon dilatation (median two dilatations, range 1–4), while two required a second operation. Similar results were described by Sweet et al. who reported on the effectiveness of dilatation for the treatment of both persistent and recurrent dysphagia [7].

Revisional Surgery

If dysphagia is not relieved by dilatations, a reoperation must be considered. When consenting the patient, it is important to stress that even though most cases can be performed laparoscopically, a laparotomy might be needed. In addition, patients must be aware that in case of severe damage to the mucosa during the course of the operation, an esophagectomy may be necessary.

The first step of the operation consists in separating the liver from the stomach and the esophagus. Subsequently the fundoplication should be taken down and the fundus brought to the left in order to fully expose the esophageal wall. Once the previous myotomy has been exposed and the area of narrowing is clearly identified, we prefer to correct the problem by performing a new myotomy on the side of the anterior esophagus opposite to the first myotomy. Rather than trying to extend the prior myotomy, it is easier to perform a new myotomy on the opposite side in order to work on an unscarred part of the esophageal wall (see Fig. 9.6) [27]. The myotomy should be extended for about 2.5–3 cm below the GEJ, and intraoperative endoscopy should be performed to evaluate for inadvertent esophageal or gastric mucosal injury. After the myotomy is completed, consideration should be given whether or not to add a fundoplication. If a mucosal injury has occurred, a Dor fundoplication should be performed to cover the area of injury.

Fig. 9.6 New myotomy on the opposite side

In the absence of a perforation, often we do not perform a fundoplication, based on the following considerations: (a) dysphagia is the primary problem necessitating repeat intervention; (b) returning to the operating room a third time to relieve dysphagia is an increasingly difficult task; (c) occasionally a fundoplication may contribute to dysphagia; and (d) abnormal reflux can be treated medically far easier than dysphagia. Loviscek et al. recently showed excellent results using this approach [27]. The outcome of 43 achalasia patients who underwent redo Heller myotomy for recurrent dysphagia between 1994 and 2011 was analyzed. Three patients underwent take down of the previous fundoplication only, while the remaining 40 patients had that and a redo myotomy that extended for 3 cm onto the gastric wall. A fundoplication was added in one third of patients only. At a median follow-up of 63 months in 24 patients, 19 patients (79%) reported improvement of dysphagia with median overall satisfaction rating of 7 (range 3–10). Four patients required esophagectomy for persistent dysphagia. Similar results have been reported by others [30–32].

Sometimes patients present with recurrent dysphagia after a Heller myotomy performed through either a left thoracotomy or a left thoracoscopic approach [33]. Because the abdomen and the right side of the esophagus are free of adhesions and scar tissue created by the first operation, a laparoscopic approach allows a myotomy to be performed on the right side of the esophagus with excellent results [33]. Depending on the size of the esophagus, a partial fundoplication can be added to the myotomy.

Peroral Endoscopic Myotomy

A peroral endoscopic myotomy (POEM) has been associated with excellent relief of dysphagia in patients with achalasia [34, 35]. Short-term follow-up in patients in whom POEM has been used as a primary treatment modality has shown improvement of the swallowing status in the majority of patients. Because the laparoscopic myotomy is performed on the anterior wall of the esophagus, POEM could be used as a remedial operation in patients with persistent or recurrent dysphagia by performing an endoscopic myotomy on the posterior wall of the esophagus.

Esophagectomy

Esophagectomy should be avoided whenever possible as it is associated with a mortality rate between 2% and 4% even in expert hands [36, 37]. In addition, it carries a high morbidity rate. For instance, Devaney and colleagues reported a 10% rate of anastomotic leak, 5% rate of hoarseness, and 2% rate of bleeding and chylothorax requiring thoracotomy among 93 patients who had an esophagectomy for achalasia [37]. Furthermore, 46% of patients had dysphagia requiring anastomotic dilatation, 42% had regurgitation, and 39% had dumping syndrome. The average hospital stay was 12.5 days.

Despite these shortcomings, esophagectomy is sometimes the only option left to treat these patients. This is particularly the case for patients with a dilated and sigmoid-shaped esophagus who have already failed Heller myotomy, dilatations, and sometimes a redo Heller or POEM. When performing an esophagectomy, we prefer to use the stomach as an esophageal substitute. Because the esophagus is frequently dilated and fed by large blood vessels, we prefer to dissect the thoracic esophagus under direct vision, either thoracoscopically or by performing a right thoracotomy. The esophagogastric anastomosis can be placed either in the neck or at the apex of the right chest.

Conclusions

A laparoscopic Heller myotomy with partial fundoplication is now considered the surgical procedure of choice for patients with achalasia. The technical steps have been clearly identified and described, and failure to follow them causes persistent or recurrent symptoms. Although the operation has a very high success rate, some patients eventually need further treatment, particularly if the first operation was done at an early age. When this happens, it is important to perform a careful workup to try to identify the cause and to have a tailored treatment plan. The best results are obtained in centers where radiologists, gastroenterologists, and surgeons have experience in the diagnosis and treatment of this rare disease.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Patti MG, Pellegrini CA, Horgan S, Arcerito M, Omelanczuk P, Tamburini A, Diener U, Eubanks TR, Way LW. Minimally invasive surgery for achalasia: an 8-year experience with 168 patients. Ann Surg. 1999;230:587–93.
2. Patti MG, Molena D, Fisichella PM, Whang K, Yamada H, Perretta S, Way LW. Laparoscopic Heller myotomy and Dor fundoplication for achalasia: analysis of successes and failures. Arch Surg. 2001;136:870–7.
3. Oelschlager BK, Chang L, Pellegrini CA. Improved outcomeafterextendedgastricmyotomy for achalasia. Arch Surg. 2003;138:490–5.

4. Patti MG, Fisichella PM, Perretta S, Galvani C, Gorodner MV, Robinson T, Way LW. Impact of minimally invasive surgery on the treatment of esophageal achalasia: a decade of change. J Am Coll Surg. 2003;196:698–703.
5. Richards WO, Torquati A, Holzman MD, Khaitan L, Byrne D, Lutfi R, Sharp KW. Heller myotomy versus Heller myotomy with Dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. Ann Surg. 2004;240:405–12.
6. Wright AS, Williams CW, Pellegrini CA, Oelschlager BK. Long-term outcomes confirm the superior efficacy of extended Heller myotomy with Toupet fundoplication for achalasia. Surg Endosc. 2007;21:713–8.
7. Sweet MP, Nipomnick I, Gasper WJ, Bagatelos K, Ostroff JW, Fisichella PM, Way LW, Patti MG. The outcome of laparoscopic Heller myotomy for achalasia is not influenced by the degree of esophageal dilatation. J Gastrointest Surg. 2008;12:159–65.
8. Wang YR, Dempsey DT, Friedenberg FK, Richter JE. Trends of Heller myotomy hospitalizations for achalasia in the United States, 1993–2005: effect of surgery volume on perioperative outcomes. Am J Gastroenterol. 2008;103:2454–64.
9. Patti MG, Fisichella PM. Laparoscopic Heller myotomy and dor fundoplication for esophageal achalasia. How I do it. J Gastrointest Surg. 2008;12:764–6.
10. Zaninotto G, Costantini M, Rizzetto C, Zanatta L, Guirroli E, Portale G, Nicoletti L, Cavallin F, Battaglia G, Ruol A, Ancona E. Four hundred laparoscopic myotomies for esophageal achalasia: a single centre experience. Ann Surg. 2008;248:986–893.
11. Tatum RP, Pellegrini CA. How I do it: laparoscopic Heller myotomy with Toupet fundoplication for achalasia. J Gastrointest Surg. 2009;13:1120–4.
12. Patti MG, Herbella FA. Fundoplication after laparoscopic Heller myotomy for esophageal achalasia: what type? J Gastrointest Surg. 2010;14:1453–8.
13. Roll GR, Ma S, Gasper WJ, Patti M, Way LW, Carter J. Excellent outcomes of laparoscopic esophagomyotomy for achalasia in patients older than 60 years of age. Surg Endosc. 2010;24:2562–6.
14. Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini C, Pierce RA, Pryor A, Martin V, Frisella MM, Cassera M, Brunt LM. Laparoscopic dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26:18–26.
15. Pellegrini C, Wetter LA, Patti M, Leichter R, Mussan G, Mori T, Bernstein G, Way L. Thoracosc opicesophagomyotomy. Initialexperience with a new approach for the treatment of achalasia. Ann Surg. 1992;216:291–6.
16. Patti MG, Feo CV, Arcerito M, De Pinto M, Tamburini A, Diener U, Gantert W, Way LW. Effects of previous treatment on results of laparoscopic Heller myotomy for achalasia. Dig Dis Sci. 1999;44:2270–6.
17. Snyder CW, Burton RC, Brown LE, Kakade MS, Finan KR, Hawn MT. Multiple preoperative endoscopic interventions are associated with worse outcomes after laparoscopic Heller myotomy for achalasia. J Gastrointest Surg. 2009;13:2095–103.
18. Smith CD, Stival A, Howell DL, Swafford V. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than Heller myotomy alone. Ann Surg. 2006;243:579–84.
19. Zaninotto G, Costantini M, Portale G, Battaglia G, Molena D, Carta A, Costantino M, Nicoletti L, Ancona E. Etiology, diagnosis, and treatment of failures after laparoscopic Heller myotomy for achalasia. Ann Surg. 2002;235:186–92.
20. Gockel I, Junginger T, Eckardt VF. Persistent and recurrent achalasia after Heller myotomy: analysis of different patterns and long-term results of reoperation. Arch Surg. 2007;142:1093–7.
21. Rossetti G, Brusciano L, Amato G, Maffettone V, Napolitano V, Russo G, Izzo D, Russo F, Pizza F, Del Genio G, Del Genio A. A total fundoplication is not an obstacle to esophageal emptying after heller myotomy for achalasia: results of a long-term follow up. Ann Surg. 2005;241:614–21.
22. Zhu ZJ, Chen LQ, Duranceau A. Long-term result of total versus partial fundoplication after esophagomyotomy for primary esophageal motor disorders. World J Surg. 2008;32:401–7.
23. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. Ann Surg. 2008;248:1023–30.
24. Csendes A, Braghetto I, Burdiles P, Korn O, Csendes P, Henríquez A. Very late results of esophagomyotomy for patients with achalasia: clinical, endoscopic, histologic, manometric, and acid reflux studies in 67 patients for a mean follow-up of 190 months. Ann Surg. 2006;243:196–203.
25. Patti MG, Diener U, Molena D. Esophageal achalasia: preoperative assessment and postoperative follow-up. J Gastrointest Surg. 2001;5:11–2.
26. Lopes AB, Fagundes RB. Esophageal squamous cell carcinoma –precursor lesions and early diagnosis. World J Gastrointest Endosc. 2012;4:9–16.
27. Loviscek MF, Wright AS, Hinojosa MW, Petersen R, Pajitnov D, Oelschlager BK, Pellegrini CA. Recurrent dysphagia after Heller myotomy: is esophagectomy always the answer? J Am Coll Surg. 2013;216:736–43.
28. Patti MG, Albanese CT, Holcomb GW 3rd, Molena D, Fisichella PM, Perretta S, Way LW. Laparoscopic Heller myotomy and Dor fundoplication for esophageal achalasia in children. J Pediatr Surg. 2001;36:1248–51.
29. Moonka R, Patti MG, Feo CV, Arcerito M, De Pinto M, Horgan S, Pellegrini CA. Clinical presentation and evaluation of malignant pseudoachalasia. J Gastrointest Surg. 1999;3:456–61.
30. Iqbal A, Tierney B, Haider M, Salinas VK, Karu A, Turaga KK, Mittal SK, Filipi CJ. Laparoscopic reoperation for failed Heller myotomy. Dis Esophagus. 2006;19:193–9.

31. Grotenhuis BA, Wijnhoven BP, Myers JC, Jamieson GG, Devitt PG, Watson DI. Reoperation for dysphagia after cardiomyotomy for achalasia. Am J Surg. 2007;194:678–82.
32. Wang L, Li YM. Recurrent achalasia treated with Heller myotomy: a review of the literature. World J Gastroenterol. 2008;14:7122–6.
33. Robinson TN, Galvani CA, Dutta SK, Gorodner MV, Patti MG. Laparoscopic treatment of recurrent dysphagia following transthoracic myotomy for achalasia. J Laparoendosc Adv Surg Tech A. 2003;13:401–3.
34. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256:659–67.
35. Hungness ES, Teitelbaum EN, Santos BF, Arafat FO, Pandolfino JE, Kahrilas PJ, Soper NJ. Comparison of perioperative outcomes between peroral esophageal myotomy (POEM) and laparoscopic Heller myotomy. J Gastrointest Surg. 2013;17:228–35.
36. Pinotti HW, Cecconello I, da Rocha JM, Zilberstein B. Resection for achalasia of the esophagus. Hepato-Gastroenterology. 1991;38:470–3.
37. Devaney EJ, Lannettoni MD, Orringer MB, Marshall B. Esophagectomy for achalasia: patient selection and clinical experience. Ann Thorac Surg. 2001;72:854–8.

10 Esophagectomy for End-Stage Achalasia

John Waters and Daniela Molena

Introduction and History

End-stage achalasia is the most severe form of the disease [1]. Current guidelines from the American College of Gastroenterology (ACG) and the International Society for Diseases of the Esophagus (ISDE) define the disease by both manometric and radiographic criteria.

Manometrically, achalasia demonstrates failure of lower esophageal sphincter relaxation, with documented integrated relaxation pressure (IRP) greater than 15 mm Hg. Disease subtypes are broken down into classes I, II, and III based on the degree of failed peristalsis, esophageal pressurization, and premature contraction (Table 10.1) [2–4]. Radiographically, end-stage achalasia is supported by evidence of megaesophagus (>6 cm), distal esophageal angulation, and sigmoid esophageal shape (Fig. 10.1) [3, 4].

Achalasia affects 1.6 per 100,000 people, occurring equally in men and women between 30 and 60 years of age [5–7]. Patients with end-stage achalasia typically experience dysphagia, recurrent food impaction, poor esophageal clearance, aspiration, recurrent pneumonia, heartburn, occasionally GI bleeding, and retrosternal chest pain [8]. They are also at increased risk for esophageal squamous cell cancer [9, 10].

Table 10.1 Manometric characteristics of achalasia's subtypes

Achalasia subtype	Integrated relaxation pressure (mm Hg)	Peristalsis	Additional considerations
Type 1	>15 mm Hg	100% failed	Premature contractions with DCI <450 mm Hg/s/cm can serve as surrogate for failed peristalsis
Type 2	>15 mm Hg	100% failed	Panesophageal pressurization with ≥20% swallows
Type 3	>15 mm Hg	No normal peristalsis	Premature contractures, DCI >450 mm Hg/s/cm with >20% swallows

Descriptions of the spectrum of achalasia presentation and esophageal morphology fill the literature. One of the earliest studies by F.G. Ellis followed 85 patients diagnosed with achalasia between 1933 and 1948 [11]. Three stages of achalasia were described: onset, silent period, and progressive deterioration. Achalasia was described as a disease with periods of quiescence and sporadic

J. Waters
Memorial Sloan Kettering Cancer Center, New York, NY, USA

D. Molena (✉)
Memorial Sloan Kettering Cancer Center, New York, NY, USA

Esophageal Surgery Program, Thoracic Surgery Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
e-mail: molenad@mskcc.org

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_10

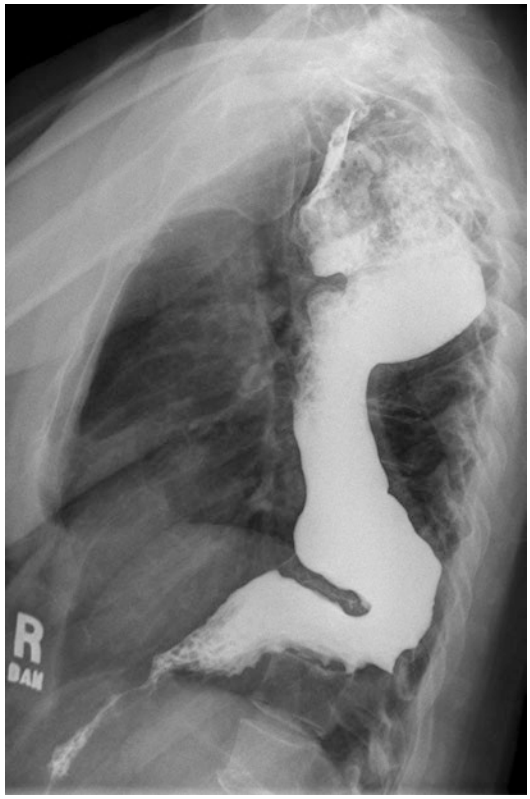


Fig. 10.1 End-stage esophagus characterized by dilation, tortuosity, and distal kinking

progression. But the exact timing and mechanisms through which a normal-sized esophagus transitioned from normal to dilated size were unclear.

More recent analyses provided description of manometric findings of achalasia. But there is little clarity on the risk of each subtype evolving into megaesophagus [12]. It is presumed that a non-resolved fixed distal esophageal obstruction eventually may lead to the development of a dilated, bag-like esophagus. Probably, it takes between 12 and 15 years for a normal-size esophagus to degenerate into a dilated and often sigmoid one [13, 14].

Achalasia Pathophysiology

Pathologic examination of surgical explants suggests that achalasia is an idiopathic neuronal degenerative disease, caused by T-cell lymphocyte destruction of enteric neurons in the distal two-thirds of the esophageal smooth muscle [15–18]. Infectious and congenital etiologies have also been suggested [19].

There is homology between end-stage achalasia and megaesophagus in Chagas disease. The flagella protozoa *Trypanosoma cruzi* is transmitted to humans by the Triatominae bug subfamily [20]. Chagas disease occurs in acute and chronic phases [21]. The acute phase can be symptom-free and occurs in patients typically under 1 year of age. If symptoms do occur, they are generalized and nonspecific: fever, inflammation at inoculation site, lymphadenopathy, and palpebral swelling. This phase lasts 4–8 weeks; approximately 30% of patients will develop subsequent systemic sequelae of the disease. In the gastrointestinal tract, this has been described as organomegaly of the esophagus, stomach, duodenum, jejunum, gallbladder, and colon [22]. Visceral explant analysis has shown that Chagas-affected esophagus demonstrates inflammation and fibrosis of the muscularis propria and myenteric plexus; mononuclear cells are surrounded by eosinophils. Mast cells and rare plasma cell also fill the muscularis and myenteric plexus.

Indications for Esophagectomy

Esophagectomy for end-stage achalasia is indicated for symptomatic patients who suffer from megaesophagus, have failed prior treatment (balloon dilation, Heller myotomy or POEM), and show radiographic evidence of disease progression [3, 4]. Careful preoperative assessment must be performed, and patients must receive full counseling on the details and potential complications of esophagectomy.

Achalasia and Esophagectomy History

In the twentieth century, surgical experiences with achalasia and esophagectomy paralleled each other. The fields did not intersect however until the late 1970s.

Surgical History of Esophageal Achalasia

On April 14, 1913, Ernst Heller (1877–1964) performed the first longitudinal esophageal myotomy in a 49-year-old German man who presented with a pharyngeal food impaction [23, 24]. He performed an anterior and posterior myotomy due to his discontent with the intraoperative visual appearance of the esophagus after anterior myotomy alone.

Four years later, Heller's original longitudinal esophagomyotomy evolved into an anterior myotomy ("modified Heller") [25, 26]. This procedure was quickly popularized and, with the addition of a partial fundoplication to reduce postoperative gastroesophageal reflux, is currently the accepted surgical technique for treating achalasia [4, 27]. The first laparoscopic Heller myotomy was performed in 1991 by Cuschieri et al. [28]. Current outcomes with Heller myotomy demonstrate up to 90% symptom improvement. Achalasia guidelines recommend Heller myotomy as the first-line treatment for achalasia. Balloon dilation and POEM also offer less invasive and promising short-term results [29, 30]; POEM and balloon dilation do not provide antireflux treatment.

Esophagectomy History

In 1913, Dr. Franz Torek at the German Hospital in New York performed the first successful esophagectomy [31]. Through a left thoracotomy, Torek removed the esophagus of a 67-year-old woman suffering from squamous cell esophageal carcinoma. Gastrointestinal continuity was reestablished through an external prosthetic tube connecting a cervical esophagostomy to gastrostomy. The prosthesis was manually removed after meals. The patient lived 13 years postoperatively.

Subsequent esophagectomy outcomes were poor [32]. Bleeding, uncontrolled pneumothorax, esophageal leak, mediastinitis, esophageal necrosis, pneumonia, and death were commonly observed complications. Suboptimal patient selection, poor understanding of esophageal carcinoma, limited anesthetic capability, lack of standardized surgical technique, and critical care and antimicrobial deficiencies contributed to these results.

Interest in esophagectomy was revived in the late 1930s. In 1938, Adams and Phimester performed esophagectomy with restoration of GI continuity through a left thoracotomy [33]. Sweet replicated this technique and published favorable results of 141 consecutive patients [34, 35].

Sweet's experience revived esophagectomy and additional surgical techniques were developed. In 1946, Ivor Lewis performed an esophagectomy through a right thoracotomy and midline laparotomy [36]. In 1969, K.C. McKeown performed esophagectomy through right thoracotomy, laparotomy, and right cervical incision [37, 38]. In 1976, Dr. Marc Orringer popularized the transhiatal esophagectomy (THE) [39].

Minimally invasive esophagectomy was developed in the 1990s. Dallemagne et al. performed the first minimally invasive McKeown esophagectomy [40]. Azagra et al. published a series of eight patients who underwent McKeown esophagectomy with thoracoscopic esophageal mobilization, cervical mobilization, and laparotomy [41]. Laparoscopic pioneers from Japan and the United States published outcomes showing reduced morbidity compared to open esophagectomy [42–45]. As the experience with laparoscopy and thoracoscopy grew, minimally invasive procedures have become more popular. Meta-analysis and prospective comparison of thoracic and non-thoracic esophagectomy for cancer patients have shown that transthoracic procedures have higher risk of pulmonary complications, lymphatic leak, and wound complications. Transhiatal surgery has a higher risk of anastomotic leak and recurrent laryngeal nerve injury.

Esophagectomy for Achalasia

In 1977, H.W. Pinotti published the technique of esophagectomy through a trans-mediastinal tunnel in a Brazilian patient suffering from end-stage esophageal dilation due to Chagas disease [46]. The high prevalence of Chagas disease in South

America led the largest early series of esophagectomy for megaesophagus to come from Brazil.

In 1988, Pinotti's group published a series of 108 patients who underwent THE for achalasia, reporting a 3.4% mortality [46]. In 1989, Devaney et al. published a series of 26 patients who underwent THE for end-stage achalasia at the University of Michigan, which observed a single reported death [47]. Several other series have been published, reporting favorable results with esophagectomy for end-stage achalasia. Tables 10.2, 10.3, 10.4, and 10.5 detail various aspects of these series.

Surgical approaches have varied between McKeown, Ivor Lewis, transhiatal, and thoracoabdominal. Conduit type has varied, depending on center experience, the two most commonly used conduits being the stomach and colon.

Technical Elements of Esophagectomy for Achalasia

Esophagectomy for achalasia requires meticulous preoperative, intraoperative, postoperative, and long-term care. While esophagectomy for esophageal cancer and achalasia have similarities, specific details for achalasia patients must be emphasized.

Preoperative

End-stage achalasia patients must undergo a thorough preoperative workup. All prior clinical data and operative reports must be studied, manometry confirmed, and updated cross-sectional imaging of the chest, abdomen, and pelvis performed.

Table 10.2 Surgical technique, anastomotic location, and follow-up period

Author (year)	*N*	Surgical technique	Anastomosis location	Follow-up range (mean)
Pinotti et al. (1988) [48]	108	THE – 108 (100%)	Neck – 108 (100%)	NA
Orringer et al. (1989) [49]	26	THE – 24 (92%) McKeown – 2 (8%)	Neck – 26 (100%)	3–91 months (30 months)
Miller et al. (1995) [14]	37	THE – 9 (24%) IL – 12 (32%) McKeown – 11 (29.5%) Distal esophagectomy RY – 5 (13%)	Neck – 20 (54%) Chest – 17 (46%)	1.4–16 years (6.3 years)
Peters et al. (1995) [50]	15	McKeown – 15 (100%)	Neck – 15 (100%)	1–14 years (median 6 years)
Banbury et al. (1999) [51]	32	THE – 21 (66%) Transthoracic – 11 (34%)	Neck – 30 (94%) Chest – 2 (6%)	3–115 months (43 months)
Hsu et al. (2003) [52]	9	Left thoracoabdominal – 9 (100%)	Chest – 9 (100%)	1–12 years (6 years)
Devaney et al. (2001) [53]	93	THE – 87 (93%) McKeown – 6 (7%)	Neck – 93 (100%)	1–190 months (38 months)
Gockel et al. (2004) [54]	8	THE – 6 (75%) McKeown – 2 (25%)	Neck – 8 (100%)	3–92 months (median 43.5 months)
Crema et al. (2005) [55]	30	Laparoscopic THE – 30 (100%)	Neck – 30 (100%)	Not provided
Glatz et al. (2007) [13]	8	IL – 8 (100%)	Chest – 8 (100%)	(median 6 years)
Schuchert (2009) [56]	6	McKeown – 6 (100%)	Neck – 6 (100%)	NA
Crema (2009) [57]	60	Laparoscopic THE – 60 (100%)	Neck – 60 (100%)	6–118 months (NA)
Crema (2017) [58]	231	Laparoscopic THE – 231 (100%)	Neck – 231 (100%)	7 months– 20 years (NA)

THE transhiatal esophagectomy, *McKeown* three field esophagectomy, *IL* Ivor Lewis, *NA* not recorded

Table 10.3 Intraoperativecomplications

Author (year)	Bleeding	Airway injury	Unplanned conversion to thoracotomy
Pinotti et al. (1988) [48]	2(1.8%)	1(0.9%)	NA
Orringer et al. (1989) [49]	2(7.7%)	0(0%)	2 (7.7%)
Peters et al. (1995) [50]	1(6.7%)	0(0%)	NA
Miller et al. (1995) [14]	2(5.4%)	0(0%)	2 (5.4%)
Banbury et al. (1999) [51]	0(0%)	0(0%)	5 (15.6%)
Devaney et al. (2001) [53]	2(2%)	1(1%)	2 (2%)
Hsu (2003) [52]	0(0%)	0(0%)	NA
Gockel et al. (2004) [54]	0(0%)	0(0%)	0 (0%)
Crema et al. (2005) [55]	0(0%)	0(0%)	0 (0%)
Glatz et al. (2007) [13]	0(0%)	0(0%)	NA
Schuchert (2009) [56]	1(16.7%)	0(0%)	NA
Crema (2009) [57]	0(0%)	0(0%)	0 (0%)
Crema (2017) [58]	0(0%)	0(0%)	0 (0%)

NA not recorded

Upper GI endoscopy should be performed by the esophagectomy surgical team. We advise at least one presurgical endoscopy, to increase surgeon familiarity with the patient's anatomy, to clean out the esophagus, and to assess for additional esophageal pathology – in particular esophageal cancer.Upper GI endoscopy has its risks. Most salient for the achalasia patient is the aspiration risk during anesthetic induction. We recommend awake fiberoptic intubation in a semi-upright or full upright position. However, rapid sequence intubation with cricoid pressure is also a good alternative but with higher risk of aspiration and resultant pneumonitis.

Full esophageal clean out should be performed using standard upper GI endoscopic equipment. Guardus esophageal overtube (US Endoscopy, Mentor, OH) assistance and pulsed irrigation systems such as EIP 2 (ERBE Corporation, Tuebingen, Germany) can be helpful adjuncts.

Once formal esophageal clean out has been performed, with confirmation of no concomitant esophageal pathology, we advise administration of a full liquid diet until 2 days prior to surgery and clear liquids only for 48 hours before surgery. A standard biochemical workup and nutritional assessment are performed. Routine colonoscopy is performed to evaluate for intraluminal malignancy or polyposis syndromes, as colon conduit may be required in patients with prior gastric surgery, complications of peptic ulcer disease, prior foregut interventions, and significant peripheral vascular disease, particularly celiac and superior mesenteric arterial (SMA) disease. History of colon cancer or colon resection, inflammatory bowel disease, diverticulitis, significant mesenteric vascular disease, and an occluded IMA preclude colon conduit use.

CT angiogram is performed to assess SMA and IMA patency. In patients with marginal renal function, diagnostic aortogram can be performed with standard contrast or CO_2 for patients with iodine contrast allergy.

Standard cardiovascular risk assessments must be performed. Performance status and revised cardiac risk index dictate preoperative workup according to American College of Cardiology guidelines.

Bowel cleansing before surgery is recommended especially for patients who had previous Heller myotomy and fundoplication as the gastroepiploic arcade might have been injured during the gastric mobilization, and this is hard to assess with preoperative radiographic imaging.

Intraoperative

Esophagectomy for achalasia can be difficult and time-consuming. The extent of esophagectomy will be dictated by length and degree of esophageal dilation. Different resection techniques include vagal-sparing esophagectomy, partial esophagectomy, and total esophagectomy.

Table 10.4 Postoperative complications

Author (year)	Anastomotic leak	Conduit necrosis	Dysphonia	Pneumonia	Pleural effusion	Pulmonary embolism
Pinotti et al. (1988) [48]	9(8.3%)	0(0%)	NA	9 (8.3%)	23 (21%)	NA
Orringer et al. (1989) [49]	1(3.8%)	0(0%)	2 (7.7%)	NA	NA	NA
Peters et al. (1995) [50]	0(0%)	0(0%)	0 (0%)	1 (6.7%)	1 (6.7% – chylothorax)	NA
Miller et al. (1995) [14]	2(6.2%)	0(0%)	2 (6.2%)	2 (6.2%)	NA	2 (6.2%)
Banbury et al. (1999) [51]	4(13%)	0(0%)	2 (6%)	7 (22%)	1 (3% – chylothorax)	NA
Devaney et al. (2001) [53]	9(10%)	1(1%)	5 (5%)	2 (2%)	2 (2% – chylothorax)	1 (1%)
Hsu et al. (2003) [52]	0(0%)	1(11%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gockel et al. (2004) [54]	1(12.5%)	0(0%)	NA	NA	1 (12.5% – chylothorax)	0 (0%)
Crema (2005) [55]	2(6.7%)	0(0%)	7 (23%)	0 (0%)	0 (0%)	0 (0%)
Glatz et al. (2007) [13]	0(0%)	0(0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Crema et al. (2009) [57]	4(6.7%)	0(0%)	9 (15%)	0 (0%)	8 (13.3%)	0 (0%)
Schuchert et al. (2009) [56]	1(16.7%)	0(0%)	0 (0%)	0 (0%)	1 (16.7%)	0 (0%)
Crema (2017) [58]	11 (4.76%)	0(0%)	18 (7.8%)	NA	22 (9.52%)	NA

NA not recorded

Table 10.5 Long-term complications

Author (year)	Dysphagia	Gastric emptying issues	Mean weight gain	Death
Pinotti et al. (1988) [48]	NA	NA	NA	4 (3.4%)
Orringer et al. (1989) [49]	10 (38.4%)	5 (19.2%)	+11.8 kg at 10 pts +5.9 kg at 12 pts	1 (3.8%)
Peters et al. (1995) [50]	3 (20%)	8 (61%)	+6.3 kg	0 (0%)
Miller et al. (1995) [14]	5 (20.8%)	0 (0%)	NA	2 (6.25%)
Banbury et al. (1999) [51]	5 (17%)	10 (34%)	NA	1 (3.1% – 6 months postsurgery)
Devaney et al. (2001) [53]	43 (46%)	36 (39%)	NA	2 (2.1%)
Hsu (2003) [52]	NA	3 (33.3%)	NA	0 (0%)
Gockel et al. (2004) [54]	3 (37.5%)	NA	NA	1 (12.5%)
Crema (2005) [55]	1 (3.3%)	NA	NA	0 (0%)
Glatz et al. (2007) [13]	0 (0%)	0 (0%)	+ 23 lbs. at 1 year	0 (0%)
Crema et al.(2009) [57]	2 (3.3%)	3 (5%)	NA	0 (0%)
Schuchert et al. (2009) [56]	NA	NA	NA	NA
Crema et al. (2017) [58]	NA	11 (4.76%)	NA	2 (0.8%)

NA not recorded

The primary decision for operators is the extent of esophagectomy. A subtotal esophagectomy with high intrathoracic anastomosis or a total esophagectomy with cervical anastomosis is the most appropriate approach due to the common presence of a tortuous, boggy, angulated intrathoracic esophagus. However, rarely a partial esophagectomy might be indicated for patients with short-segment esophageal dilation and angulation with a relatively straight, normal-

sized mid- and upper esophagus. Reconstruction techniques vary according to the length of esophagus resected. For short segment distal esophageal resections, reconstruction with long-segment jejunal Roux-en-Y configuration can be performed through laparotomy. For long-segment interposition, gastric, colon, and small bowel interposition can be used through transhiatal, Ivor Lewis, and three field techniques.

A dilated and inflamed esophagus, fed by enlarged aorto-esophageal collateral branches, should be anticipated. The esophagus can partially or totally fill either the left or right pleural space and be densely adherent to surrounding mediastinal structures. The safest esophagectomy technique will be dictated by surgeon experience and associated anatomic findings.

Esophagectomy should be performed by keeping the dissection as close to the esophagus as possible to limit injury to surrounding structures. Transthoracic and transhiatal techniques can be performed. Should total esophagectomy be performed, we use thoracoscopic surgery to assist with the dissection. This allows for direct visualization and mobilization of the thoracic esophagus and opportunity for rapid thoracotomy with good exposure should untoward bleeding be encountered. Thoracotomy however is safe and should be performed initially if operators are not experienced with thoracoscopy.

Transhiatal Esophagectomy

THE is performed with the patient in the supine position, beginning with a full and wide prep of the entire chest prior to starting the operation. Simultaneous abdominal and cervical procedures are performed. The abdominal team performs a midline laparotomy and mobilizes the left lateral segmental of the liver. The lesser sac is entered. The left gastric artery is divided and the proximal stomach mobilized. The gastrocolic ligament is incised and the greater curve of the stomach mobilized to the level of the left crus. Blunt mediastinal dissection is performed. A gastric emptying procedure is performed, and the stomach is tubularized with gastrointestinal staplers. The cervical team identifies and mobilizes the esophagus in the neck. Mediastinal dissection is completed from cephalad and caudal approaches.

It should be emphasized that with this technique, there is an increased risk of injury to aorto-esophageal collateral vessels, the left atrium, and the airway during the posterior mediastinal dissection, which may result in significant blood loss: for this reason, we prefer the transthoracic approach. In the event of massive bleeding with poor visualization of the bleeding area, a thoracotomy should be performed. Exposure of the posterior mediastinum through an anterolateral thoracotomy can be difficult if bleeding occurs and a right posterior thoracotomy offers the best exposure.

The stomach is transected in the abdomen and the specimen is delivered into the neck. An esophagogastrostomy is performed using hand-sewn or stapled techniques. A jejunal feeding tube and drains are placed, and the abdominal and neck incisions are closed.

Ivor Lewis Esophagectomy (IL)

Ivor Lewis esophagectomy is performed in two stages. The operation is begun with abdominal exploration. If the procedure is performed open, laparotomy is used to dissect the stomach and lower esophagus, fashion the conduit, perform a gastric emptying procedure, and place the J tube. The patient is then placed in the left lateral decubitus position, and a right-sided thoracoscopy or thoracotomy is performed. The esophagus is mobilized. The azygous vein is divided. Perforating aorto-esophageal branches are ligated, as are lymphatic channels. The esophagus is transected above the level of the azygous vein. The specimen is pulled into the chest with the conduit; the specimen is removed, and an anastomosis is performed with stapled or hand-sewn techniques. Drains are placed and the chest is closed.

McKeown Esophagectomy

Three-field esophagectomy is performed initially via a right-sided thoracoscopy or thoracotomy. The esophagus is mobilized and separated from the mediastinum, identical to the Ivor

Lewis technique. The esophagus is mobilized to the level of the thoracic inlet, taking care to stay close to the esophagus in the upper portion of the chest. The dissected esophagus is encircled proximally with a ½" Penrose drain. Simultaneous abdominal and cervical procedures are performed, identical to the transhiatal technique to transpose the conduit to the neck.

Conduit Options

The stomach is the most commonly used conduit following esophagectomy for achalasia. It is easy to mobilize, requires a single anastomosis, and can be adequately lengthened to traverse the entire chest. Additional conduit options include the right and left colon and the small bowel.

There are no guidelines to conduit selection following esophagectomy. Conduit selection requires consideration of patient comorbidities and operative conditions.

Technical Conduit Considerations

Stomach

The stomach is the most commonly used conduit for esophageal resection in achalasia. When fashioning the gastric conduit, the lesser curve of the stomach at the level of the incisura angularis should be identified and dissected.Either an EndoGIA or GIA stapler can be used to perform the gastric tubularization. GIA blue or EndoGIA purple or black load staplers will be used for this portion of the procedure. The tissue can be thicker, and the wider stapler loads can assist with tissue apposition. Tubularization then proceeds cephalad to create a conduit that is approximately 4 cm in diameter. Narrower conduits are prone to ischemia and anastomotic complications [56–58]. Esophagogastrostomy can be performed with hand-sewn, stapled, or hybrid techniques. Healthy tissue apposition without tension is essential. The conduit should be oriented so that the greater curve is positioned toward the patient's left-hand side.

Colon

The large bowel is the second most commonly used conduit in achalasia patients. The left or right colon, preferentially in isoperistaltic configurations, can be used. Advantages of colon interposition include length and reduced incidence of reflux. Disadvantages include the need for three anastomoses and poor long-term peristaltic function.

Arterial supply to the left colon conduit relies on the ascending branch of the left colic artery from the inferior mesenteric artery. The right colon conduit receives arterial supply from the middle colic system. Colonic venous drainage parallels arterial supply. The left colic vein merges with the splenic and portal vein; the marginal vein drains via the hemorrhoidal system and the inferior vena cava. The right-sided venous drainage is more variable, frequently with no dominant draining vein.

Regardless of whether the right or left colon is used, the entire colon is mobilized at the time of surgery via laparotomy. If the left colon is used, the middle colic artery and vein must be identified and dissected to their origin along the superior mesenteric artery and vein. Bulldog clamps should be placed at the origin of these vessels and along ileocolic and right colic collateral vessels to assess for arterial sufficiency. Visual inspection, doppler examination with a strong biphasic signal or fluorescence imaging will assist with determining adequate perfusion to the left and transverse colon. In cases of inadequate perfusion, supercharging the left colon blood supply in the neck can be considered.The colon is typically placed through the posterior mediastinum and tunneled to the neck in a laparoscopic camera bag. Proper length is determined using umbilical tape. Esophago-colostomy and colo-gastrostomy are performed using hand-sewn or stapled techniques. Colo-colostomy reestablishes colon continuity.

Right colon grafts are supplied by the middle colic artery. The right colic and ileocolic arterial branches are temporarily clamped, and graft viability is assessed. These arteries are then ligated proximally to preserve collateral flow, and the colon is transected distal to the cecum (although

some authors prefer to transpose the distal ileum as well). The colon is delivered to the neck with the assistance of a sterile laparoscopic camera bag. The distal colon is divided at the splenic flexure. Esophago-colostomy and colo-gastrostomy are performed using hand-sewn or stapled techniques. Colo-colostomy reestablishes colon continuity.

While the posterior mediastinal route is the shortest, the colon can be tunneled in a retrosternal or subcutaneous location.The retrosternal location mandates a left hemi-manubrial resection to avoid narrowing the conduit at the thoracic inlet. Care must be taken to avoid conduit compression and injury to nearby venous and arterial structures [59].

Small Bowel

Supercharged pedicled jejunum as interposition technique was first used in 1957 by Thomas and Merendino [60]. A 35–40 cm segment of jejunum is harvested, 20 cm distal to the ligament of Treitz. The first arterial arcade is preserved, receiving blood supply from the superior mesenteric artery (SMA). The second is divided proximally – preserved for future anastomosis to the left internal thoracic artery. The third arcade is divided; the fourth arcade is preserved, receiving blood supply from the SMA. The small bowel can be tunneled through the posterior mediastinum or retrosternal location [61]. There is a small amount of experience with supercharged jejunal conduit in the achalasia populations.

Complications

Esophagectomy is a morbid procedure. Patients undergoing esophagectomy for achalasia experience similar complications to patients undergoing esophagectomy for other indications: anastomotic leaks and stenosis, conduit necrosis, cardiac-related issues, deep venous thrombosis, dumping syndrome, gastric outlet obstruction, respiratory failure, chylothorax, and recurrent laryngeal nerve injury.

Anastomotic Leak/Conduit Necrosis

Anastomotic leak is well-described in achalasia patients undergoing esophagectomy. Leak rates vary between 0% and 16%. Diagnoses hinges on clinical observation, radiographic assessment using esophagram or CT esophagram, and upper GI endoscopy. Management revolves around prompt drainage and debridement of devitalized tissue.

Conduit necrosis is an infrequent complication in the achalasia literature. Nonetheless, operators must be cognizant of it. Diagnosis hinges on high clinical suspicion and urgent upper GI endoscopy. Fever, hypotension, tachycardia, and respiratory insufficiency can be markers of conduit death. Conduit necrosis is managed with rapid administration of IV antibiotics, urgent surgery, resection of necrotic tissue, and esophageal diversion. GI continuity can be reestablished at a later time.

Tracheal Injury

Tracheal injury is a rare but serious complication in the achalasia literature. It has been described mostly when surgery is performed using the transhiatal technique. The risk of this injury can be reduced by performing a transthoracic mobilization and keeping the dissection close to the esophagus. Management revolves around prompt identification and urgent repair using pedicled muscle flaps through a right posterolateral thoracotomy.

Cardiac Dysrhythmia

Up to 40% of patients experience cardiac dysrhythmia after esophagectomy [62]. The most common dysrhythmia is atrial fibrillation, but certainly other dysrhythmias can result. For stable atrial fibrillation, we advocate ruling out concurrent myocardial ischemia, optimized depleted electrolyte levels, and rapid chemical cardioversion. For unstable patients, synchronized cardioversion should be performed.

Pneumonia and Pulmonary Embolism

Respiratory complications affect 20–30% of patients undergoing esophagectomy. Pneumonia, pulmonary embolism, aspiration, and pleural effusions are the most common diagnoses [62–65]. Pneumonia rates vary between 0% and 9% in the achalasia literature. Management revolves around prompt administration of directed antibiotics. We advocate for urgent bronchoscopy for patients with mucus plugging and evidence of lobar atelectasis on plain radiograph. Pulmonary embolism should be diagnosed with CT angiogram PE protocol and treated with systemic anticoagulation.

Pleural Effusion and Chylothorax

The incidence of pleural effusion in the achalasia population is difficult to ascertain. In the transhiatal literature, operators have described placing pleural drains in as many as 76% of patients during surgery for inadvertent entry into the pleural space. When identified, pleural effusions should be managed with percutaneous of formal chest tube procedures.

The incidence of chylothorax varies between 0% and 13% in the achalasia literature. Diagnosis is determined clinically and biochemically – pleural triglyceride level greater than 110 mg/dL and lymphocyte percentage >90% in pleural assay. Treatment of high-output chylothorax should be surgical ligation of the thoracic duct. Low-output fistula can be conservatively managed with NPO and parental nutrition, with octreotide administration. Failure to resolve mandates surgical re-exploration. Refractory fistulas after thoracic duct ligation may require pleurodesis or pleural-peritoneal shunting.

Vocal Cord Paresis

Temporary vocal cord paresis occurs in 0–20% of achalasia patients after esophagectomy. Typically it is associated with cervical dissection. Cervical esophageal exploration using techniques published by Orringer (bipolar energy use in the neck, minimal cautery use in the deep cervical fascia, and no metal retractor placement beneath the deep cervical fascia) may reduce the incidence of injury. When suspected, injury should be confirmed with indirect laryngoscopy and cord paresis managed with cord injection. Bilateral cord injury may require tracheostomy tube placement.

Anastomotic Stenosis

In the achalasia literature, up to 46% of patients undergoing esophagectomy will experience postoperative dysphagia. Treatment of postoperative dysphagia is guided by upper GI endoscopy. We routinely perform upper GI endoscopy and serial dilation using balloon dilators; however Maloney or Savary bougies over a wire and under fluoroscopic guidance can be used.

Conduit-Emptying Issues

After esophagectomy, up to 60% of patients will experience conduit-emptying problems. The highest incidence is in patients with colon conduit, but this is well-described in gastric conduit series. Some groups have shown that vagal preservation techniques can reduce the incidence of this complication. Management revolves around administration of prokinetic agents and in select cases gastric-emptying procedures.

Conclusions

Esophagectomy for achalasia is reserved for patients with refractory disease, unmitigated by treatment other forms of treatment. Esophagectomy can be performed through a variety of techniques, but a transthoracic approach is preferred. Conduit options include the stomach, colon, and small intestine. Complications following esophagectomy occur frequently, and prompt diagnosis is necessary to improve outcomes. Overall outcomes of esophagectomy for

achalasia are good when performed in high-volume centers by experienced surgeons.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Boeckxstaens GE, Zaninotto G, Richter JE. Achalasia. Lancet. 2014;383:83–93.
2. Kahrilas PJ, Bredenoord AJ, Fox M, Gyawali CP, Roman S, Smout AJ, Pandolfino JE. The Chicago Classification of esophageal motility disorders, v3.0. Neurogastroenterol Motil. 2015;27(2):160–74.
3. Zaninotto G, Bennett C, Boeckxstaens G, Costantini M, Ferguson MK, Pandolfino JE, et al. The 2018 ISDE achalasia guidelines. Dis Esophagus. 2018;31:1–29.
4. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108(8):1238–49.
5. O'Neill OM, Johnston BT, Coleman HG. Achalasia: a review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol. 2013;19(35):5806–12.
6. Sadowski DC, Ackah F, Jiang B, Svenson LW. Achalasia: incidence, prevalence and survival. A population-based study. NeurogastroenterolMotil. 2010;22(9):e256–61.
7. Tuason J, Inoue H. Current status of achalasia management: a review on diagnosis and treatment. NeurogastroenterolMotil. 2010;22:e256–61.
8. Winter H, Shukla R, Elshaer M, Ali RA. Current management of achalasia – areview. Br JMedPract. 2015;8(2):a810.
9. Leeuwenburgh I, Scholten P, Alderliesten J, Tilanus HW, Looman CW, Steijerberg EW, Kuipers EJ. Long-term esophageal cancer risk in patients with primary achalasia: a prospective study. Am J Gastroenterol. 2010;105(10):2144–9.
10. Zendehdel K, Nyrén O, Edberg A, Ye W. Risk of esophageal adenocarcinoma in achalasia patients, a retrospective cohort study in Sweden. Am J Gastroenterol. 2011;106(1):57–61.
11. Ellis FG. The natural history of achalasia of the cardia. Proc R Soc Med. 1960;53(8):663–6.
12. Salvador R. The natural history of achalasia: evidence of a continuum- "The evolutive pattern theory". Dig Liver Dis. 2018;50(4):342–7.
13. Glatz SM, Richardson JD. Esophagectomy for end stage achalasia. J Gastrointest Surg. 2007;11:1134–7.
14. Miller DL, Allen MS, Trastek VF, Deschamps C, Pairolero P. Esophageal resection for recurrent achalasia. Ann Thorac Surg. 1995;60:922–6.
15. Goldblum JR, Whyte RI, Orringer MB, Appelman HD. Achalasia. A morphologic study of 42 resected specimens. Am J Surg Pathol. 1994;18(4):327–37.
16. Qualman SJ, Haupt HM, Yang P, Hamilton SR. Esophageal Lewy bodies associated with ganglion cell loss in achalasia. Similarity to Parkinson's disease. Gastroenterology. 1984 Oct;87(4):848–56.
17. Csendes A, Srnok G, Braghetto I. Gastroesphagealsphincter pressure and histologic changes in distal esophagus in patients with achalasia of the esophagus. Dig Dis Sci. 1985;30:941–5.
18. Singaram C, Koch J, Gaumnitz EA. Nature of neuronal loss in human achalasia. Gastroenterology. 1996;110:A259.
19. Stavrapoulos SN, Friedel D, Modayil R, Parkman HP. Diagnosis and management of esophageal achalasia. Clin RevBMJ. 2016;354:i2785.
20. Ximenes-Netto M. Chapter 68. In: Pearson's thoracic and esophageal surgery. 3rd ed. 2002.
21. Pérez-Molina JA, Molina I. Chagas disease. Lancet. 2018;391:82–94.
22. Matsuda NM, Miller SM, Barbosa Evora PR. The chronic gastrointestinal manifestations of chagasdisease. Clinics (Sao Paulo). 2009;64(12):1219–24.
23. Heller E. ExtramukoseCardiaplastikbeimchronischen Cardiospasmusmit Dilatation des Oesophagus. Mitt Grenzgeb Med Chir. 1914;27:141–9.
24. Gottstein G. Technik und Klinik der Oesophagoskopie. Mitt Grenzgeb Med Chir. 1901;8:57–152.
25. De Brui'neGroeneveldt JR. Over cardiospasmus. Ned Tijd- schrGeneeskd. 1918;54(Sect 2):1281–2.
26. Zaaijer JH. Cardiospasm in the aged. Ann Surg. 1923;77:615.
27. Stefanidis D, Richardson W, Farrell TM, Kohn GP, Augenstein V, Fanelli RD. SAGES guidelines for the surgical treatment of esophageal achalasia. SurgEndosc. 2012;26:296–311.
28. Shimi S, Nathanson LK, Cuschieri A. Laparoscopic cardiomyotomy for achalasia. J R Coll Surg Edinb. 1991;36:152–4.
29. Vela MF, Richter JE, Khandwala F, Blackstone EH, Wachsberger D, Baker ME, Rice TW. The long-term efficacy of pneumatic dilatation and Heller myotomy for the treatment of achalasia. Clin Gastroenterol Hepatol. 2006;4(5):580–7.
30. Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, Ciovica R. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249(1):45–57.
31. Torek F. The first successful case of resection of the thoracic portion of the oesophagus for carcinoma. Surg GynecolObstet. 1913;16:614–7.
32. Torek F. The causes of failure in the operative treatment of carcinoma of the esophagus. Ann Surg. 1929 Oct;90(4):496–506.
33. Klingman RR, DeMeester TR. Surgery for carcinoma of the thoracic esophagus: Adams and Phemister in perspective. AnnThorac Surg. 1988;46(6):699–702.
34. Sweet RH. Surgical management of carcinoma of the midthoracic esophagus: preliminary report. N Engl J Med. 1945;233(1):1–7.
35. Sweet RH. Carcinoma of the esophagus and the cardiac end of the stomach: immediate and late results of

treatment by resection and primary esophagogastric anastomosis. JAMA. 1947;135(8):485–90.
36. Lewis I. The surgical treatment of carcinoma of the oesophagus with special reference to a new operation for growths of the middle third. Br JSurg. 1946;34:18–31.
37. McKeown KC. Total oesophagectomy. British Medical Association Film 439, 1969, "By kind permission of Editor Surgery Annual".
38. McKeown KC. Total three-stage oesophagectomy for cancer of the oesophagus. Ann R Australas Coll Dent Surg. 1972;51:213–38.
39. Orringer MB. Esophagectomy without thoracotomy. JTCVS. 1978;76:643–54.
40. Dallemagne B, Weerts JM, Jehaes C, Markiewicz S, Bona S, Hosselet JL, et al. Case report: subtotal oesophagectomy by thoracoscopy and laparoscopy. Minim Invasive Ther. 1992;1:183–5.
41. Azagra JS, Ceuterick M, Goergen M. Thoracoscopy in oesophagectomy for oesophageal cancer. Br J Surg. 1993;80:320–1.
42. Akaishi T, Kaneda I, Higuchi N, Kuriya Y, Kuramoto J, Toyoda T, Wakabayashi A. Thoracoscopic en bloc total esophagectomy with radical mediastinal lymphadenectomy. J Thorac Cardiovasc Surg. 1996;112:1533–41.
43. Kawahara K, Maekawa T, Okabayashi K, Hideshima T, Shirashi T, Yoshinaga Y, et al. Video-assisted thoracoscopic esophagectomy for esophageal cancer. Surg Endosc. 1999;13:218–23.
44. Taguchi S, et al. Comparison of three-field esophagectomy for esophageal cancer incorporating open or thoracoscopic thoracotomy. Surg Endosc. 2003;17:1445–50.
45. Osugi H, et al. Learning curve of video-assisted thoracoscopic esophagectomy and extensive lymphadenectomy for squamous cell cancer of the thoracic esophagus and results. Surg Endosc. 2003;17:515–9.
46. Luketich JD, Nguyen NT, Weigel T, Ferson P, Keenan R, Schauer P. Minimally invasive approach to esophagectomy. JSLS. 1998;2(3):243–7.
47. Pinotti HW. Esofagectomia subtotal por túneltransmediastinalsemtoracotomia. Rev da Assoc MedBrasil. 1977;23:395–8.
48. Pinotti HW, Nasi A, Cecconello I, Zilberstein B, Pollara W. Chagas' disease of the esophagus. Dis Esophagus. 1988;1(1):65–71.
49. Orringer MB, Stirling MC. Esophageal resection for achalasia: indications and results. AnnThorac Surg. 1989;47:340–5.
50. Peters JH, Kauer WK, Crookes PF, Ireland AP, Bremner CG, DeMeester TR. Esophageal resection with colon interposition for end-stage achalasia. Arch Surg. 1995;130:632–7.
51. Banbury MK, Rice TW, Goldblum JR, et al. Esophagectomy with gastric reconstruction for achalasia. J Thorac Cardiovasc Surg. 1999;117:1077–85.
52. Hsu H-S, Wang C-Y, Hsieh C-C, et al. Short-segment colon interposition for end-stage achalasia. Ann Thorac Surg. 2003;76:1706–10.
53. Devaney EJ, Iannettoni MD, Orringer MB, Marshall B. Esophagectomy for achalasia: patient selection and clinical experience. Ann Thorac Surg. 2001;72:854–8.
54. Gockel I, Kneist W, Eckardt VF, et al. Subtotal esophageal resection in motility disorders of the esophagus. Dig Dis. 2004;22:396–401.
55. Crema E, Ribeiro LBP, Terra JA Jr, Silva AA. Laparoscopic transhiatal subtotal esophagectomy for the treatment of advanced megaesophagus. Ann Thorac Surg. 2005;80:1196–201.
56. Schuchert MJ, Luketich JD, Landreneau RJ, et al. Minimally invasive surgical treatment of sigmoidal esophagus in achalasia. J Gastrointest Surg. 2009;13:1029–35.
57. Crema E, Ribeiro LB, Sousa RC, et al. Laparoscopic transhiatal esophagectomy for the treatment of advanced megaesophagus: an analysis of 60 cases. Rev Col Bras Cir. 2009;36:118–22.
58. Crema E, JAT J, Terra GA, Teles CJO, da Silva AA. Minimally invasive esophagectomy in achalasia: a more liberal approach to esophageal resection. Minim Invasive Surg. 2017;1:160–6.
59. Collard JM, Tinton N, Malaise J, Romagnoli R, Otte JB, Kestens PJ. Esophageal replacement: gastric tube or whole stomach? Ann Thorac Surg. 1995;60:261–7.
60. Pierie JP, de Graaf PW, van Vroonhoven TJ, Obertop H. The vascularization of a gastric tube as a substitute for the esophagus is affected by its diameter. Dis Esophagus. 1998;11(4):231–5.
61. Liebermann-Meffert DM, Meier R, Siewert JR. Vascular anatomy of the gastric tube used for esophageal reconstruction. Ann Thorac Surg. 1992;54(6):1110–5.
62. Bakshi A, Sugarbaker DJ, Burt BM. Alternative conduits for esophageal replacement. AnnCardiothor Surg. 2017;6(2):137–43.
63. Thomas GI, Merendino KA. Jejunal interposition operation: analysis of thirty-three clinical cases. JAMA. 1958;168:1759–66.
64. Al-Tarshihi MI, Ghanma IM, Khamash FA, AlIbrahim AE. Cardiac complications in the first week post transhiatal esophagectomy for esophageal cancer. JRMS. 2008;15(3):29–33.
65. Avendano CE, Flume PA, Silvestri GA, King LB, Reed CE. Pulmonary complications after esophagectomy. Ann Thorac Surg. 2002;73:922–6.

11 Comparison of Different Treatment Modalities and Treatment Algorithm for Esophageal Achalasia

Nicolás H. Dreifuss, Francisco Schlottmann, Marco Di Corpo, and Marco G. Patti

Introduction

There are many treatment modalities for esophageal achalasia, and they all aim to decrease the lower esophageal sphincter (LES) pressure and improve the emptying of the esophagus into the stomach. Available treatments are not curative but rather help to relieve patient's symptoms. Nonsurgical modalities include pharmacological therapy, endoscopic botulinum toxin injection (EBTI), pneumatic dilatation (PD), and per-oral endoscopic myotomy (POEM). Surgical treatments include laparoscopic Heller myotomy (LHM) and esophagectomy [1, 2].

N. H. Dreifuss
Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine and Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti
Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Pharmacologic Therapy

Pharmacologic agents include smooth muscle relaxants, such as long-lasting nitrates, calcium channel blockers, and 5′-phosphodiesterase inhibitors. Mechanism of action of these drugs is relaxation of the smooth muscle of the LES. Most of these agents are administered sublingually because the prolonged esophageal transit and emptying make absorption and kinetics unpredictable (e.g., nifedipine 10–30 mg sublingually 30–45 min before meals or isosorbide dinitrate 5 mg sublingually 10–15 min before a meal) [3, 4].

Several factors limit the use of these agents for the treatment of esophageal achalasia. The duration of action is short, the symptom improvement is very limited, and their efficacy decreases over time. In addition, these drugs are associated with side effects such as peripheral edema, headache, and hypotension that occur in up to 30% of patients [5].

Both the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) 2012 guidelines [2] and the International Society for Diseases of the Esophagus (ISDE) 2018 guidelines [6] recommend against the use of nitrates, calcium blockers, or phosphodiesterase inhibitors treatment for symptomatic relief of achalasia because of lack of convincing evidence. Medical therapy should only be considered in patients unwilling or unable to tolerate more invasive therapies.

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_11

Endoscopic Botulinum Toxin Injection

Botulinum toxin is a potent inhibitor of acetylcholine released from nerve endings, thus decreasing LES pressure. The standard protocol for EBTI into the LES consists of the injection of 100 units of toxin with a sclerotherapy needle in four quadrants, about 1 cm above the esophagogastric junction [7]. Endoscopic botulinum toxin injection (EBTI) was first described by Pasricha et al. [8] in 1995. He demonstrated symptomatic improvement in 82% of patients after EBTI compared with 10% of placebo group. After 6 months, response rate drops to 57% (range 33–77%), and by 12 months, it drops to around 48% (range 15–76%) [8–13]. A previous systematic review and meta-analysis showed relief or improvement of symptoms in about 80% of patients within 1 month after EBTI [14]. Nevertheless, symptoms' relief decreased at 3 months (70%), 6 months (53%), and 12 months (40%). At least a second EBTI was done in 47% of patients.

EBTI is a safe procedure; possible complications are transient chest pain (20% of patients) and heartburn (5–10% of patients). Few reports have included pneumothorax, heart block, mediastinitis, gastroparesis, and arrhythmia [7].

Predictors for the long-term success of botulinum toxin are the presence of vigorous achalasia, an LES pressure not exceeding the upper normal limit by more than 50% in patients without vigorous achalasia, and age greater than 55 years [11, 15]. Main predictors of poor response to EBTI are lack of an initial symptomatic response and residual LES pressure of 18 mmHg or greater after EBTI.

Overall, the effect of EBTI progressively diminishes over time, with more than 60% of patients experiencing recurrent symptoms after 1 year [16]. In addition, EBTI needs to be repeated in most patients to achieve some benefits that usually have a short duration due to the regeneration of the axons and the development of antibodies [17–19]. Furthermore, in patients with history of EBTI, a subsequent surgical myotomy is usually more challenging because of fibrosis at the level of the gastroesophageal junction with consequent loss of the normal anatomic planes [20]. In cases when fibrosis is present, the risk of mucosal perforation is higher and the results are less predictable.

Endoscopic Botulinum Injection Versus Pneumatic Dilatation

A recent Cochrane systematic review [21] of 7 randomized controlled trials (RCTs) including 178 achalasia patients compared EBTI and PD [22–27]. Clinical and manometric evaluations were performed between 1 and 4 weeks after the initial treatment in all studies. Symptom scores at 1-year follow-up were available in all studies, while LES pressure values at 12 months were assessed only in 3 RCTs. Five RCTs reported [23–27] the response to the initial endoscopic treatment modality at 6 and 12 months. Overall, there were no significant differences in symptom remission and LES pressure within 1 month of the endoscopic treatment between EBTI and PD. At 6 months and 12 months, symptom remission rates were lower after EBTI than PD (52% vs. 81%, $p = 0.0015$ and 37.5% vs. 73%, $p = 0.0002$, respectively). Esophageal perforation occurred in 3 (1.6%) patients after PD.

Based on these data, EBTI seems to be associated with worse clinical mid- and long-term outcomes than PD.

Endoscopic Botulinum Injection Versus Laparoscopic Heller Myotomy

It is well known that the outcomes of LHM are better than EBTI. Zaninotto et al. [28] randomly assigned to EBTI or LHM 100 patients with new diagnosis of esophageal achalasia. Six months after the index procedure, there was no significant difference in LES pressure between the two groups, but symptom scores improved more after LHM than EBTI, and a greater reduction in the esophageal diameter was also observed after surgery. At 2-year follow-up, the percentage of asymptomatic patients was significantly lower in the EBTI group (35% vs. 87.5%, $p < 0.05$).

The ISDE 2018 achalasia guidelines [6] recommend that EBTI should be reserved for patients who are unfit for surgery or as a bridge to more effective therapies such as surgery or endoscopic dilation.

Pneumatic Dilatation

Pneumatic dilatation (PD) has been considered the first-line nonsurgical therapy for esophageal achalasia for many years. The goal of this procedure is to weaken the lower esophageal sphincter by tearing its muscle fibers by generating radial force. This procedure is done using a Rigiflex balloon (Boston Scientific Corporation, MA, USA). There is so far no clear consensus on the optimal method for performing PD regarding the balloon diameter, duration of inflation, balloon pressure, or interval between the successive dilations. Some groups [29, 30] recommend a graded approach using a 30 mm balloon in the first session and larger balloons (35 mm and 40 mm in diameter) 2 to 4 weeks later in the presence of persistent symptoms secondary to inadequate dilatation. Graded PD is an effective treatment in terms of symptoms relief, but success rate declines over time, and further dilatations are usually required. Patients should be advised that when dysphagia rapidly recurs after a PD with a 40-mm balloon, the response to further PDs is unlikely [31].

Esophageal perforation is the most serious complication after PD and should be suspected in patients who experience thoracic pain, subcutaneous emphysema, shortness of breath, and/or fever after the procedure. The rate of perforation after PD varies from 2.0% to 5.4% and is more frequent in patients older than 65 years old, with high amplitude of contractions in the distal esophagus and with the use of Witzel dilators [32].

The 2018 ISDE achalasia guidelines [6] recommend that patients should be observed for at least 4 hours after PD, and selective gastrografin (water-soluble iodine contrast) esophagogram or CT scan with oral contrast should be performed if any symptoms suggest perforation.

Long-term studies have reported different rates of relief of dysphagia at 5 years (40% to 78%) or beyond (12% to 58% at 15 years) after PD. These wide ranges depend on the definition of success, on the methods used to evaluate patient's symptoms, and on the number of PDs. Even in the series reporting the best long-term outcomes, repeated PD sessions are needed in up to one-third of patients [33].

Well-recognized predictors of poor response after PD are failure after the first or second PD, age less than 40 years, male sex, large esophageal diameter, type I and III achalasia, and post-procedural reduction in LES pressure less than 50% [34–37].

Pneumatic Dilatation Versus Laparoscopic Heller Myotomy

During the last 10 years, several RCTs comparing PD and LHM have been published [38–47].

The pooled analysis of these RCTs showed higher rates of symptom remission after LHM at 3 months and 1 year, while the outcomes at 2 and 5 years seemed to be equivalent (remission rate at 5 years was 85.3% after LHM and 78.2% after PD). Overall, 25% of patients required a re-treatment, more frequently after PD. Post-procedural LES pressure and the rate of pathologic reflux did not significantly differ between the two treatment modalities. Similarly, quality of life improvement showed no significant differences between the two groups.

Although these data support the equivalence of both treatment modalities, postoperative complications requiring medical care (mainly esophageal perforations) occurred more frequently after PD than LHM (4.9% vs. 0.8%). In addition, the interpretation of these results might be biased by some methodological issues of these RCTs (small sample size in most of the trials, different PD and LHM techniques, and lack of objective data about esophageal acid exposure and its correlation with symptoms).

Pneumatic Dilatation Versus POEM

A retrospective study that compared PD with POEM in elderly patients (>65 years) found that treatment success (Eckardt score<3) rates at 3, 6,

12, 24, and 36 months after treatment were comparable between both treatment modalities [48]. The study also showed that the presence of megaesophagus was a predictive factor of failure for both POEM and PD. Meng et al. [49] conducted another study that compared POEM ($n = 32$) with PD ($n = 40$) for newly diagnosed achalasia. Success rates for PD at 3, 6, 12, 24, and 36 months were 95, 88, 75, 72, and 60% respectively. For POEM, these were 96, 96, 96, 93, and 93% ($p = 0.013$). On subgroup analysis, the success rate was higher for POEM than with PD in all 3 manometric subtypes, but only in patients with type III achalasia, this difference was statistically significant.

A recent multicenter randomized controlled trial conducted by Ponds et al. [50] compared PD ($n = 66$) with POEM ($n = 67$) in patients with treatment naïve achalasia. After 1 year, 92% of POEM patients were in clinical remission versus 70% after PD ($p < 0.01$). One perforation occurred after PD and no severe adverse events related to POEM were reported.

Laparoscopic Heller Myotomy

LHM for esophageal achalasia has shown excellent results with low morbidity. Boec kxstaens et al. [39] studied 106 patients who underwent LHM and Dor fundoplication and reported a therapeutic success (reduction of Eckardt symptoms score to 3 or less) of 93% and 90% at 1 and 2 years of follow-up, respectively. Moonen et al. [40] from the same group, with longer follow-up, demonstrated a treatment success at 5 years of 82%. Another randomized trial found that with a minimal follow-up of 5 years, only 8% of the patients after LHM had recurrence of symptoms [42].

Zaninotto et al. [51] studied 407 consecutive patients who underwent LHM and Dor fundoplication during the period 1992–2007 and reported a 90% success rate at a median follow-up of 30 months. Perrone and colleagues [52] analyzed a consecutive series of patients who underwent LHM and Toupet fundoplication and described excellent results in 97% of patients at a median follow-up of 26 months.

Several studies have shown that the best outcomes for LHM are achieved in Chicago type I and II achalasia patients. Pandolfino et al. [53] found that type II patients were significantly more likely to respond to LHM (100%) than type I (56%) and type III (29%). Salvador and colleagues [54] reported that in 246 patients who underwent LHM treatment, failure rates were significantly different: type I 14.6%, type II 4.7%, and type III 29%.

Symptomatic gastroesophageal reflux has been reported to occur in up to 48% of patients after a myotomy for achalasia, so it is well recognized that a fundoplication should be added [55].

At first, Nissen fundoplication (360°) was the procedure of choice to reduce myotomy-related reflux [56]. However, nowadays there is a general consensus that a 360° fundoplication can lead to an increased rate of postoperative dysphagia. Rebecchi et al. [57] conducted a RCT comparing anterior partial fundoplication (Dor) versus 360° fundoplication (Nissen) and confirmed that the Nissen fundoplication has higher rates of postoperative dysphagia than the Dor procedure (15% vs. 2.8%), without significant difference in reflux control.

The 2018 ISDE achalasia guidelines [6] recommend a partial fundoplication but not a Nissen fundoplication to reduce long-term risk of gastroesophageal reflux and dysphagia after myotomy. The choice between anterior 180° (Dor) or posterior 270° (Toupet) fundoplication should be based on surgeon's experience and preference [58, 59].

Per-oral Endoscopic Myotomy

In 2010, Haruhiro Inoue from the Showa University Northern Yokohama Hospital, Japan, published the results of a new endoscopic technique called per-oral endoscopic myotomy (POEM) in 17 patients with esophageal achalasia [60]. This procedure includes four steps (see Fig. 1.11):

1. Submucosal injection and mucosal incision (Fig. 11.1)
2. Submucosal tunnel creation (Fig. 11.2)

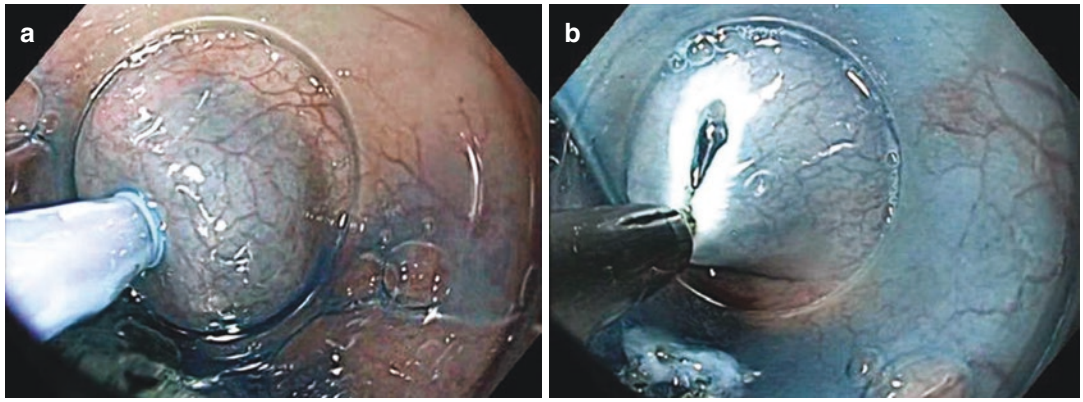


Fig. 11.1 Submucosal injection and mucosal incision. (**a**) Submucosal injection with a solution of saline, indigocarmine, and dilute epinephrine; (**b**) Mucosectomy with electrocautery. (Reprinted with permission © Springer Nature [95])

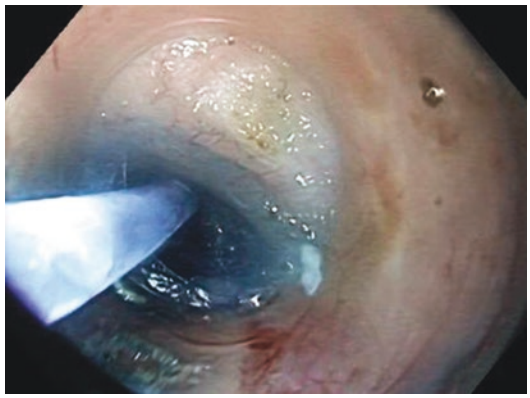


Fig. 11.2 Submucosal tunnel creation. (Reprinted with permission © Springer Nature [95])

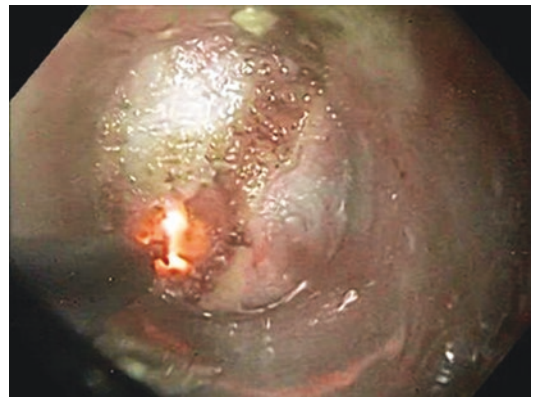


Fig. 11.3 Myotomy. (Reprinted with permission © Springer Nature [95])

3. Myotomy (Fig. 11.3)
4. Closure of the mucosal entry (Fig. 11.4)

The study showed that POEM significantly improved the dysphagia score in every patient (from mean 10 to 1.3) and reduced the resting LES pressure from a mean of 52.4 mmHg to 19.9 mmHg, without serious complications related to the procedure. This report represented a milestone in the history of the treatment of achalasia. Following Inoue's study, POEM was introduced in the treatment algorithm of achalasia across the world, and soon many gastroenterologists and surgeons started considering POEM as the primary treatment for achalasia.

Von Renteln et al. [61] conducted a prospective, international, multicenter study involving 70 patients who underwent POEM in 5 centers in Europe and North America, showing improvement at 12 months in 82.4% of patients. In 2015 Inoue [62] studied a cohort of 500 POEM patients and found a significant reduction in Eckardt scores and LES pressure at 2 months, 1 year, and 3 years post procedure. Adverse events rate were 3.2% and there were no mortalities. In 2016, Familiari and colleagues [63] reported the results of POEM in 94 patients, and at a mean follow-up of 11 months, clinical success was achieved in 94.5% of patients. A recent meta-analysis including 36 studies with 2373 patients reported that clinical success (Eckardt score ≤ 3) was achieved in 98% of the patients after POEM [64].

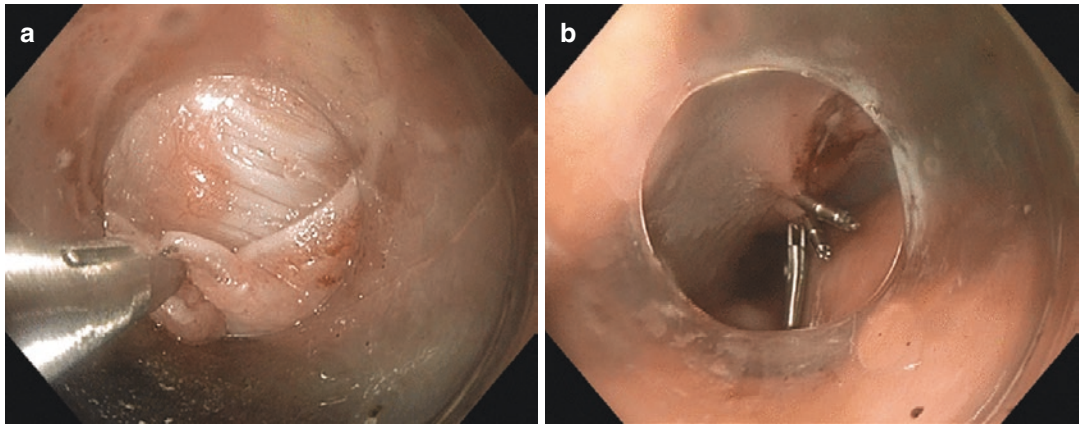


Fig. 11.4 Closure of the mucosal entry. (**a**) First clip applied to close the mucosectomy; (**b**) Mucosectomy clip closure in progress. (Reprinted with permission © Springer Nature [95])

A major concern with POEM has been the high rate of gastroesophageal reflux related to the ablation of LES without any antireflux procedure. In the RCT comparing POEM to PD[50], endoscopy at 1 year follow-up showed that reflux esophagitis was significantly more common in patients treated with POEM (40.0% Los Angeles A or B, 8.3% grade C/D), compared to 13% in those treated with PD (all Los Angeles A or B). Inoue [62] reported on their series of 500 patients that 268 of 414 patients (64.7%) had endoscopic findings of reflux esophagitis. In 2017, Kumbhari et al. [65] performed a multicenter case-control series studying 282 patients and found post-POEM gastroesophageal reflux disease either by endoscopy or pH monitoring in 58% of the patients. Sharata et al. [66] studied with pH monitoring 68 patients after a mean follow-up of 20 months and found an incidence of reflux of 38.2%. Worrell et al. [67] found that 70% of the patients studied with pH monitoring 12 months after POEM had pathologic reflux.

Laparoscopic Heller Myotomy Versus POEM

Potential advantages of POEM over LHM include lack of abdominal incisions, faster recovery, ease of performing a longer myotomy, avoidance of vagal nerve injury, and lack of intra-abdominal adhesions in case surgery is required [68].

Data comparing LHM with POEM are very limited, and to date there have been no randomized controlled trials comparing these treatment modalities. Swanstrom et al. [69] compared the results of LHM ($n = 64$) and POEM ($n = 37$), and at a mean follow-up of 6 months, both groups had sustained similar improvements in their Eckardt scores (1.7 vs. 1.2, $p = 0.1$). Interestingly, post-myotomy resting pressures were higher for POEM than for LHM (16 vs. 7.1 mm Hg, $p = 0.006$). Bhayani et al. [70] compared LHM and POEM, and at 6 months both groups had similar improvements in their Eckardt score (1.7 vs. 1.2, $p = 0.1$). Postoperative pH monitoring showed abnormal acid exposure in 39% and 32% of the patients after POEM and LHM, respectively. Chan et al. [71] performed a retrospective cohort study and compared clinical outcomes and quality of life after LHM and POEM; 33 patients underwent POEM and 23 patients underwent LHM. Both procedures achieved similar dysphagia scores at 1, 3, and 6 months and comparable quality-of-life outcomes.

Schlottmann et al. [72] conducted a systematic review and meta-analysis which comprised 53 studies reporting data on LHM (5834 patients) and 21 studies examining POEM (1958 patients). At 24 months, improvement in dysphagia for LHM and POEM was 90.0% and 92.7%, respec-

tively (p = 0.01). Patients undergoing POEM were more likely to develop GERD symptoms (OR 1.69), GERD evidenced by erosive esophagitis (OR 9.31), and GERD evidenced by pH monitoring (OR 4.30).

In patients with type III achalasia ("spastic achalasia"), POEM seems to achieve better outcomes. Kumbhari et al. [65] reported that in patients with type III achalasia, the success rate was 80.8% after LHM and 98.0% after POEM (p = 0.01). Khashab et al. [73] reported a 96.3% successful clinical rate after POEM in 54 patients with type III achalasia refractory to medical therapy. Recently, Zhang et al. [74] studied 32 consecutive patients with type III achalasia treated with POEM, and at a median follow-up of 27 months treatment success was achieved in 90.6% of the patients.

Table 11.1 summarizes outcomes of LHM and POEM in terms of improvement of dysphagia and post-procedural GERD by pH monitoring.

Overall, laparoscopic myotomy and POEM seem to achieve comparable symptomatic improvement rates. However, patients undergoing POEM have a high risk of post-procedural GERD. In patients with type III achalasia, POEM could be considered as the first-line treatment modality.

Failed Laparoscopic Heller Myotomy: What Next?

Approximately 10–20% of patients undergoing LHM will relapse in the mid- or long term and need further treatment. The best treatment for these patients is still under discussion with many options: PD, EBTI, POEM, redo-myotomy, or esophagectomy.

Zaninotto et al. [51] performed 407 LHM with a failure of 10% (39/407 patients). Most of these failures were treated with PD and overcome symptoms in 75% of patients. Schlottmann et al. [75] treated 147 achalasia patients with LHM. At a median follow-up of 22 months, 19 patients had recurrence of symptoms and required additional treatment: 12 patients were successfully treated with PD alone (median 2 PDs/patient), and 4 were successfully treated with combination of PD and EBTI (one session/patient).

PD success rate after LHM seems to be lower than primary PD. However, comparing patients treated with PD after failed myotomy to patients directly undergoing additional surgery showed that the efficacy of PD and redo-surgery were similar [76].

POEM is indeed another option after a failed LHM. A recent study reported 90 patients treated

Table 11.1 Outcomes of laparoscopic Heller myotomy (LHM) and per-oral endoscopic myotomy (POEM)

Study (year)	Technique	*N*	Follow-up (months)	Improvement dysphagia (%)	Reflux pH monitoring (%)
Rossetti (2005) [85]	LHM	195	83.2	91.8	0/15 (0)
Katada (2006 [86]	LHM	30	51	80	3/25 (12)
Zaninotto (2008) [51]	LHM	407	30	90.4	17/260 (6.5)
Rebecchi (2008) [57]	LHM	138	125	91.3	2/138 (1.4)
Sasaki (2010) [87]	LHM	35	94	94.3	0/35 (0)
Parise (2011) [88]	LHM	137	65	94.8	2/15 (13.3)
Di Martino (2011) [89]	LHM	56	24	92.9	4/56 (7.1)
Cuttitta (2011) [90]	LHM	49	75	93.9	2/49 (4.1)
Rosati (2013) [91]	LHM	173	50	99.4	8/47 (17)
Salvador (2016) [92]	LHM	806	49	88.9	40/463 (8.6)
Sharata (2015)[66]	POEM	75	20.1	97.9	26/68 (38.2)
Schneider (2016) [93]	POEM	25	9	91	4/8 (50)
Worrell (2016) [67]	POEM	35	12	90.9	7/10 (70)
Hungness (2016) [94]	POEM	112	28	92	10/22 (45.4)
Familiari (2016) [63]	POEM	100	11	94.5	39/73 (53.4)

LHM laparoscopic Heller myotomy, *POEM* per-oral endoscopic myotomy

with POEM after LHM failure with clinical success rates of 81% [77].

The 2018 ISDE Achalasia guidelines [6] state that PD rather than repeat myotomy or POEM is the first option for treatment after failed Heller myotomy.

Treatment of End-Stage Achalasia

A severely dilated and sigmoid-shaped esophagus is the final outcome of long-standing untreated achalasia or the result of recurrences and failures of previous treatments (Fig. 11.5). Traditionally, end-stage achalasia was managed by performing an esophagectomy. However, it is well known the high morbidity and mortality associated with this procedure.

PD is considered difficult in patients with end-stage achalasia, and there is limited evidence that PD may be used as first-line therapy. Khan et al. [78] reported 9 patients with megaesophagus (>7 cm diameter) that underwent PD with good symptomatic improvement and no complications at 12 months of follow-up.

A LHM is challenging in these patients because an extensive dissection in the posterior mediastinum is needed to straighten the esophageal axis. In addition, there is usually significant periesophageal inflammation secondary to prior interventions or esophagitis due to long-standing retention of food. Mineo et al. [79] reported their experience in a small cohort of patients and LHM proved to be effective in improving subjective, objective, and quality of life outcome measures in patients with sigmoid esophagus. Similarly, Sweet et al. [80] showed that the outcome of LHM was not influenced by the degree of esophageal dilatation. In 12 patients with an esophageal diameter >6 cm and sigmoid-shaped esophagus, excellent or good results were obtained in 91% of patients, and none required esophagectomy.

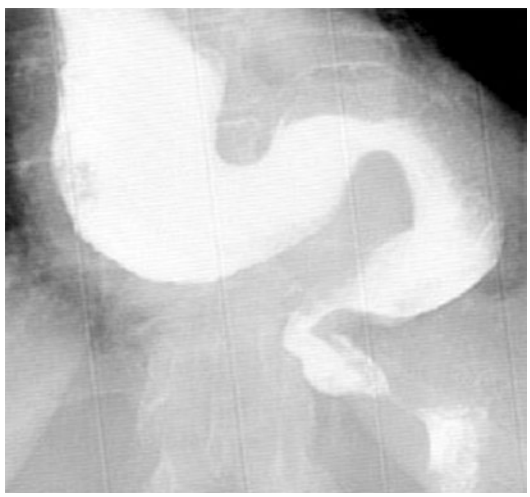


Fig. 11.5 End-stage achalasia: barium swallow showing a dilatated and sigmoid-shaped esophagus

POEM also seems to be effective in patients with end-stage achalasia. Hu et al. [81] performed a prospective study in which patients with advanced sigmoid-shaped achalasia were assigned to POEM. In this study, 32 consecutive patients underwent POEM with a treatment success of 96.8% with a mean follow-up of 30 months.

After the failure of all other treatment modalities, esophagectomy should be considered. It is important to promptly identify patients in whom surgical resection will be needed before patients' nutritional and general conditions become too deteriorated increasing the risk of this major surgery.

The ISDE 2018 Achalasia guidelines [6] recommend standard endoscopic (PD or POEM) or surgical therapies (LHM) in sigmoid-shaped esophagus, leaving esophagectomy as the last option in case of failure of the other treatment modalities.

Algorithm for Achalasia Treatment

Medical therapy and/or endoscopic Botox injection should be considered in patients with advanced age or significant comorbidities who are not candidates for LHM or POEM. Patients who are deemed good surgical candidates should undergo LHM (types I and II) or POEM (type III). Patients who have failed initial treatment should be referred for pneumatic dilatation. If symptoms persist, it is reasonable to consider

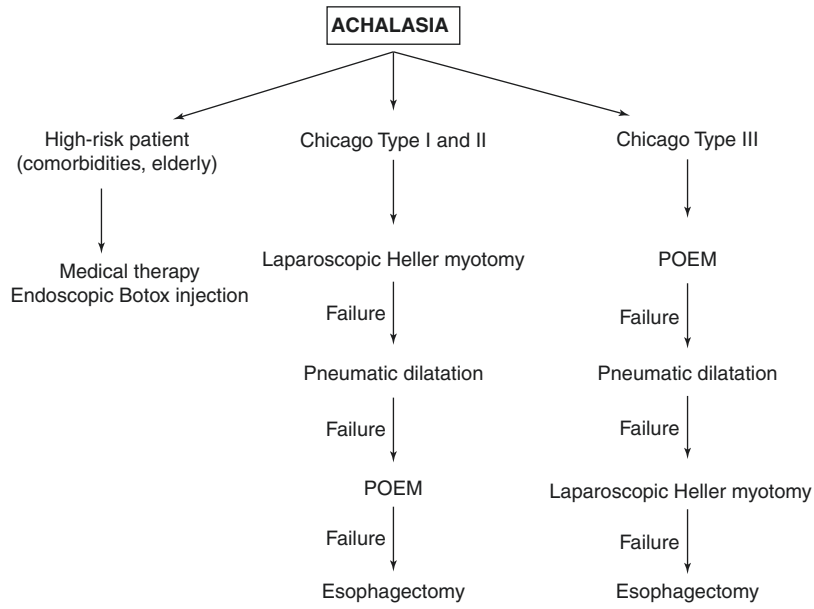


Fig. 11.6 Treatment algorithm of esophageal achalasia

POEM for those who underwent LHM initially and LHM for those who underwent POEM at first [77, 82–94]. Esophagectomy should be reserved for patients who have failed all these previous interventions (Fig. 11.6).

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Vaezi MF, Pandolfino JE, Vela MF. ACG clinical guideline: diagnosis and management of achalasia. Am J Gastroenterol. 2013;108(8):1238–49.
2. Stefanidis D, Richardson W, Farrell TM, Kohn GP, Augenstein V, Fanelli RD. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc. 2012;26(2):296–311.
3. Wen ZH, Gardener E, Wang YP. Nitrates for achalasia. Cochrane Database Syst Rev. 2004;(4):CD002299.
4. Eckardt AJ, Eckardt VF. Current clinical approach to achalasia. World J Gastroenterol. 2009;15:3969–75.
5. Vaezi MF, Richter JE. Diagnosis and management of achalasia. American College of Gastroenterology PracticeParameter Committee. Am J Gastroenterol. 1999;94:3406–12.
6. Zaninotto G, Bennett C, Boeckxstaens G, Costantini M, et al. The 2018ISDE achalasia guidelines. Dis Esophagus. 2018;31(9). https://doi.org/10.1093/dote/doy071.
7. Shim CS. Endoscopic botulinum toxin injection: benefit and limitation. Gastrointest Interv. 2014;3:19–23.
8. Pasricha P, Ravich W, Hendrix T, Sostre S, et al. Intrasphinteric botulinum toxin for the treatment of achalasia. N Engl J Med. 1995;332:774–8.
9. Pasricha P, Ravich W, Hendrix T, Kalloo A, et al. Treatment of achalasia with intrasphinteric injection of botulinum toxin: a plot trial. Ann Intern Med. 1994;121:590–1.
10. Cuilliere C, Ducrotte P, Zerbib F, Metman E, de Looze D, Guillemot F, et al. Achalasia: outcome of patients treated with intrasphinteric injection of botulinum toxin. Gut. 1997;41:87–92.
11. Pasricha P, Rai R, Ravich W, Hendrix T, Kaloo A. Botulinum toxin for achalasia: long term outcomes and predictors of response. Gastroenterology. 1996;110:1410–5.
12. Fishman V, Parkman H, Schiano T, Hills C, Dabezies M, et al. Symptomatic improvement in achalasia after botulinum toxin injection of the lower esophageal sphincter. Am J Gastroenterol. 1996;91:1724–30.
13. Annesse V, Basciani M, Borrelli O, Leandro G, Simone P, et al. Intrasphinteric injection of botulinum toxin is effective in long-term treatment of esophageal achalasia. Muscle Nerve. 1998;21:1540–2.
14. Campos GM, Vittinghoff E, Rabl C, Takata M, Gadenstätter M, Lin F, et al. Endoscopic and surgical treatments for achalasia: a systematic review and meta-analysis. Ann Surg. 2009;249:45–57.
15. Neubrand M, Scheurlen C, Schepke M, Sauerbruch T. Long-term results and prognostic factors in the treatment of achalasia with botulinum toxin. Endoscopy. 2002;34:519–23.
16. Allescher HD, Storr M, Seige M, Gonzales-Donoso R, Ott R, Born P, et al. Treatment of achalasia: botulinum toxin injection vs. pneumatic balloon dilation. A prospective study with long-term follow-up. Endoscopy. 2001;33:1007–17.

17. Pasricha PJ, Rai R, Ravich WJ, Hendrix TR, Kalloo AN. Botulinum toxin for achalasia: long-term outcome and predictors of response. Gastroenterology. 1996;110:1410–5.
18. Fishman VM, Parkman HP, Schiano TD, Hills C, Dabezies MA, Cohen S, et al. Symptomatic improvement in achalasia after botulinum toxin injection of the lower esophageal sphincter. Am J Gastroenterol. 1996;91:1724–30.
19. Annese V, Basciani M, Perri F, Lombardi G, Frusciante V, Simone P, et al. Controlled trial of botulinum toxin injection versus placebo and pneumatic dilation in achalasia. Gastroenterology. 1996;111:1418–24.
20. Patti MG, Feo CV, Arcerito M, De Pinto M, Tamburini A, Diener U, et al. Effects of previous treatment on results of laparoscopic Heller myotomy for achalasia. Dig Dis Sci. 1999;44(11):2270–6.
21. Leyden JE, Moss AC, MacMathuna P. Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia. Cochrane Database Syst Rev. 2014;12:CD005046.
22. Vaezi MF, Richter JE, Wilcox CM, Schroeder PL, Birgisson S, Slaughter RL, et al. Botulinum toxin versus pneumatic dilatation in the treatment of achalasia: a randomized trial. Gut. 1999;44(2):231–9.
23. Muehldorfer SM, Schneider TH, Hochberger J, Martus P, Hahn EG, Ell C. Esophageal achalasia: intrasphincteric injection of botulinum toxin A versus balloon dilation. Endoscopy. 1999;31(7):517–21.
24. Ghoshal UC, Chaudhuri S, Pal BB, Dhar K, Ray G, Banerjee PK. Randomized controlled trial of intrasphincteric botulinum toxin A injection versus balloon dilatation in treatment of achalasia cardia. Dis Esophagus. 2001;14(3–4):227–31.
25. Mikaeli J, Fazel A, Montazeri G, Yaghoobi M, Malekzadeh R. Randomized controlled trial comparing botulinum toxin injection to pneumatic dilatation for the treatment of achalasia. Aliment Pharmacol Ther. 2001;15(9):1389–96.
26. Bansal R, Nostrant TT, Scheiman JM, Koshy S, Barnett JL, Elta GH, et al. Intrasphincteric botulinum toxin versus pneumatic balloon dilation for treatment of primary achalasia. J Clin Gastroenterol. 2003;36(3):209–14.
27. Zhu Q, Liu J, Yang C. Clinical study on combined therapy of botulinum toxin injection and small balloon dilation in patients with esophageal achalasia. Dig Surg. 2009;26:493–8.
28. Zaninotto G, Annese V, Costantini M, Del Genio A, Costantino M, Epifani M, et al. Randomized controlled trial of botulinum toxin versus laparoscopic Heller myotomy for esophageal achalasia. Ann Surg. 2004;239:364–70.
29. Karamanolis G, Sgouros S, Karatzias G, Papadopoulou E, Vasiliadis K, Stefanidis G, et al. Long-term outcome of pneumatic dilation in the treatment of achalasia. Am J Gastroenterol. 2005;100:270–4.
30. Mikaeli J, Bishehsari F, Montazeri G, Yaghoobi M, Malekzadeh R. Pneumatic balloon dilatation in achalasia: a prospective comparison on safety and efficacy with different balloon diameters. Aliment Pharmacol Ther. 2004;20(4):431–6.
31. Hungness ES, Kahrilas PJ. Endoscopic management of achalasia. In: Fisichella PM, Soper NJ, Pellegrini CA, Patti MG, editors. Surgical management of benign esophageal disorders. The Chicago approach. London: Springer; 2014. p. 141–54.
32. Borotto E, Gaudric M, Danel B, et al. Risk factor of esophageal perforation during pneumatic dilatation for achalasia. Gut. 1996;39:9–12.
33. Zerbib F, Thetiot V, Richy F, Benajah D, Message L, et al. Repeated pneumatic dilations as long-term maintenance therapy for esophageal achalasia. Am J Gastroenterol. 2006;101:692–7.
34. Eckardt VF, Gockel I, Bernhard G. Pneumatic dilation for achalasia: late results of a prospective follow up investigation. Gut. 2004;53:629–33.
35. Gockel I, Junginger T, Bernhard G, Eckardt VF. Heller myotomy for failed pneumatic dilation in achalasia: how effective is it? Ann Surg. 2004;239:371–7.
36. Farhoomand K, Connor JT, Richter JE, Achkar E, Vaezi MF. Predictors of outcome of pneumatic dilation in achalasia. Clin Gastroenterol Hepatol. 2004;2:389–94.
37. Dagli U, Kuran S, Savas N, Ozin Y, Alkim C, Atalay F, et al. Factors predicting outcome of balloon dilatation in achalasia. Dig Dis Sci. 2009;54:1237–42.
38. Cheng JW, Li Y, Xing WQ, Lv HW, Wang HR. Laparoscopic Heller myotomy is not superior to pneumatic dilation in the management of primary achalasia: conclusions of a systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2017;96(7):e5525.
39. Boeckxstaens GE, Annese V, des Varannes SB, et al. Pneumatic dilation versus laparoscopic Heller myotomy for idiopathic achalasia. N Engl J Med. 2011;364:1807–16.
40. Moonen A, Annese V, Belmans A, et al. Long-term results of the European achalasia trial: a multicentre randomized controlled trial comparing pneumatic dilation versus laparoscopic Heller myotomy. Gut. 2016;65:732–9.
41. Kostic S, Kjellin A, Ruth M, et al. Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. World J Surg. 2007;31:470–8.
42. Persson J, Johnsson E, Kostic S, et al. Treatment of achalasia with laparoscopic myotomy or pneumatic dilatation: long-term results of a prospective, randomized study. World J Surg. 2015;39:713–20.
43. Borges AA, Lemme EM, Abrahao LJ Jr, et al. Pneumatic dilation versus laparoscopic Heller myotomy for the treatment of achalasia: variables related to a good response. Dis Esophagus. 2014;27:18–23.
44. Hamdy E, El Nakeeb A, El Hanfy E, et al. Comparative study between laparoscopic Heller myotomy versus pneumatic dilatation for treatment of early achalasia: a prospective randomized study. J Laparoendosc Adv Surg Tech A. 2015;25:460–4.

45. Novais PA, Lemme EM. 24-h pH monitoring patterns and clinical response after achalasia treatment with pneumatic dilation or laparoscopic Heller myotomy. Aliment Pharmacol Ther. 2010;32:1257–65.
46. Wang L, Li YM, Li L. Meta-analysis of randomized and controlled treatment trials for achalasia. Dig Dis Sci. 2009;54(11):2303–11.
47. Richter JE, Boeckxstaens GE. Management of achalasia: surgery or pneumatic dilation. Gut. 2011;60(6):869–76.
48. Wang X, Tan Y, Lv L, Zhu H, Chu Y, Li C, et al. Peroral endoscopic myotomy versus pneumatic dilation for achalasia in patients aged >65 years. Rev Esp Enferm Dig. 2016;108(10):637–41.
49. Meng F, Li P, Wang Y, Ji M, Wu Y, Yu L, et al. Peroral endoscopic myotomy compared with pneumatic dilation for newly diagnosed achalasia. Surg Endosc. 2017;31(11):4665–72.
50. Ponds F, Fockens P, Neuhaus H, et al. Peroral endoscopic myotomy (POEM) versus pneumatic dilatation in therapy naïve patients with achalasia: results of a randomized controlled trial. Gastroenterology. 2017;152(5 Suppl 1):S139.. (abstract)
51. Zaninotto G, Costantini M, Rizzetto C, Zanatta L, Guirroli E, Portale G, et al. Four hundred laparoscopic myotomies for esophageal achalasia: a single centre experience. Ann Surg. 2008;248(6):986–93.
52. Perrone JM, Frisella MM, Desai KM, Soper NJ. Results of laparoscopic Heller-Toupet operation for achalasia. Surg Endosc. 2004;18(11):1565–71.
53. Pandolfino JE, Kwiatek M, Nealis T, Bulsiewicz W, et al. Achalasia: a new clinically relevant classification by high-resolution manometry. Gastroenterology. 2008;135:1526–33.
54. Salvador R, Constantini M, Zaninotto G, et al. The preoperative manometric pattern predicts the outcome of surgical treatment for esophageal achalasia. J Gastrointest Surg. 2010;14:1635–45.
55. Richards WO, Torquati A, Holzman MD, Khaitan L, Byrne D, Lutfi R, et al. Heller myotomy versus Heller myotomy with Dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. Ann Sug. 2004;240(3):405–12.
56. Falkenback D, Johansson J, Öberg S, Kjellin A, Wenner J, Zilling T, et al. Heller's esophagomyotomy with or without a 360° floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. Dis Esophagus. 2003;16(4):284–90.
57. Rebecchi F, Giaccone C, Farinella E, Campaci R, Morino M. Randomized controlled trial of laparoscopic Heller myotomy plus Dor fundoplication versus Nissen fundoplication for achalasia: long-term results. Ann Surg. 2008;248(6):1023–30.
58. Rawlings A, Soper NJ, Oelschlager B, Swanstrom L, Matthews BD, Pellegrini CA, et al. Laparoscopic Dor versus Toupet fundoplication following Heller myotomy for achalasia: results of a multicenter, prospective, randomized-controlled trial. Surg Endosc. 2012;26(1):18–26.
59. Kumagai K, Kjellin A, Tsai JA, Thorell A, Granqvist S, Lundell L, et al. Toupet versus Dor as a procedure to prevent reflux after cardiomyotomy for achalasia: results of a randomized clinical trial. Int J Surg. 2014;12(7):673–80.
60. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265–71.
61. Von Renteln D, Fuchs KH, Fockens P, Bauerfeind P, Vassiliou MC, Werner YB, et al. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. Gastroenterology. 2013;145(2):309–11.
62. Inoue H, Sato H, Ikeda H, et al. Per –oral endoscopic myotomy: a series of 500 patients. J Am Coll Surg. 2015;221:256–64.
63. Familiari P, Gigante G, Marchese M, Boskoski I, Tringali A, Perri V, et al. Peroral endoscopic myotomy for esophageal achalasia: outcomes of the first 100 patients with short-term follow-up. Ann Surg. 2016;263(1):82–7.
64. Akintoye E, Kumar N, Obaitan I, Alayo QA, Thompson CC. Peroral endoscopic myotomy: a meta-analysis. Endoscopy. 2016;48(12):1059–68.
65. Kumbhari V, Familiari P, Bjerregaard NC, et al. Gastroesophageal reflux after peroral endoscopic myotomy: a multicenter case-control study. Endoscopy. 2017;49:634–42.
66. Sharata AM, Dunst CM, Pescarus R, Shlomovitz E, Wille AJ, Reavis KM, et al. Peroral endoscopic myotomy (POEM) for esophageal primary motility disorders: analysis of 100 consecutive patients. J Gastrointest Surg. 2015;19(1):161–70.
67. Worrell SG, Alicuben ET, Boys J, DeMeester SR. Peroral endoscopic myotomy for achalasia in a thoracic surgical practice. Ann Thorac Surg. 2016;101(1):218–24.
68. Kahrilas P, Katzka D, Richter J. Clinical practice update: the use of per-oral endoscopic myotomy in achalasia: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology. 2017;153(5):1205–11.
69. Swanstrom LL, Kurian A, Dunst CM, Sharata A, Bhayani N, Rieder E. Long-term outcomes of an endoscopic myotomy for achalasia: the POEM procedure. Ann Surg. 2012;256(4):659–67.
70. Bhayani NH, Kurian AA, Dunst CM, Sharata AM, Rieder E, Swanstrom LL. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Ann Surg. 2014;259(6):1098–103.
71. Chan S, Wu J, Teoh A, et al. Comparison of early outcomes and quality of life after laparoscopic Heller's cardiomyotomy to peroral endoscopic myotomy for treatment of achalasia. Dig Endosc. 2016;28:27–32.
72. Schlottmann F, Luckett DJ, Fine J, Shaheen NJ, Patti MG. Laparoscopic Heller myotomy versus Peroral Endoscopic Myotomy (POEM) for achala-

sia: asystematic review and meta-analysis. Ann Surg. 2018;267(3):451–60.
73. Khashab MA, Messallam AA, Onimaru M, Teitelbaum EN, Ujiki MB, Gitelis ME, et al. International multicenter experience with peroral endoscopic myotomy for the treatment of spastic esophageal disorders refractory to medical therapy (with video). Gastrointest Endosc. 2015;81(5):1170–7.
74. Zhang W, Linghu EQ. Peroral endoscopic myotomy for type III achalasia of Chicago classification: outcomes with a minimum follow-up of 24 months. J Gastrointest Surg. 2017;21(5):785–91.
75. Schlottmann F, Andolfi C, Kavitt RT, Konda VJA, Patti MG. Multidisciplinary approach to esophageal achalasia: asingle center experience. J Laparoendosc Adv Surg Tech A. 2017;27(4):358–62.
76. Vela MF, Richter JE, Wachsberger D, Connor J, et al. Complexities of managing achalasia at tertiary referral center: use of pneumatic dilatation, Heller myotomy and botulinum toxin injection. Am J Gastroenterol. 2004;99:1029–36.
77. Ngamruengphong S, Inoue H, Ujiki MB, Patel LY, Bapaye A, Desai PN, et al. Efficacy and safety of Peroral endoscopic myotomy for treatment of achalasia after failed Heller myotomy. Clin Gastroenterol Hepatol. 2017;15(10):1531–7.
78. Khan A, Shah S, Alam A, Butt A, et al. Massively dilated esophagus in achalasia: response to balloon pneumatic dilation. Am J Gastroenterol. 1999;94:2363–6.
79. Mineo TC, Pompeo E. Long-term outcome of Heller myotomy in achalasic sigmoid esophagus. J Thorac Cardiovasc Surg. 2004;128(3):402–7.
80. Sweet MP, Nipomnick I, Gasper WJ, Bagatelos K, Ostroff JW, Fisichella PM, et al. The outcome of laparoscopic Heller myotomy for achalasia is not influenced by the degree of esophageal dilatation. J Gastrointest Surg. 2008;12(1):159–65.
81. Hu J, Li Q, Zhou P, Yao L, et al. Peroral endoscopic myotomy for advanced achalasia with sigmoid-shaped esophagus: long term outcomes from a prospective, single center study. Surg Endosc. 2015;29:2841–50.
82. Zhang X, Modayil RJ, Friedel D, Gurram KC, Brathwaite CE, Taylor SI, et al. Per-oral endoscopic myotomy in patients with or without prior Heller myotomy: comparing long-term outcomes in a large U.S. single-center cohort (with videos). Gastrointest Endosc. 2018;87(4):972–85.
83. Tyberg A, Sharaiha RZ, Familiari P, Costamagna G, Casas F, Kumta NA, et al. Peroral endoscopic myotomy as salvation technique post-Heller: international experience. Dig Endosc. 2018;30(1):52–6.
84. van Hoeij FB, Ponds FA, Werner Y, Sternbach JM, Fockens P, Bastiaansen BA, et al. Management of recurrent symptoms after per-oral endoscopic myotomy in achalasia. Gastrointest Endosc. 2018;87(1):95–101.
85. Rossetti G, Brusciano L, Amato G, Maffettone V, Napolitano V, Russo G, et al. A total fundoplication is not an obstacle to esophageal emptying after Heller myotomy for achalasia: results of a long-term follow up. Ann Surg. 2005;241(4):614–21.
86. Katada N, Sakuramoto S, Kobayashi N, Futawatari N, Kuroyama S, Kikuchi S, et al. Laparoscopic Heller myotomy with Toupet fundoplication for achalasia straightens the esophagus and relieves dysphagia. Am J Surg. 2006;192(1):1–8.
87. Sasaki A, Obuchi T, Nakajima J, Kimura Y, Koeda K, Wakabayashi G. Laparoscopic Heller myotomy with Dor fundoplication for achalasia: long-term outcomes and effect on chest pain. Dis Esophagus. 2010;23(4):284–9.
88. Parise P, Santi S, Solito B, Pallabazzer G, Rossi M. Laparoscopic Heller myotomy plus Dor fundoplication in 137 achalasic patients: results on symptoms relief and successful outcome predictors. Updat Surg. 2011;63(1):11–5.
89. Di Martino N, Brillantino A, Monaco L, Marano L, Schettino M, Porfidia R, et al. Laparoscopic calibrated total vs partial fundoplication following Heller myotomy for oesophageal achalasia. World J Gastroenterol. 2011;17(29):3431–40.
90. Cuttitta A, Tancredi A, Andriulli A, De Santo E, Fontana A, Pellegrini F, et al. Fundoplication after Heller myotomy: a retrospective comparison between Nissen and Dor. Eurasian J Med. 2011;43(3):133–40.
91. Rosati R, Fumagalli Romario U, Ceolin M, Massaron S, Peracchia A. Laparoscopic Heller-Dor for primary esophageal achalasia: outcomes in 173 patients. Ann Ital Chir. 2013;84(5):515–9.
92. Salvador R, Pesenti E, Gobbi L, Capovilla G, Spadotto L, Voltarel G, et al. Postoperative gastroesophageal reflux after laparoscopic Heller-Dor for achalasia: true incidence with an objective evaluation. J Gastrointest Surg. 2017;21(1):17–22.
93. Schneider AM, Louie BE, Warren HF, Farivar AS, Schembre DB, Aye RW. A matched comparison of per oral endoscopic myotomy to laparoscopic Heller myotomy in the treatment of achalasia. J Gastrointest Surg. 2016;20(11):1789–96.
94. Hungness ES, Sternbach JM, Teitelbaum EN, Kahrilas PJ, Pandolfino JE, Soper NJ. Per-oral Endoscopic Myotomy (POEM) after the learning curve: durable long-term results with a low complication rate. Ann Surg. 2016;264(3):508–17.
95. Hungness ES, El Khoury F. Peroral Endoscopic Myotomy (POEM). In: Risichella PM, Patti MG, editors. Atlas of esophageal surgery. Springer International Publishing Switzerland; 2015. p. 85–93.

Part II

GERD

Historical Notes on the Surgical Treatment of GERD

12

Vera Lucia Ângelo Andrade
and Fernando A. M. Herbella

Introduction

Gastroesophageal reflux disease (GERD) is a highly prevalent disease associated to heavy burden in quality of life. An appropriate treatment is thus essential. Conservative treatment aims to alleviate symptoms, heal lesions, and prevent relapses and complications by using behavioral and pharmacologic therapy. On the other hand, surgical treatment has the ability to correct the defective barrier between the stomach and the esophagus. A tailored approach should be used to identify the best treatment for each individual [1, 2].

The goal of surgery for GERD is to re-establish the antireflux barrier without creating obstacles to the transit of the bolus from the esophagus into the stomach. In other words, GERD surgery needs to achieve a balance between flux and reflux. Esophageal surgery, however, was a challenge for surgeons due to anatomical, histological, and physiological issues [3]. The beginning of the surgical approach to the esophagus dates from the seventeenth century for the treatment of trauma and subsequently of esophageal cancer. Operations for GERD were first reported in the twentieth century. The delay in the development of surgical intervention for GERD is probably related to lack of understanding of the pathophysiology of GERD and the limitation of diagnostic methods [4].

GERD symptoms have been reported since ancient Rome, but they received little clinical relevance until the last century. Only in 1935, Winkelstein popularized reflux esophagitis as a new pathological entity [5], even though it had first been reported by Quincke in 1859 [6]. Rokitansky in 1855 demonstrated that esophagitis was due to gastroesophageal reflux [7].

The history of antireflux surgery reflects a progressive understanding of the pathophysiology of GERD. Allison, as an example, was a pioneer of antireflux operations, but at his time, GERD and hiatal hernia (HH) were considered synonyms [8]. He proposed HH reduction to solve GERD symptoms [8, 9]. Predictably, the recurrence rate was very high, and symptoms control suboptimal. The role of Nissen in the history of fundoplication should be highlighted, as well as the various technical changes that were later proposed [10–12]. However, today many lessons from the past are ignored and those who fail to remember them are doomed to repeat the same mistakes.

This chapter will review important aspects of the history of GERD treatment.

V. L. Â. Andrade
Department of Pathology, Faculdade de Medicina da UninCor, Universidade Vale do Rio Verde, Belo Horizonte, Brazil

F. A. M. Herbella (✉)
Department of Surgery, Escola Paulista de Medicina, Federal University of Sao Paulo, Sao Paulo, Brazil
e-mail: herbella.dcir@epm.br

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_12

Hiatal Hernia Repair: Early Attempts to Control GERD

GERD was a synonym for HH for a long time [7, 9, 13]. The description of HH – as we understand today – was initially reported based on *post-mortem* examination by Morgagni [14] (Fig. 12.1) in 1769 and *in vivo* by Eppinger in 1909 [15].

It is interesting to note that the first description of a HH was performed by X-ray. In that same year, the first surgical intervention for HH was described [16]. Eppinger in 1911 summarized the literature on diaphragmatic hernia and reported that of 635 cases of herniation through various portions of the diaphragm, only 11 involved the esophageal hiatus [15]. Akerlund in 1926 proposed the term HH and classified it in the three types we use today [7]. Bernstein in 1947 reviewed the HH theme and concluded that one of the reasons for the low number of diagnoses was that HH could be missed by autopsy as muscles are relaxed and intra-abdominal pressure decreased [17]. The technique of X-ray examination with the patient in the upright posture generally also fails to visualize these hernias. Examination in a reclining or even Trendelenburg position with application of manual pressure to the upper abdomen is necessary to demonstrate HH. These hernias may disappear as soon as the patient is brought back into the upright posture, or the increased abdominal pressure is released [16].

The first elective surgical repair of HH entitled "diaphragmatica" repair was reported in 1919 by Angelo Soresi [18], although the physiopathological link between HH and gastroesophageal reflux was only established in the second half of the twentieth century by Allison in Leeds and Barrett in London. We feel that the modern age of antireflux surgery was initiated by the English surgeon Allison (Fig. 12.2) who in 1951 repositioned the stomach into the abdo-

Fig. 12.1 Giovanni Battista Morgagni(1682–1771) was an Italian anatomist, regarded as the father of modern anatomical pathology. (Public domain reproduced from Wikipedia.org)

Fig. 12.2 Philip R. Allison (1908–1974) a thoracic surgeon from Leeds, UK. (Reproduced with permission ©Nuffield Department of Surgical Sciences, University of Oxford)

men and approximated the crural fibers behind the esophagus [19].

Allison's 20-year follow-up showed good results with improvement of symptoms in 80% of patients. Modern attempts to correct HH without other procedure such as a fundoplication failed to control GERD adequately [20]. HH repair, however, was granted as a necessary part of anatomical restoration to control GERD.

Angle of His Restoration: Early Attempts to Control GERD

Parallel to hiatal hernia repair, some surgeons focused on the angle of His as antireflux mechanism (Fig. 12.3) [21].

Barrett [22] (Fig. 12.4) and latter Lortat-Jacob [23] (Fig. 12.5) were pioneers on the restoration of the cardioesophageal (His) angle as an element for GERD prevention.

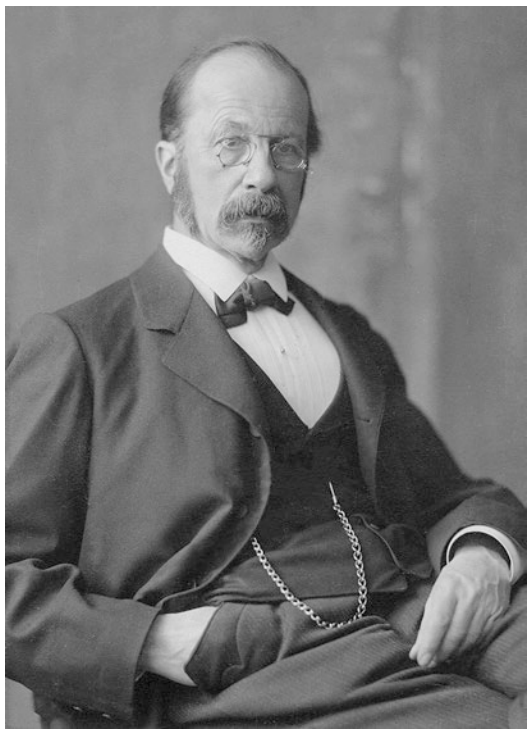


Fig. 12.3 Wilhelm His (1831–1904) a German anatomist that described the angle named after him. (Public domain reproduced from Wikipedia.org)

Fig. 12.4 Norman R. Barret (1903–1979) a thoracic surgeon who is primarily remembered for describing Barrett's esophagus. (Reproduced from Researchgate under CC BY 2.0 license)

Fig. 12.5 Jean-Louis Lortat-Jacob (1908–1922) a French surgeon also recognized as the first one to reconstruct the alimentary tract after an esophagectomy in France and to perform the first anatomic hepatectomy

As a consequence, the angle of His gained importance as an indispensable antireflux mechanism. It is important to note that while Allison focused on the reduction of HH and adequate closure of the diaphragmatic sling, Barrett prioritized restoration of the cardioesophageal angle as a critical element in preventing reflux [7].

The Rise of the Fundoplication

It is impossible to talk about the history of GERD surgery without citing the key role of Rudolph Nissen (Fig. 12.6). Nissen was born in Schlesien in 1896, began his career in German in 1921, and died in Basel in 1981. Of historical importance are his work in thoracic surgery such as the first successful pneumonectomy in man; however, it was his antireflux operation that made him famous worldwide [24–28].

The Nissen technique was first introduced during the operation of a young patient with a distal esophageal ulcer penetrating the pericardium. After resection of the distal esophagus and cardia, the anastomosis was protected wrapping the distal esophagus with the posterior wall of the stomach. The patient had an excellent recovery and did not develop esophagitis. It is of notice that the short gastric blood vessels were not ligated, and the hiatus was not approximated. As such, the ideal antireflux operation was not perfected yet [25–28].

The Technical Evolution of the Fundoplication

André Toupet (Fig. 12.7) played an important role in the development of many operations, but he is recognized for the antireflux procedure that bears his name. Unlike Nissen who performed a 360-degree wrap, Toupet proposed a 270-degree posterior wrap, which would produce less postoperative dysphagia than Nissen fundoplication [29].

Other authors such as Jacques Dor [30] and Vicente Guarner [31] also proposed different partial fundoplications [32]. Dor proposed an anterior 180-degree fundoplication, while Guarner used a posterior partial fundoplication with closure of the hiatus.

Studies comparing Lortat-Jacob [23], Toupet, and Nissen procedures proved that isolated restoration of the cardioesophageal angle has inferior outcomes as compared to a fundoplication

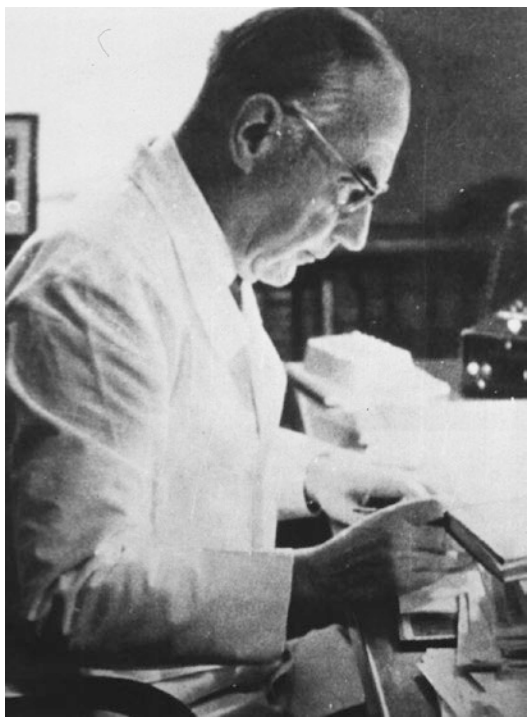


Fig. 12.6 Rudolph Nissen (1896–1981) a German surgeon that also acted in Turkey, the Unites States, and Switzerland. (Reproduced from Images from the History of Medicine – National Library of Medicine)

Fig. 12.7 André Toupet (1915–2015) a Parisian surgeon that also developed 20 new instruments and 40 procedures. (Reused with permission ©French Academie Nationale de Chirurgie)

[33–35]. History showed that correction of a single natural antireflux mechanism is not enough.

Some authors have performed a Nissen fundoplication without a hiatoplasty, neglecting the diaphragm as an antireflux mechanism. The results showed a large number of HH recurrences and consequently very poor control of reflux. This experience further strengthened the role of the diaphragm as an antireflux mechanism. In 1965 Nissen and Rossetti proposed a variation of the technique in overweight patients, using the anterior wall of the stomach to wrap the distal esophagus [27]. The follow-up of 590 cases showed 90% relief of symptoms [36, 37]. Other technical changes were made but were eventually abandoned such as the addition of pyloroplasty or vagotomy [38–42].

Two modifications, however, showed improvement in results especially decreasing the rate of dysphagia and gas symptoms. Donahue et al. made the Nissen valve "floppy," with a loose wrapping of the esophagus [43]. The advantages of a loose "floppy" wrap in avoiding the gas bloat syndrome have been well documented, and it was an important historical learning (Fig. 12.8) [44].

DeMeester et al. (Fig. 12.9) made the valve shorter, decreasing significantly the size of the fundoplication from the original 5 cm to 1.5–2 cm. Evaluation of primary repair in 100 consecutive patients showed excellent results, and currently most surgeons prefer this shorter wrap[45].

The first minimally invasive (laparoscopic Nissen fundoplication) was performed in 1991 by Bernard Dallemagne [46]. Robotic arms were used the first time in 1998 [47, 48]. Figure 12.10 shows Nissen fundoplication and its modifications.

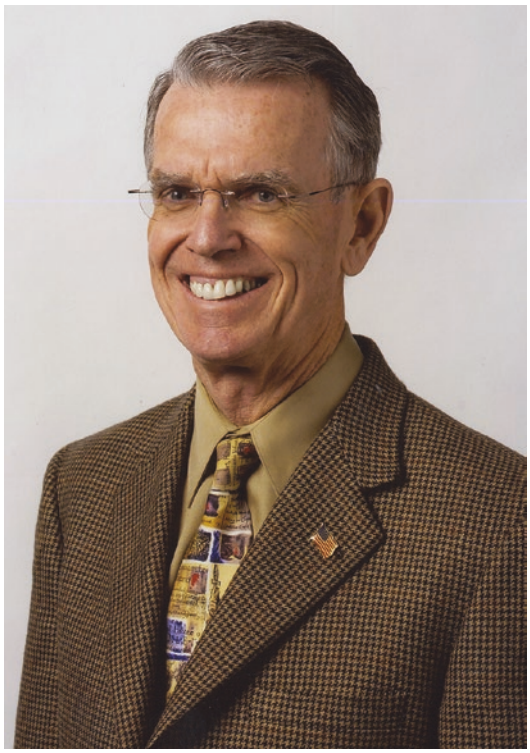


Fig. 12.8 Philip E. Donahue (1942–2009) an American surgeon and pioneer in laparoscopic surgery. (Reuse with permission ©Department of Surgery, University of Illinois at Chicago)

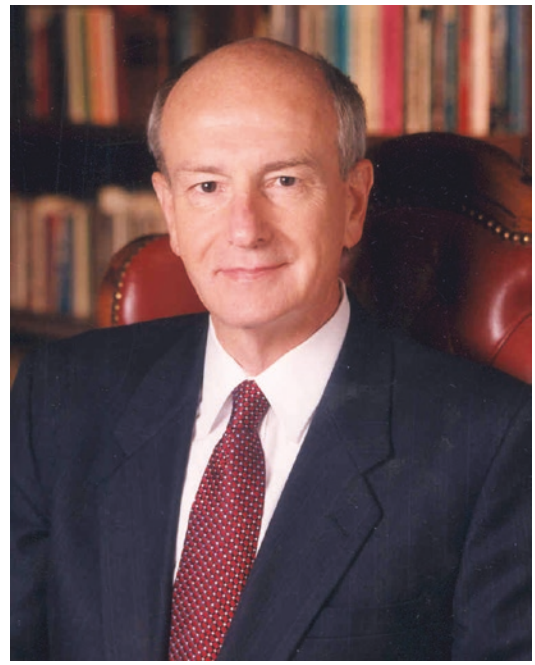


Fig. 12.9 Tom Ryan DeMeester (1938–) an American surgeon that dedicated his entire career to the esophagus, and it is also known by the composite score that defines reflux on pH monitoring. (Courtesy Ms. Carol DeMeester)

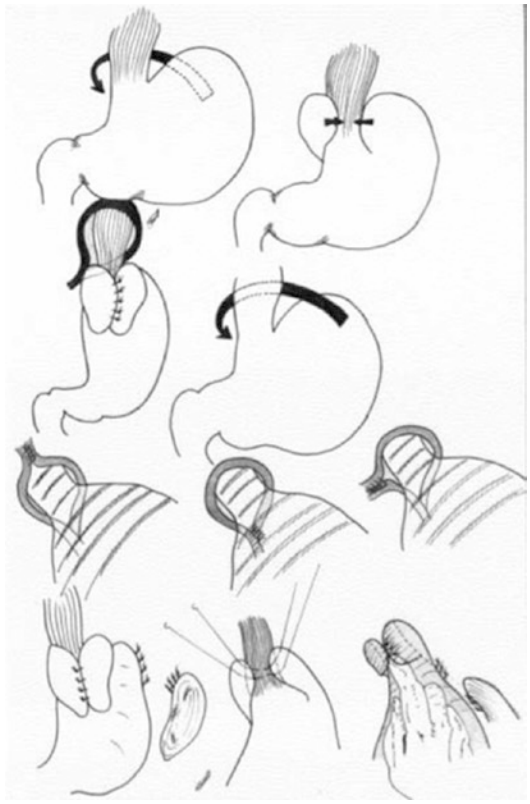


Fig. 12.10 Nissen fundoplication and its modifications. (Reproduced with permission © Oxford University Press [48])

Beyond Fundoplication

There are modern attempts to create alternative procedures to Nissen fundoplication. These techniques act on the augmentation of the esophagogastric barrier by decreasing the complacency of the esophagogastric junction, artificial sphincters implantation, endoluminal plication, or electric stimulation of the lower esophageal sphincter. Neither one restores all-natural mechanisms like a Nissen fundoplication and hiatoplasty does. Time will tell if these procedures will persist in the armamentarium to treat GERD [49–51].

Conclusions

Current gold standard surgical therapy for GERD is the procedure created by Nissen and modified along time to reach the modern laparoscopic 360-degree short-floppy fundoplication associated to a hiatoplasty (Fig. 12.11). Current and future developments must be compared to this time-proven operation.

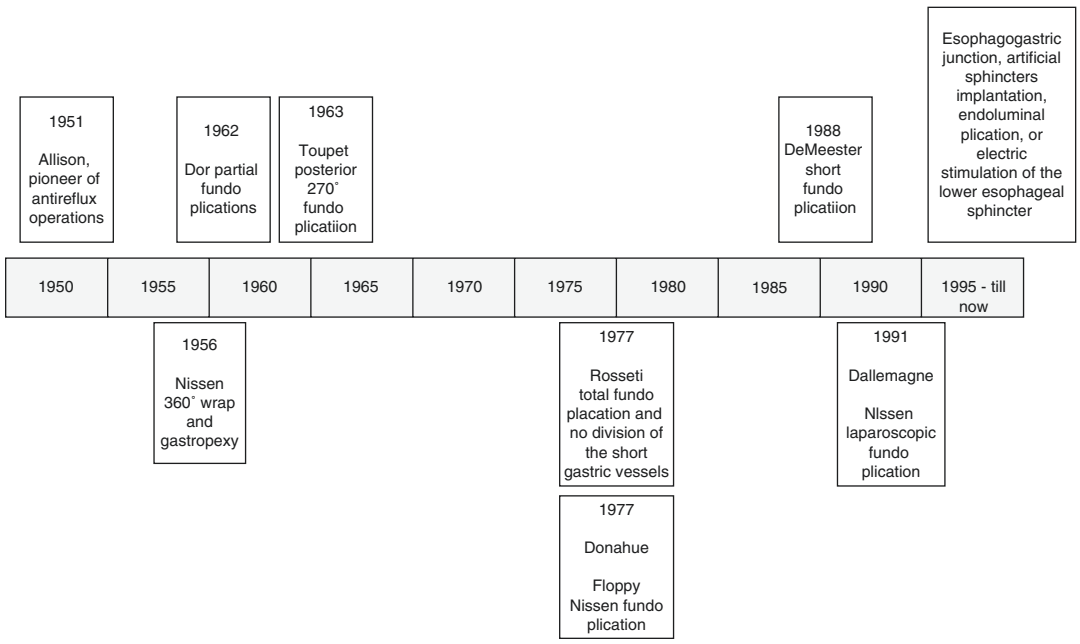


Fig. 12.11 Gastroesophageal reflux treatment timeline

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Wiklund I. Review of the quality of life and burden of illness in gastroesophageal reflux disease. Dig Dis. 2004;22(2):108–14.
2. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63(6):871–80.
3. Takassi GF, Herbella FA, Patti MG. Anatomic variations in the surgical anatomy of the thoracic esophagus and its surrounding structures. Arq Bras Cir Dig. 2013;26(2):101–6.
4. Modlin IM, Kidd M, Lye KD. Historical perspectives on the treatment of gastroesophageal reflux disease. Gastrointest Endosc Clin N Am. 2003;13:19–55.
5. Winkelstein A. Peptic esophagitis: a new clinical entity. JAMA. 1935;104:906–11.
6. Quincke H. Ulcusoesophagiexdigestione. Deutsch Arch KilnMed. 1879;24:72–9.
7. Stylopoulos N, Rattner DW. The history of hiatal hernia surgery: from Bowditch to laparoscopy. Ann Surg. 2005;241(1):185–93.
8. Anonymous. Philip Rowland Allison. Lancet. 1974;16:465–6.
9. Cross FS, Kay EB, Smith GV Jr. The treatment of regurgitant esophagitis by reconstruction of the cardiac sphincter mechanism in patients with no demonstrable hiatal hernia. Dis Chest. 1961;39:530–4.
10. Hunter JG, Trus TL, Branum GD, et al. A physiologic approach to laparoscopic fundoplication for gastroesophageal reflux disease. Ann Surg. 1996;223(6):673–85; discussion 685–7
11. Bhandarwar AH, Kasat GV, Palep JH, et al. Impact of laparoscopic Nissen's fundoplication on response of disease specific symptoms and quality of life. Updat Surg. 2013;65(1):35–41.
12. Kamolz T, Granderath FA, Bammer T, et al. Dysphagia and quality of life after laparoscopic Nissen fundoplication in patients with and without prosthetic reinforcement of the hiatal crura. Surg Endosc. 2002;16(4):572–7.
13. Jobe BA, Richter JE, Hoppo T, et al. Preoperative diagnostic workup before antireflux surgery: an evidence and experience-based consensus of the Esophageal Diagnostic Advisory Panel. J Am Coll Surg. 2013;217(4):586–97.
14. Ghosh SK. Giovanni Battista Morgagni (1682–1771): father of pathologic anatomy and pioneer of modern medicine. Anat Sci Int. 2017;92(3):305–12.
15. Eppinger H. Pathologie des Zwerchfelles. Supplement zuNorthmageSpeziellePathologie und Therapie. Wien und Leipzig: Holder; 1911.
16. Herbella FA, Patti MG, Del Grande JC. When did the esophagus start shrinking? The history of the short esophagus. Dis Esophagus. 2009;22(7):550–8.
17. Bernstein A. Hiatal hernia, a frequent and clinically important condition. Univ W Ont J. 1947;17:159.
18. Soresi AL. Diaphragmatic hernia: its unsuspected frequency: diagnosis and technique for radical cure. Ann Surg. 1919;69:254–70.
19. Allison PR. Reflux esophagitis, sliding hiatal hernia, and the anatomy of repair. Surg Gynecol Obstet. 1951;92(4):419–31.
20. Allison PR. Hiatus hernia: (a 20-year retrospective survey). Ann Surg. 1973;178(3):273–6.
21. Lortat–Jacob JL. Traitment chirurgical du cardiospasme. Ann Chir. 1997;51:403–4.
22. Barrett NR. Hiatus hernia: a review of some controversial points. Br J Surg. 1954;42:231–43.
23. Boutelier P. Eulogy of Jean-Louis Lortat-Jacob (1908–1992). Chirurgie. 1996;21(8):589–96.
24. Nissen R. Die transpleurale Resection der Kardia. Dtsch Z Chir. 1937;249:311–6.
25. Nissen R. Gastropexy as lone procedure in surgical repair of hiatus hernia. Am J Surg. 1956;92:389–92.
26. Nissen R. Gastropexy and "fundoplication" in surgical treatment of hiatal hernia. Am J Dig Dis. 1961;6:95441.
27. Nissen R, Rossetti M. Surgery of hiatal and other diaphragmatic hernias. J Int Coll Surg. 1965;43:663–74.
28. Liebermann-Meffert D, Rossetti M. The 100th birthday of Rudolf Nissen. Chirurgie. 1996;67(10):1053–9.
29. Toupet A. Techinic of esophago-gastroplasty with phenp-gastropexy used in radical treatment of hiatal hernia as a supplement to Heller's operation in cardiospasms. Mem Acad Chir. 1963;89:284–389.
30. Dor J, Humbet P, Dor V, et al. L'intéret de la technique de Nissenmodifféedans la prévention du reflux après cardiomyotomie extra-muqueuse de Heller. Mem AcadChir. 1962;3:877–84.
31. Guarner V, Degollade JR, Tore NM. A new antireflux procedure at the esophagogastric junction: experimental and clinical evaluation. Arch Surg. 1975;110(1):101–6.
32. Patti MG, Robinson T, Galvani C, et al. Total fundoplication is superior to partial fundoplication even when esophageal peristalsis is weak. J Am Coll Surg. 2004;198(6):863–9; discussion 869–70
33. Erenoğlu C, Miller A, Schirmer B. Laparoscopic Toupet versus Nissen fundoplication for the treatment of gastroesophageal reflux disease. Int Surg. 2003;88(4):219–25.
34. Segol P, Hay JM, Pottier D. Surgical treatment of gastroesophageal reflux: which operation to choose: Nissen, Toupet or Lortat-Jacob? A multicenter randomized trial. GastroenterolClin Biol. 1989;13(11):873–9.
35. Herbella FA, Tedesco P, Nipomnick I, et al. Effect of partial and total laparoscopic fundoplication on esophageal body motility. Surg Endosc. 2007;21(2):285–8.
36. Rossetti M, Hell K. Fundoplication for the treatment of gastroesophageal reflux in hiatal hernia. World J Surg. 1977;1:43.
37. Chysos F, Tzortzinis A, Tsiaoussis J, et al. Prospective randomized trial comparing Nissen to Nissen-Rosseti technique for laparoscopic fundoplication. Am J Surg. 2001;182(3):215–21.

38. Watson DI, Jamieson GG, Devitt PG, et al. Changing strategies in the performance of laparoscopic Nissen fundoplication as a result of experience with 230 operations. Surg Endosc. 1995;9(9):961–6.
39. Hunter JG, Swanstrom L, Waring JP. Dysphagia after laparoscopic antireflux surgery. The impact of operative technique. Ann Surg. 1996;224(1):51–7.
40. Soper NJ, Dunnegan D. Antomic fundoplication failure after laparoscopic antireflux surgery. Ann Surg. 1999;229(5):669–77.
41. Perez AR, Moncure AC. Obesity adversely affects the outcome of antireflux operations. SurgEndosc. 2001;15(9):986–5.
42. Farah JF, Grande JC, Goldenberg A, et al. Randomized trial of total fundoplication and fundal mobilization with or without divisor of short gastric vessels: a short-term clinical evaluation. Acta Cir Bras. 2007;22(6):422–39.
43. Donahue PE, Larson GM, Stewardson RH, et al. "Floppy" Nissen fundoplication. Rev Surg. 1977;34:223–4.
44. Donahue PE, Samelson S, Nyhus LM, Bobeck T. The floppy Nissen fundoplication: effective long-term control of pathologic reflux. Arch Surg. 1985;120:663–8.
45. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg. 1986;204(1):9–20.
46. Dallemagne B, Weents JM, Jehaes C, et al. Laparoscopic Nissen fundoplication: preliminary report. Surg Laparosc Endosc. 1991;1(3):138–43.
47. Davis CS, Baldea JR, Johns JR, et al. The evolution and long-term results of laparoscopic antirefluz surgery for the treatment of gastroesphageal reflux disease. JSLS. 2010;14(3):332–41.
48. Herbella FA, Oliveira DR, Del Grande JC. Eponyms in esophageal surgery. Dis Esophagus. 2004;17(1):1–9.
49. Watson TJ, Peters JH. Lower esophageal sphincter injections for the treatment of gastroesophageal reflux disease. Thorac Surg Clin. 2005;15(3):405–15.
50. Lo W-K, Mashimo H. Critical assessment of endoscopic techniques for gastroesophageal reflux disease. J Clin Gastroent. 2015;49(9):720–4.
51. Catarci M, Gentileschi P, Papi C, et al. Evidence-based appraisal of antireflux surgery. Ann Surg. 1996;224(1):51–7.

Clinical and Diagnostic Evaluation of GERD

13

Francisco Schlottmann, Martín Galvarini, and Marco G. Patti

Introduction

Gastroesophageal reflux disease (GERD) affects approximately 20% of the population in the United States, and its prevalence is increasing worldwide, mostly due to the epidemic of obesity [1]. The economic impact of this disease is remarkable, with direct healthcare costs of approximately $10 billion per year, being proton-pump inhibitors (PPI) the largest contributors of these expenses (nearly $6 billion) [2, 3].

Patients with GERD may present with a wide variety of symptoms. The Montréal classification was created in 2006 to provide a diagnostic standardization of the symptomatology of the disease [4]. This classification defined GERD as "a condition resulting from reflux of stomach contents and causing troublesome symptoms or complications, occurring at least 2 times per week, with an adverse effect on an individual's well-being." The consensus group stated that GERD might present with typical or "*esophageal*" symptoms (heartburn, regurgitation, and dysphagia) and atypical or "*extraesophageal*" symptoms (such as chronic cough, laryngitis, hoarseness, or even asthma).

Due to the complex clinical manifestations of GERD, the diagnostic evaluation of patients with suspected GERD should include multiple tests. The Esophageal Diagnostic Advisory Panel (multidisciplinary team of experienced gastroenterologists and surgeons) achieved a consensus on the optimal preoperative evaluation for patients with GERD, indicating that upper endoscopy, barium esophagram, esophageal manometry, and pH monitoring are always required before surgery. The panel also recommended that a gastric emptying study and combined multichannel impedance pH (MII-pH) should be performed in selected patients [5].

Clinical Findings

Heartburn, regurgitation, and dysphagia are considered *typical esophageal* symptoms of the disease. GERD can also cause *atypical or extra-esophageal* symptoms such as cough, wheezing, chest pain, hoarseness, and dental erosions. Two

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Galvarini
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

M. G. Patti
Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_13

Table 13.1 Gastroesophageal reflux disease esophageal and extraesophageal symptoms

Gastroesophageal reflux disease symptoms	
Esophageal	Heartburn
	Regurgitation
	Dysphagia
Gastric	Bloating
	Early satiety
	Belching
	Nausea
Pulmonary	Aspiration
	Dyspnea
	Wheezing
	Cough
	Asthma
Ears-nose-throat	Globus
	Hoarseness
Cardiac	Chest pain

mechanisms have been postulated for GERD-induced respiratory symptoms: (1) a vagal reflex arc resulting in bronchoconstriction and (2) microaspiration into the tracheobronchial tree. Hoarseness and dental erosions are instead secondary to the upward extent of the acid with direct damage of the vocal cords or teeth (Table 13.1).

The clinical evaluation should also investigate the effect of antireflux medications on symptoms relief. In fact, a good response to therapy with proton-pump inhibitors (PPI) is a good predictor of both the presence of abnormal reflux and success after antireflux surgery [6–8].

A diagnosis of GERD based only on symptoms is wrong in many patients because clinical findings are neither sensitive nor specific, and there is considerable overlap with other gastrointestinal disorders [9]. For instance, Patti and colleagues [10] showed that after performing pH monitoring in 822 patients referred for antireflux surgery with the diagnosis of GERD based on symptom evaluation, 247 (30%) had a normal reflux score. Thus, objective esophageal testing is mandatory to document the presence of GERD, particularly when surgical treatment is considered.

Diagnostic Evaluation

Patients with suspected GERD should be evaluated with upper endoscopy, barium swallow, esophageal manometry, and ambulatory pH monitoring. A gastric emptying study and combined multichannel impedance pH may be needed in selected cases.

Upper Endoscopy

An upper endoscopy is often the first test performed in patients with suspected GERD. However, around 50–60% of patients with abnormal reflux evidenced by pH monitoring do not have any evidence of mucosal damage [11, 12]. A diagnosis of erosive reflux esophagitis is established when there are patchy, striated, or circular and confluent epithelial defects (erosions) in the mucosa in the distal esophagus.

The Los Angeles (LA) classification is the most validated classification system for esophagitis (Table 13.2). LA grade A refers to one or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds (Fig. 13.1). LA grade B refers to one or more mucosal breaks more than 5 mm long that does not extend between the tops of two mucosal folds (Fig. 13.2). LA grade C is defined by one or

Table 13.2 Los Angeles classification system for esophagitis

Los Angeles classification	
Grade A	Mucosal breaks ≤5 mm long, none of which extends between the tops of the mucosal folds
Grade B	Mucosal breaks >5 mm long, none of which extends between the tops of two mucosal folds
Grade C	Mucosal breaks that extend between the tops of ≥2 mucosal folds, but which involve <75% of the esophageal circumference
Grade D	Mucosal breaks which involve ≥75% of the esophageal circumference

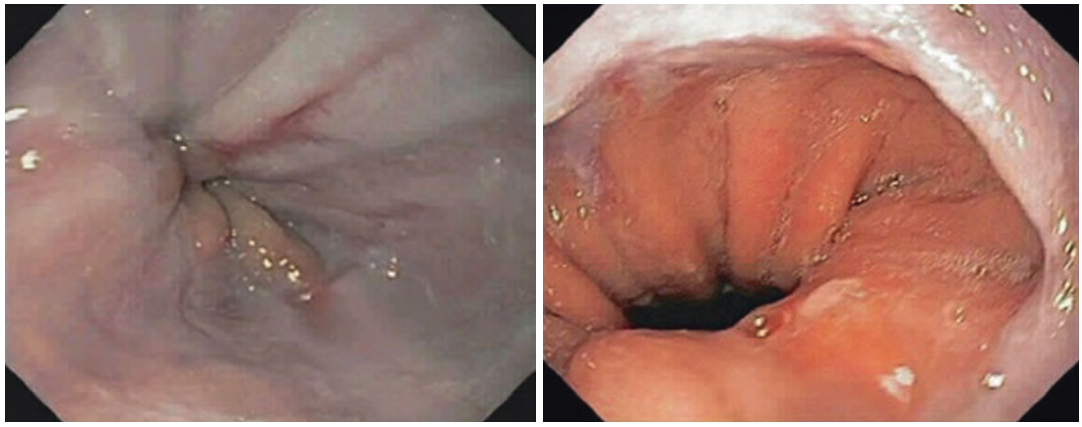


Fig. 13.1 LA grade A: one or more mucosal breaks no longer than 5 mm, not bridging the tops of mucosal folds

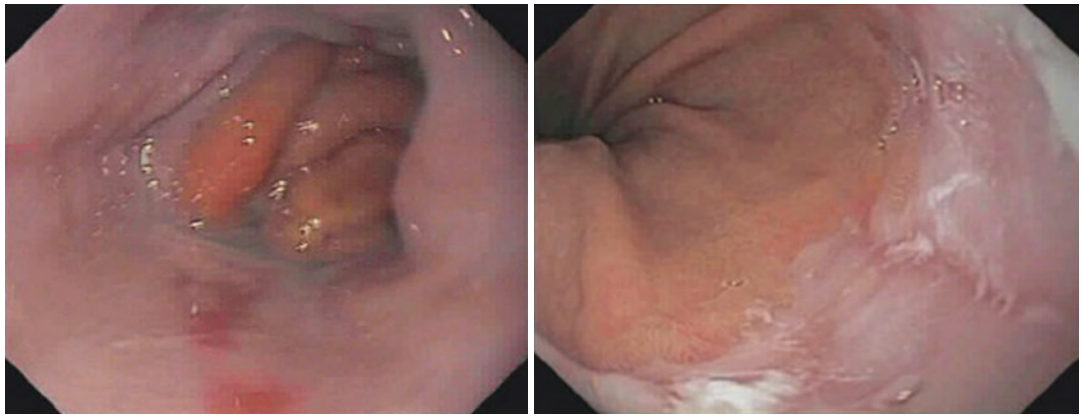


Fig. 13.2 LA grade B: one or more mucosal breaks more than 5 mm long that does not extend between the tops of two mucosal folds

more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference (Fig. 13.3). LA grade D is defined by one or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference (Fig. 13.4). Unfortunately, particularly for low-grade esophagitis, a high interobserver variability has been shown for the determination of the LA grade [13].

The endoscopy is also useful for diagnosing complications of GERD such as Barrett's esophagus and/or strictures. In addition, this study is valuable for excluding other pathologies such as eosinophilic esophagitis, gastritis, peptic ulcer, and cancer.

Barium Swallow

The barium swallow test has no diagnostic role per se because the presence of gastroesophageal reflux during the test does not correlate with the pH monitoring data. For instance, a previous study demonstrated the absence of any radiological sign of reflux in 53% of patients with GERD confirmed by ambulatory 24-hour pH monitoring [14].

Although this test does not provide objective evidence of GERD, it has a great value in preoperative planning because it gives information about different anatomic variables (i.e., presence and degree of esophageal shortening, diverticulum, stricture, or hiatal hernia). In particular, the

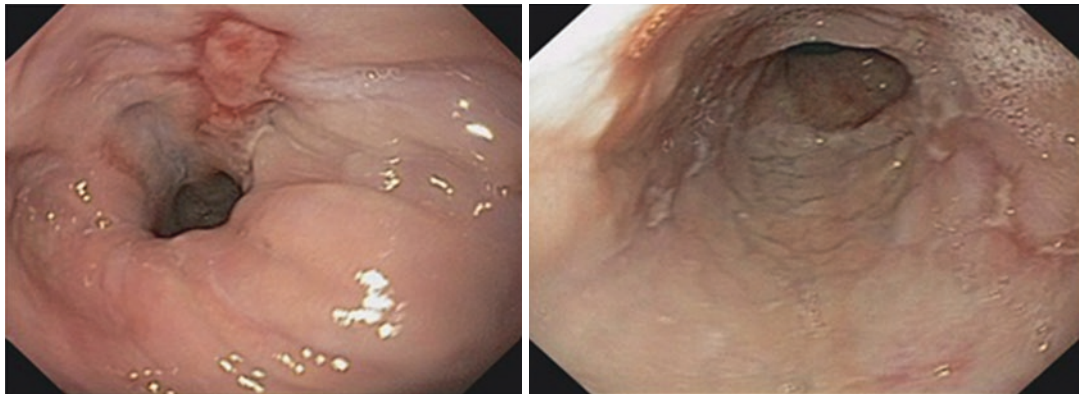


Fig. 13.3 LA grade C: one or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference

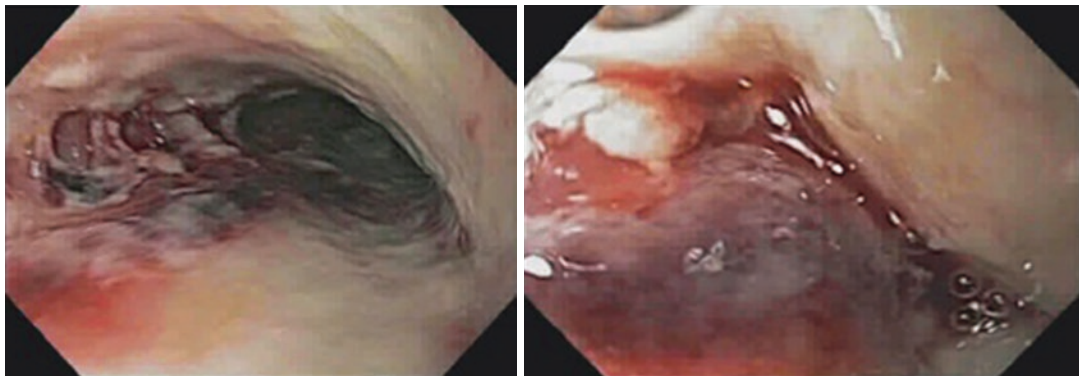


Fig. 13.4 LA grade D: one or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference

ability to distinguish between a type I sliding hiatal hernia and a type III paraesophageal hernia has implications for the complexity of the operation.

Esophageal Manometry

The esophageal manometry has limited valued for the diagnosis of GERD. However, it plays an important role during the evaluation of a patient with suspected GERD. First, the manometry is necessary for the correct placement of the pH monitoring probe (5 cm above the upper border of the lower esophageal sphincter). Second, it can rule out primary esophageal motility disorders (mainly achalasia) that present with similar symptoms to those with GERD. Finally, most surgeons will tailor the degree of fundoplication (total vs. partial) based on the peristaltic coordination and contractile force of the esophageal body (Fig.13.5).

Ambulatory pH Monitoring

The ambulatory pH monitoring provides objective evidence of abnormal reflux and is considered the gold standard for the diagnosis of GERD. This test should be performed: (1) in patients with persistent symptoms on PPI or in those who complain of symptoms without endoscopic evidence of esophagitis; (2) in patients who relapse after discontinuation of medical therapy; (3) before an antireflux

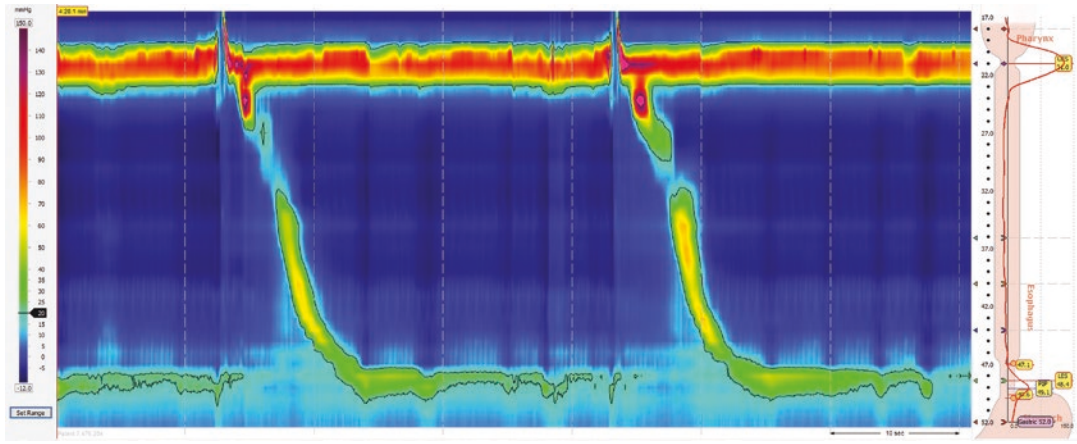


Fig. 13.5 High-resolution manometry showing normal peristalsis. (Reused with permission © Springer Nature [23])

operation; or (4) when evaluating atypical symptoms such as cough, hoarseness, and chest pain.

Acid-suppression medications should be discontinued on patients undergoing this test (H2 blocking agents for 3 days and PPIs for 7 days before the test) [15]. Diet and exercise are unrestricted during the test in order to mimic a typical day of the patient's life. The DeMeester score is a composite score calculated by points attributed to each standard deviation above the reference value for six parameters evaluated and has been used since 1970s to categorize patients as GERD + or GERD - by pH monitoring (Table 13.3) [16]. The temporal correlation between patients' symptoms and reflux events (a given symptom is considered associated with a reflux event if it occurs within the 2-minute interval after the reflux event) is also important and can be established by either the symptom index or the symptom association probability [17, 18].

Table 13.3 Ambulatory pH monitoring normal values

Normal values for 24-hour pH monitoring	
Percentage of total time pH < 4.0	4.5%
Percentage of upright time pH < 4.0	8.4%
Percentage of supine time pH < 4.0	3.5%
Number of episodes of reflux	47
Number of episodes >5 minutes	3.5
Longest episode (minutes)	20
DeMeester score[a]	14.7

[a]The DeMeester score is a composite score calculated by points attributed to each standard deviation above the reference value for the six parameters evaluated

The pH monitoring can be performed by either a transnasal catheter placement (5 cm above the manometrically determined lower esophageal sphincter) for *24 hours* or an endoscopically placed BRAVO wireless capsule (6 cm above the squamocolumnar junction) which collects pH data for *48 hours*. Both conventional pH monitoring and wireless 48-h pH monitoring represent valid diagnostic methods for GERD, and centers should select the study based on their clinical experience and expertise [19].

Esophageal pH testing can also be combined with *impedance* to detect any type of reflux event (acid, weakly acidic, or nonacidic). This study may have particular value in patients who are refractory or unresponsive to PPI therapy [20, 21]. However, impedance testing is prone to interpretation error and the role of antireflux surgery in patients with abnormal non-acid reflux on acid suppression remains unclear (Fig. 13.6) [22].

Gastric Emptying Study

Gastroparesis may be associated with GERD in a very small percentage of patients. Therefore, this

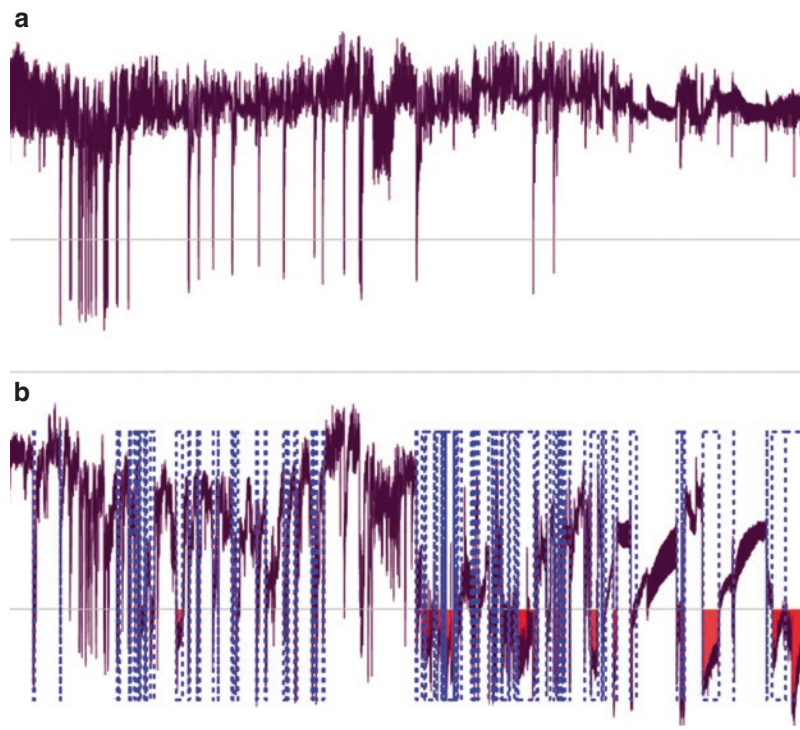


Fig. 13.6 24-h pH monitoring. (**a**) Normal results; (**b**) abnormal results

study should not be performed routinely during the evaluation of patients with GERD in preparation for antireflux surgery but should be rather indicated in selected cases: patients with nausea and postprandial bloating, patients with evidence of food in the stomach despite an overnight fast, and patients with other risk factors such as diabetes and chronic opiate use.

Conclusions

Patients with GERD may present with a wide variety of symptoms. Clinical findings are not specific and there is considerable overlap with other gastrointestinal disorders. Therefore, an extensive diagnostic workup that includes upper endoscopy, barium swallow, esophageal manometry, and ambulatory pH monitoring is needed for patients with suspected GERD planning to undergo antireflux surgery.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. El-Serag HN, Sweet S, Winchester CC, et al. Update on the epidemiology of gastro-esophageal reflux disease: a systematic review. Gut. 2014;63:871–80.
2. Sandler RS, Everhart JE, Donowitz M, et al. The burden of selected digestive diseases in the United States. Gastroenterology. 2002;122:1500–11.
3. Shaheen NJ, Hansen RA, Morgan DR, et al. The burden of gastrointestinal and liver diseases, 2006. Am J Gastroenterol. 2006;101(9):2128–38.
4. Vakil N, van Zanten SV, Kahrilas P, Dent K, Jones R, Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am J Gastroenterol. 2006;101(8):1900–20.
5. Jobe BA, Richter JE, Hoppo T, et al. Preoperative diagnostic workup before antireflux surgery: an evidence and experience-based consensus of the Esophageal Diagnostic Advisory Panel. J Am Coll Surg. 2013;217(4):586–97.
6. Campos GM, Peters JH, DeMeester TR, et al. Multivariate analysis of factors predicting outcome after laparoscopic Nissen fundoplication. J Gastrointest Surg. 1999;3(3):292–300.
7. Morgenthal CB, Lin E, Shane MD, et al. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. Surg Endosc. 2007;21:1978–84.

8. Schlottmann F, Herbella FA, Allaix ME, et al. Surgical treatment of gastroesophageal reflux disease. World J Surg. 2017;41(7):1685–90.
9. Gerson LB, Kahrilas PJ, Fass R. Insights into gastroesophageal reflux diseases-associated dyspeptic symptoms. Clin Gastroenterol Hepatol. 2011;9:824–33.
10. Patti MG, Diener U, Tamburini A, et al. Role of esophageal function tests in diagnosis of gastroesophageal reflux disease. Dig Dis Sci. 2001;46(3):597–602.
11. Sonnenberg A, Delcò F, El-Serag HB. Empirical therapy versus diagnostic tests in gastroesophageal reflux disease: a medical decision analysis. Dig Dis Sci. 1998;43(5):1001–8.
12. Ates F, Vaezi MF. New approaches to management of PPI-refractory gastroesophageal reflux disease. Curr Treat Options Gastroenterol. 2014;12(1):18–33.
13. Nasseri-Moghaddam S, Razjouyan H, Nouraei M, et al. Inter and intra-observer variability of the Los Angeles classification: a reassessment. Arch Iran Med. 2007;10:48–53.
14. Bello B, Zoccali M, Gullo R, et al. Gastroesophageal reflux disease and antireflux surgery-what is the proper preoperative work-up? J Gastrointest Surg. 2013;17(1):14–20.
15. Hirano I, Richter JE, Practice Parameters Committee of the American College of Gastroenterology. ACG practice guidelines: esophageal reflux testing. Am J Gastroenterol. 2007;102(3):668–85.
16. Neto RML, Herbella FAM, Schlottmann F, et al. Does DeMeester score still define GERD? Dis Esophagus. 2019;32(5):doy118.
17. Wiener GJ, Morgan TM, Cooper JB, et al. Ambulatory 24-hour esophageal ph monitoring. Reproducibility and variability of ph parameters. Dig Dis Sci. 1988;33:1127–33.
18. Weusten BL, Roelofs JM, Akkermans LM, et al. The symptom-association probability: an improved method for symptom analysis of 24-hour esophageal ph data. Gastroenterology. 1994;107:1741–5.
19. Schlottmann F, Andolfi C, Herbella FA, et al. GERD: presence and size of hiatal hernia influence clinical presentation, esophageal function, reflux profile, and degree of mucosal injury. Am Surg. 2018;84(6):978–82.
20. Agrawal A, Castell DO. Clinical importance of impedance measurements. J Clin Gastroenterol. 2008;42:579–83.
21. Vela MF. Non-acid reflux: detection by multichannel intraluminal impedance and ph, clinical significance and management. Am J Gastroenterol. 2009;104:277–80.
22. Francis DO, Goutte M, Slaughter JC, et al. Traditional reflux parameters and not impedance monitoring predict outcome after fundoplication in extraesophageal reflux. Laryngoscope. 2011;121:1902–9.
23. Allaix ME, Borraez BA, Patti MG. Gastroesophageal reflux disease: diagnostic evaluation. In: Fisichella PM, Allaix ME, Morino M, Patti MG, editors. Esophageal disease. New York: Springer Nature; 2014. p. 53–67.

Medical Treatment of GERD

14

Charles Muller, Natalie Tapaskar, and Robert T. Kavitt

Lifestyle Modification

Lifestyle modifications are considered first line for treatment of gastroesophageal reflux disease (GERD). The abnormal reflux of acidic gastric secretions beyond the lower esophageal sphincter (LES) into the esophagus is responsible for the symptoms and mucosal injury associated with GERD. Avoidance of certain foods or behaviors that facilitate the pathologic reflux of gastric contents to the esophagus and symptoms of acid exposure have therefore traditionally been recommended for patients with GERD [1–4]. These recommendations can be grouped into three categories: avoidance of foods that precipitate reflux (coffee, chocolate, peppermint, alcohol, fatty foods), avoidance of spicy or acidic foods that cause heartburn (citrus, tomatoes), and adoption of behaviors that promote LES integrity to prevent esophageal acid exposure (smoking cessation, avoidance of recumbent position for 2–3 hours after meals, raising head of bed, and weight loss).

Although studies have demonstrated the ability of such lifestyle modifications to improve physiologic parameters of GERD (e.g., LES tone, esophageal pH), data supporting the ability of such interventions to improve symptoms or other measurable disease endpoints are lacking. A systematic review of dietary and lifestyle modifications for GERD demonstrated that there is little evidence to support the notion that cessation of alcohol, smoking, chocolate, coffee, or acidic foods results in improvement of GERD [5], despite studies demonstrating the influence of these substances on LES pressure [6–13] or esophageal pH [14–19]. In spite of the fact that the recommendations for dietary and substance avoidance are based on observational evidence without proven improvements in GERD outcomes, a subset of patients receive symptomatic benefit from such interventions. It is therefore recommended that association between dietary exposures and symptoms be explored with consideration of trigger avoidance.

Postprandial recumbency is thought to promote esophageal acid exposure through decreased gravity-mediated acid clearance. This principle guides the recommendations to raise the head of the bed and to avoid eating for 2–3 hours before sleeping. Head-of-bed elevation by 6–8 inches with foam wedges or blocks has been shown in

C. Muller
Department of Medicine, Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago, Chicago, IL, USA

N. Tapaskar
Department of Medicine, University of Chicago, Chicago, IL, USA

R. T. Kavitt (✉)
Center for Esophageal Diseases, Department of Medicine, Section of Gastroenterology, Hepatology, and Nutrition, University of Chicago, Chicago, IL, USA

University of Chicago Medicine, Chicago, IL, USA
e-mail: rkavitt@bsd.uchicago.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_14

several RCTs to improve esophageal acid exposure [20, 21], reduce symptoms [7], and heal esophagitis in patients with GERD [22]. Data regarding late evening meals has been conflicting. Whereas one study demonstrated lower intragastric nocturnal pH in healthy patients following a late evening meal [23], a study of patients with GERD showed that timing of evening meal had no impact on esophageal pH or symptoms of reflux [24].

Obesity contributes to the development of GERD via multiple mechanisms, including increased gastroesophageal pressure gradient, increased incidence of hiatal hernia, and attenuated integrity of the esophagogastric junction [25]. Multiple large observational studies have demonstrated a dose-dependent relationship between BMI and GERD symptoms and complications [26–28]. Weight loss has been shown to have beneficial effects on LES function and esophageal acid exposure [29–31]. A large case-control study further demonstrated a reduction in GERD symptoms by up to 40% with significant loss of weight [26]. Although earlier prospective studies on the effects of weight loss on GERD symptoms have produced conflicting results [32, 33], more recent data suggest that weight loss is efficacious [34]. Despite the mixed results of well-designed prospective studies, weight loss remains a promising therapeutic option and continues to be recommended for overweight patients with GERD [4].

Non-Proton Pump Inhibitor-Based Medical Therapy

Nonabsorbable agents

Antacids

Antacids are over-the-counter medications typically utilized for temporary relief of episodic mild GERD symptoms that occur less than once a week [35]. They are inorganic salts with wide variability in their chemical composition consisting of aluminum, calcium, magnesium, and/or sodium. They were traditionally believed to partially neutralize gastric hydrochloric acid. However, recent data has challenged this mechanism and demonstrates that some antacids exert more of an effect on raising esophageal rather than gastric pH [36–38]. Calcium carbonate formulations are the most potent followed by sodium bicarbonate, then magnesium, and lastly aluminum salts (Table 14.1) [39].

Studies comparing the different methods of delivery of antacids demonstrate that antacid chewing gums provider faster and more prolonged symptom relief and pH control than chewable tabs and liquids, respectively. This may be because chewable tabs remain in the mouth longer and expose the esophagus to numerous smaller boluses of antacid over a longer time period than do liquids [38, 40, 41]. While antacids have rapid onset, their effect is short acting, and because they do not significantly alter gastric pH, they do not prevent subsequent reflux episodes from exposing the esophagus to caustic gastric acids.

Limited data exists comparing antacids to other medications. Two studies evaluated the effect of antacids on healing rates of esophagitis and found no improvement compared to placebo [2, 42–44]. Two studies found an improvement in symptoms with antacids compared to placebo, though this was only significant in one study [2, 42, 43]. Three studies have compared cimetidine 1200 mg/day [45, 46] or ranitidine 300 mg/day [47] with antacids for 6 and 12 weeks. It was found that the symptomatic response was equivalent or better with H2Ras; however, this was significant in only one study [45].

Antacids are generally well tolerated, with adverse effects being of greater significance with higher doses and prolonged use. Antacids have many potential drug interactions, some of which are outlined in Table 14.2. Overall antacids have little effect on healing erosive esophagitis but are likely nearly as effective as H2RAs. For patients with milder disease, antacids are likely more effective than placebo and, because of their rapid onset, may be useful to those with milder symptoms or for use as breakthrough relief while on a PPI or H2RA.

Table 14.1 Characteristics of non-PPI GERD therapy [39]

Drug	Mechanism	Acid-neutralizing capacity (mEq/15 mL of commercial product)	Dosage	Adverse reactions
Antacids				
Aluminum hydroxide	Neutralizes hydrochloride in the stomach to form Al $(Cl)_3$ salt + H_2O, resulting in increased gastric pH and inhibition of pepsin activity	29	640 mg five to six times daily after meals and at bedtime (maximum, 3840 mg in 24 hours)	Constipation Significant aluminum retention may occur in renal failure causing neurotoxicity
Calcium Carbonate	Neutralize gastric acidity resulting in increased gastric and duodenal bulb pH; inhibit proteolytic activity of pepsin if the pH is increased >4 and increase lower esophageal sphincter tone	58	One to four tabs as needed; (maximum, 8000 mg in 24 hours	Milk alkali syndrome is a rare complication of excessive calcium carbonate antacid intake along with other calcium containing compounds
Magnesium hydroxide	Reacts with gastric hydrochloric acid producing magnesium chloride and water raising pH	35	311 mg/tab: two to four tabs every 4 hours (maximum, 1244 mg in 24 hours)	Diarrhea Use with extreme caution in patients with myasthenia gravis or other neuromuscular disease as may exacerbate muscle weakness Significant magnesium retention may occur in renal failure leading to hypermagnesemia
Magnesium oxide	Reacts with gastric hydrochloric acid producing magnesium chloride and water raising pH	8–20	400 mg/tab: one tab twice a day (maximum, 800 mg in 24 hours)	
Sodium bicarbonate	Dissociates to provide bicarbonate ion which neutralizes hydrogen ion concentration and raises blood and urinary pH	17	325 mg – 2 g tabs (maximum, one to four tabs in 24 hours)	When taken with calcium in excess, may lead to milk-alkali syndrome Significant sodium retention may occur in renal failure
Alginate: aluminum hydroxide/magnesium carbonate/alginate	Viscous gel formation of near-neutral pH within minutes of contacting gastric acid triggering sodium bicarbonate in the formulation to release carbon dioxide, which becomes trapped in the alginate gel, causing it to float to the top of the gastric contents		Aluminum hydroxide 160 mg/ magnesium carbonate 105 mg; 2–4 tabs 4 times daily (maximum, 16 tabs per 24 hours)	Significant aluminum retention may occur in renal failure causing neurotoxicity Constipation Some dosage forms may contain benzyl alcohol which may cause fatal toxicity in neonates taking large doses

(continued)

Table 14.1 (continued)

Drug	Mechanism	Acid-neutralizing capacity (mEq/15 mL of commercial product)	Dosage	Adverse reactions
Baclofen	Selective GABA(B) receptor agonist Inhibits the transmission of monosynaptic and polysynaptic reflexes at the spinal cord level, resulting in relief of muscle spasticity		Initial: 5 mg three times daily. Increase by 5 mg per dose every 3 days until optimal response is reached. Usual dosage range: 40 to 80 mg daily. (maximum, 80 mg per 24 hours)	Crosses the blood–brain barrier: Somnolence Confusion Dizziness Drowsiness Headache Nausea, vomiting

Alginate

An alternative method to managing GERD is to impede the flow of acidic refluxate. The acid pocket is an area of relatively unbuffered highly acidic material localized to the proximal stomach postprandially. Alginates are natural polysaccharide polymers that create a mechanical barrier to acid reflux. In the presence of gastric acid, they precipitate into a viscous gel of near-neutral pH and form a raft that floats within the stomach and displace the postprandial acid pocket away from the gastroesophageal junction. This mechanical barrier reduces reflux for up to 4 hours after ingestion [2, 48]. A 2017 meta-analysis of alginate-based therapy compared to placebo, antacids, H2RAs, and PPIs included 14 randomized controlled trials and demonstrated that alginate therapy was favored over placebo and antacids in resolution of symptoms in those with nonerosive GERD [48]. There was a trend toward alginates being less effective at symptom control than H2RAs and PPI therapy, but this was not statistically significant [48].

Alginate–antacid formulations can have variable compositions Table 14.1. Alginates should be considered as an alternative to other antacids in patients with infrequent, mild symptoms, especially if they occur predominantly postprandially. They can also be considered as adjunctive therapy for those on maintenance PPIs [49].

Sucralfate

The use of sucralfate is discussed later in this chapter in the section "Management of GERD in Pregnancy."

Inhibitors of Transient Lower Esophageal Sphincter Relaxations (TLESRs)

Baclofen

Persistent GERD symptoms in patients on PPI maintenance therapy may be due to ongoing weakly acidic or alkaline reflux, in which further reduction of symptoms is unlikely to occur with increased gastric acid suppression [2, 50]. Inhibiting TLESRs via neurotransmitters and receptors such as gamma-aminobutyric acid (GABA), nitric oxide, cholecystokinin, and metabotropic glutamate receptor 5 (mGluR5) may improve symptoms. Thus far, GABA and mGluR5 are considered the dominant signaling pathways, but baclofen (a GABA-B agonist) is the only medication that has demonstrated efficacy in reducing TLESRs and reflux [2, 51].

A meta-analysis of nine randomized controlled trials comparing baclofen to placebo concluded that baclofen reduced the number of reflux episodes, average length of episodes, and the incidence of TLESRs [52]. Small uncontrolled trials have demonstrated a benefit for baclofen

when used for refractory duodenal reflux in patients with ongoing symptoms on PPI therapy [53]. The use of baclofen three times a day before meals may be considered as an adjunct for patients with persistent symptoms on PPI therapy. Pharmacokinetics and adverse reactions are noted in Tables 14.1 and 14.2.

Antisecretory Agents

Histamine-2 Receptor Blockers (H2RAs)

H2RAs slow gastric acid production by competitively and reversibly binding to H2 receptors on gastric parietal cells. Compared to antacids, H2RAs have a slower onset of action (reaching

Table 14.2 Drug interactions related to the use of antacids and drug interactions

Drug	Antacid drug interaction (effect on drug in first column)	Mechanism
Aspirin (enteric coated)	Increased rate of absorption	Enhanced drug release from dosage form
Beta blockers		
Atenolol	Decreased bioavailability and prolonged half-life (Ca-containing antacids)	Unknown
Metoprolol	Increased bioavailability (Mg- and Al-containing antacids)	Unknown
Propranolol	Decreased bioavailability and rate of absorption (aluminum hydroxide containing antacids)	Decreased rate of gastric emptying
Corticosteroids (prednisone, dexamethasone)	Decreased absorption	Unknown, adsorption suspected
Digoxin	Decreased absorption	Adsorption and faster gastric emptying
Indomethacin	Decreased bioavailability	Increased gastric pH resulting in increased ionized indomethacin and less absorption
Ketoconazole	Decreased bioavailability	Increased gastric pH resulting in decreased dissolution in the stomach
Levodopa	Decreased breakdown in the stomach, with increased absorption	Increased gastric emptying rate
Lithium	Decreased serum concentrations with sodium bicarbonate	Alkalization of the urine enhances renal clearance
Methotrexate	Decreased effect with sodium bicarbonate	Alkalization of the urine enhances renal clearance
Phenytoin	Decreased absorption	Unknown
Salicylates	Decreased serum concentrations due to decreased urinary reabsorption	Increased urinary pH decreased urinary reabsorption
Sulfonylureas	Increased absorption with increased effect and possible hypoglycemia with Mg antacids	Unknown
Tetracycline	Decreased absorption of tetracycline (significant interaction)	Chelation
Drug	*Baclofen drug interaction (effect on drug in first column)*	
Azelastine	Enhances CNS depressant effect	
Bromperidol	Enhances CNS depressant effect	
Orphenadrine	Enhances CNS depressant effect	
Oxomemazine	Enhances CNS depressant effect	
Thalidomide	Enhances CNS depressant effect	

Related to the use of baclofen [39]

peak concentrations 1–3 hours after administration) but have a longer duration of action (up to 4–10 hours) [1, 38]. A single dose of H2RA can be effective for short-term heartburn relief but has limited efficacy in patients with erosive esophagitis and is inferior to PPIs in symptom relief and maintenance of symptom remission at 6 months [2]. Repeated use of H2RAs can also lead to tachyphylaxis. The mechanism of this tolerance is unclear but has been observed in both fasting and fed conditions. Increasing the dose of H2RA does not overcome the tolerance, and the effects persist for several days after discontinuation of H2RAs [38, 54].

Despite H2RAs' propensity for tolerance, they have been shown to be useful as short-term reflux relief and for PPI refractory nocturnal symptoms. Nocturnal acid breakthrough (NAB) occurs in more than 70% of patients on PPI therapy. Adding a bedtime H2RA to once or twice-daily PPI can reduce the percentage of NAB as well as improve reflux-associated sleep disturbance [55–58]. A recent meta-analysis comparing efficacy of different H2RAs showed that famotidine had the best short-term therapeutic benefit in GERD when compared to ranitidine, cimetidine, and nizatidine [59]. Pharmacokinetics and major drug interactions are listed in Tables 14.3, 14.4, and 14.5.

Table 14.3 Pharmacokinetics of H2RAs [1, 196]

	Cimetidine	Ranitidine	Nizatidine	Famotidine
Bioavailability (%)	80	50	70	40
Relative potency	1	5–10	5–10	32
Half-life (hours)	6	8	8	12
Time to peak concentration (hours)	1–2	1–3	1–3	1–3.5
Hepatic clearance (%)				
Oral	60	73	22	50–80
Intravenous	25–40	30	25	25–30
Renal clearance (%)				
Oral	40	27	57–65	25–30
Intravenous	50–80	50	75	65–80
Relative effect on P450 metabolism	1	0.1	0	0

Table 14.4 Dosing adjustments of H2Ras and adverse effects [1, 96]

	Creatinine clearance (mL/min)	Dose (mg/day)	Adverse effects
Cimetidine	>30	800	Gynecomastia, impotence, diarrhea, CNS: confusion, dizziness, agitation, headache[a]
	15–30	600	
	<15	400	
Ranitidine	>75	300	Gynecomastia, CNS: confusion, dizziness, agitation, headaches[a]
	30–75	225	
	15–30	150	
	<15	75	
Famotidine	>75	40	CNS: confusion, dizziness, agitation, headaches
	30–75	30	
	15–30	20	
	<15	10	
Nizatidine	>75	300	CNS: confusion, dizziness, agitation, headaches
	30–75	225	
	15–30	150	
	<15	75	

[a]Rare adverse reactions (<1%), hepatitis, pancytopenia, polymyositis, anaphylaxis; cardiac, AV block, QT prolongation, hypotension (with rapid infusion)

Table 14.5 Cimetidine drug interactions [196]

Drug	Effect of cimetidine		Mechanism
	serum concentration of drug	Clearance of drug (% decrease)	
Caffeine	Increased	31–42	Decreased demethylation
Carbamazepine	Increased	10–20	Decreased epoxidation
Desipramine	Increased	36	Decreased hydroxylation in rapid metabolizers
Ketoconazole	Decreased	No change	Decreased absorption due to elevation of gastric pH, slowing dissolution
Lidocaine	Increased	14–30	Decreased N-dealkylation
Metronidazole	Increased	29	Decreased hydroxylation
Nifedipine	Increased	38	Uncertain
Phenytoin	Increased	21–24	Decreased hydroxylation
Propranolol	Increased	20–27	Decreased hydroxylation
Procainamide	Increased	28	Competition for renal tubular secretion
Warfarin	Increased	23–36	Decreased hydroxylation

Proton Pump Inhibitor Therapy

History of PPIs

In the late 1960s, the pharmaceutical company Hassle (division of Astra) initiated a gastrointestinal research division with the aim of finding a drug for inhibition of gastric acid secretion for patients with peptic ulcer disease. The momentous recognition that the H^+/K^+ ATPase (proton pump) was the final step of acid secretion resulted in the development of the class of drugs knows as proton pump inhibitors (PPIs) [60]. In 1975, timoprazole was found to inhibit acid secretion irrespective of stimulus; however, it caused enlargement of the thyroid gland due to inhibition of iodine uptake. After multiple animal models and trials, a derivative of timoprazole, omeprazole, was discovered in 1979. Omeprazole was found to be the most potent inhibitor of gastric acid secretion in rats and dogs in vivo, with no effect on iodine uptake [61, 62]. An Investigational New Drug (IND) application was filed in 1980, and omeprazole was taken into human trials in 1982. Omeprazole was found to be superior to H2RAs for GERD symptoms [63] and duodenal [64] and gastric ulcers [65]; thus omeprazole was launched in Europe as Losec in 1988 and in the United States as Prilosec in 1990 [62].

Omeprazole had significant inter-individual variability dependent on rapidity of metabolism. In Western populations, about 2–4% of people lack 2C19, one of the P450 enzymes, which is important for metabolism of many drugs, including omeprazole [66]. Thus, Astra started a new research program in 1987 with the goal of finding an acid suppression compound with reduced clearance by the liver and increased bioavailability. Several hundred compounds were screened, and finally an isomer of omeprazole was found to exceed omeprazole, esomeprazole [62]. Since then, several additional PPIs have been introduced into the market.

Benefits of PPI Therapy in GERD

Via inhibition of the final step in acid secretion, PPIs are the most potent acid suppressants available. In a Cochrane Review of 34 trials with 1300 patients, PPIs were more effective than H2RAs in reducing heartburn symptoms in those treated empirically for GERD and in those with nonerosive reflux on endoscopy [67]. PPIs have also been shown to be more effective than H2RAs and placebo in healing of erosive esophagitis and reducing relapse rates [68, 69]. Meta-analyses have demonstrated PPI superiority in healing of all grades of erosive esophagitis when compared to H2RAs, sucralfate, and placebo [70]. Thus PPIs

are currently the first-line treatment of GERD [4] and are initiated for 8 weeks for symptom relief and healing of erosive esophagitis [4, 56].

Pharmacology of PPIs

As of 2015, the US Food and Drug Administration (FDA) had approved 6 PPIs: omeprazole, esomeprazole, lansoprazole, dexlansoprazole, pantoprazole, and rabeprazole (Table 14.6) [71]. All PPIs share a common structural motif. They accumulate selectively in the acid space (canaliculi) of the secreting gastric parietal cell, and within that space they undergo a conversion to permanent cations. These compounds bind to cysteine residues (cys 813 subunit) on the H^+/K^+ ATPase, thereby inhibiting acid secretion until replacement pumps are synthesized (up to 36 hours). All PPIs require accumulation and acid activation; thus their onset of action is delayed [1, 71].

PPIs are the most potent inhibitors of gastric acid secretion; however, they are most effective when parietal cells are stimulated in response to a meal. Thus, PPIs should only be taken before meals (30–60 minutes prior) and should not be used along with H2RAs or other antisecretory agents, as this will reduce the acid-inhibitory effect of PPIs [72]. PPIs are most effective after a prolonged fast when a large amount of inactive H^+/K^+ ATPase is present [1]. During meals, not all of the parietal cells or proton pumps are active. Thus, the PPI will only inhibit activated H^+/K^+ ATPase, and only two-thirds of proton pumps are inhibited by a single dose of PPI. As more inactive enzyme is recruited, acid secretion will continue (although reduced). Once-daily dosing of PPI results in 66% inhibition of acid after 5 days, while initial twice-daily dosing may be helpful to achieve more rapid inhibition of acid secretion in the first 2–3 days. Due to these properties, sporadic use of PPIs is not likely to be effective [1, 73].

Omeprazole

Omeprazole was the first PPI to be developed in the 1970s. It has the fastest onset of action at 1.5 to 3.5 hours but the shortest half-life of all the PPIs. It is metabolized almost entirely by CYP2C19, thereby offering the greatest potential for drug interactions (Tables 14.6 and 14.7) [71].

Table 14.6 Pharmacodynamics of commercially available PPIs in the United States [71]

	Omeprazole	Esomeprazole	Lansoprazole	Dexlansoprazole	Pantoprazole	Rabeprazole
Dose (mg)	10, 20, 40	20, 40	15, 30	30, 60	20, 40	20
Treatment of erosive or nonerosive GERD	20 or 40 mg daily or 20 mg twice daily	20 or 40 mg daily	30 mg daily or 30 mg twice daily	30 mg daily or 30 mg twice daily	40 mg daily or 40 mg twice daily	20 mg daily or 20 mg twice daily
IV Formulation	Yes	Yes	Yes	No	Yes	No
Liquid or suspension	No	Yes	Yes	No	Yes	No
Generic	Yes	Yes	Yes	No	Yes	Yes
Over the counter	Yes	Yes	Yes	No	No	No
Bioavailability (%)	30–40	64–90	80–85	–	77	52
Time to peak plasma level (tmax, hours)	0.5–3.5	1.5	1.7	1–2, 4–5	2–3	2–5
Half-life (hours)	0.5–1	1–1.5	1.6	1–2	1–1.9	1–2
Protein binding (%)	95	97	97	96	98	96.3
Primary excretion	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic	Hepatic
Liver metabolism	CYP2C19	CYP2C19	CYP2C19	CYP2C19, CYP3A4	CYP2C19, CYP3A4	CYP2C19

Table 14.7 PPI drug interaction [197–199]

	Omeprazole	Esomeprazole	Lansoprazole	Dexlansoprazole	Pantoprazole	Rabeprazole
Phenazone (antipyrine)	↓ Clearance		↑ Clearance		None	
Carbamazepine	↓ Clearance				↓ Clearance	
Citalopram	↓ Clearance					
Clopidogrel	↓ Absorption	↓ Absorption	None	None	None	
Diazepam	↓ Clearance	↓ Clearance	None		None	None
Digoxin	↑ Absorption			None	None	↑ Absorption
Etravirine	↓ Clearance					
HIV protease inhibitors	↓ Absorption		↓ Absorption			
Methotrexate	↓ Clearance					
Nifedipine	↑ Absorption ↓ Clearance				None	
Phenprocoumon	↓ Clearance					
Phenytoin	↓ Clearance	↓ Clearance	None	None	None	None
Tacrolimus			↓ Clearance		None	None
Theophylline			↑ Absorption	None		
Warfarin	↓ Clearance	↓ Clearance	None	None	None	None

Conventional PPIs are delayed release for their enteric coating and generally require several doses to achieve adequate acid suppression. To overcome this, efforts have been taken to develop novel PPI formulations with rapid onset, extended release, or longer half-life. Immediate-release (IR) omeprazole is administered at bedtime rather than before dinner to provide improved control of nocturnal reflux. The IR formulation is non-enteric coated and is combined with sodium bicarbonate to protect the PPI from acid degradation. IR omeprazole has a more rapid onset of antisecretory action without sacrificing the duration of acid suppression when compared with delayed release PPIs and is designed to decrease nocturnal acid breakthrough [71–74]. When compared to pantoprazole, esomeprazole, and lansoprazole, bedtime dosing of IR omeprazole provided faster control of nighttime gastric pH and acid breakthrough [75]. IR omeprazole also achieved better control of 24-hour intragastric acidity when compared to lansoprazole and pantoprazole [76]. However, despite its improved control of acidity in the stomach and esophagus when compared to delayed-release PPIs, this does not correspond to better symptom control for GERD. In multicenter randomized controlled trials, IR omeprazole has failed to show faster heartburn relief when compared to omeprazole [77].

Esomeprazole

Esomeprazole is an isomer of omeprazole that is available in intravenous, liquid, and IR formulations. It has a higher bioavailability than omeprazole (Table 14.6) [71]. Large meta-analyses demonstrate at 8 weeks a 5% relative increase in probability of healing erosive esophagitis with esomeprazole when compared to omeprazole, lansoprazole, and pantoprazole with an associated 8% relative increase in GERD symptom relief [78]. Many other analyses over the years have consistently concluded that esomeprazole 40 mg was the only PPI to have higher healing rates than omeprazole 20 mg [79–81]. However, the clinical relevance of these small differences remains unclear [4, 78].

Pantoprazole

Pantoprazole was the first PPI to be available in both oral and intravenous formulations. It was initially approved for the treatment and maintenance of erosive esophagitis (40 mg/day for 8–16 weeks), but later the intravenous formulation was approved for short-term treatment (7–10 days) of GERD patients with a history of erosive esophagitis (40 mg/day) who were unable to tolerate oral pantoprazole [82]. Compared to other PPIs, it is less likely to become activated in neutral to moderately acidic environments, thus preventing it from acting on other areas of the body and reducing adverse effects (Table 14.7) [83]. Pantoprazole has a longer duration of action than other PPIs because it binds two cysteine subunits of the H^+/K^+ ATPase (Table 14.6). Unlike other PPIs, the serum concentration is not dose-dependent; thus the concentration after one dose is similar to that after multiple doses [82].

When compared to esomeprazole 40 mg/day, pantoprazole 40 mg/day produced equivalent esophageal pH profiles [84]. Endoscopic healing rates at 4 and 8 weeks showed no difference among pantoprazole 40 mg/day, omeprazole 20 mg/day, and lansoprazole 30 mg/day [85]. However, patients taking pantoprazole 40 mg/day compared to esomeprazole 40 mg/day had less symptom relapse and fewer symptomatic episodes at 1 week [86]. Since pantoprazole is effective at controlling GERD symptoms and improving quality of life, there is interest in using it as on-demand therapy. This is not currently FDA approved but has been shown to be effective in mild GERD [87].

Rabeprazole

Rabeprazole is a prescription PPI with a slow onset of action (2–5 hours) and a short half-life (1–2 hours) (Table 14.6). Rabeprazole extended release (ER) was designed to prolong the effects by releasing a single delayed-release tablet and multiple pulsatile-release tablets in the intestine and colon separately, thereby achieving acid suppression over 24 hours. Once-daily rabeprazole-ER 50 mg showed longer acid suppressed time and better control of nocturnal acid suppression when compared to esomeprazole 40 mg in

healthy patients [88]. However, it failed to show superiority in healing esophagitis and heartburn symptoms compared to esomeprazole in patients with severe erosive esophagitis [89]. After this study, no further studies were performed to evaluate rabeprazole-ER, and the development of this drug seemed to be discontinued [56].

Lansoprazole

Lansoprazole is available in oral tablets, liquid suspensions, oral disintegrating tablets (LFDT), and intravenous forms. It has a relatively quick onset of action, increasing gastric pH to greater than four within 130 minutes (Table 14.6) [71–90]. When compared to omeprazole, lansoprazole-treated patients were less likely to experience daytime heartburn on the first day of therapy for erosive esophagitis [75].

Lansoprazole's primary formulation is an oral capsule that contains active granules, which can be removed from the capsule and mixed into foods and beverages as well as flushed through nasogastric tubes [91]. LFTD has the same pharmacological properties as lansoprazole capsules. LFTD offers increased flexibility as it can be taken with or without water and may be of use to special populations such as children, the elderly, and those with dysphagia [91].

Dexlansoprazole

Dexlansoprazole-modified release (MR) is a novel PPI with a longer half-life achieved by a dual delayed-release formulation. Because of the dual delayed-release nature, it reaches peak concentrations at 1–2 hours and 4–5 hours after administration (Table 14.6). It contains two types of granules in one capsule and provides two distinct drug release periods in the small intestine to improve the therapeutic time. In patients with nonerosive GERD, dexlansoprazole MR 30 mg was superior to esomeprazole 20 or 40 mg in symptom control [92]; however it has failed to provide better efficacy in healing esophagitis [93]. The advantage of using dexlansoprazole MR is in greater dosing flexibility without restriction to mealtime, its control of nocturnal symptoms [94, 95], and as a step-down therapy for patients taking twice-daily PPI [96]. It also has a greater affinity for CYP3A4 than CYP2C19, thereby making significant drug interactions less likely Table 14.7 [71].

Approach to GERD Therapy

The overall approach to selecting an initial agent for GERD remains relatively unclear. Both step-up and step-down approaches have been utilized. It is reasonable to utilize a step-up approach in patients with mild and intermittent symptoms without evidence of erosive esophagitis. Treatment may start with antacids/alginate along with H2RAs and increasing potency of therapy until symptom control is achieved, generally making changes every 2–4 weeks. If this is ineffective, initiation of daily PPI is recommended, and treatment is continued for 8 weeks once symptoms are controlled. Alternatively, patients with erosive esophagitis, frequent symptoms, or severe symptoms may benefit from initiating daily PPI for 8 weeks first and can be stepped down to H2RAs if symptoms are under control. Maintenance PPI therapy may be continued in those with severe erosive disease [97–99].

Selection of optimal dose of PPI is also a well-studied topic of interest. When assessing control of gastric pH as the model for PPI efficacy, PPIs show a dose response [100]. Over-the-counter (OTC) omeprazole 20.6 mg was superior to OTC lansoprazole 15 mg for maintaining gastric pH >4 [101]. However, esomeprazole 20 mg was no different than omeprazole 20 mg for maintenance of gastric pH >4 [102]. Overall, PPIs show significant differences in duration of gastric pH >4 across a range of doses, but do not show a difference at equivalent OTC (20 mg) doses [38]. Furthermore, while the differences in duration of gastric pH >4 can be correlated to relative healing rates for erosive esophagitis, there is no similar correlation with symptom control [38]. This is due to a dose ceiling effect at PPI doses of 20 mg. PPI doses less than or equal to 20 mg have a dose response, while doses greater than or equal to 20 mg fail to show consistent dose responsiveness [38, 103, 104]. Overall, when treating frequent

heartburn, a PPI dose of 20 mg is optimal, and while doses greater than 20 mg demonstrate differences in acid control, these are not predictive of superior clinical benefit [38].

Switching PPIs is common but has limited supporting data. One study demonstrated equal efficacy in switching patients from daily lansoprazole to daily esomeprazole or twice-daily lansoprazole [105]. A randomized control trial of patients on daily PPI showed 20% had symptomatic improvement by increasing to twice-daily PPI or switching to another PPI [106]. However, even on twice-daily PPI, nearly 10% of patients still have persistent symptoms [107]. Meta-analyses demonstrate no significant difference in efficacy among PPIs in symptom relief and healing of erosive esophagitis [56, 78, 81].

There is no universal method for discontinuing PPIs. In a prospective study analyzing the efficacy of step-down therapy, 117 patients on greater than single-dose PPI therapy were stepped down to single-dose PPI and were assessed for symptom recurrence for 6 months. Recurrent symptoms occurred in only 20.5% of patients and were more likely in patients that had used PPIs for a longer duration before the study [98]. Another study evaluated quality of life and symptom recurrence in patients after discontinuation of PPIs in 73 patients. At 1 year follow-up, 41% were asymptomatic off PPIs, 34% required H2RAs, 7% prokinetic agents, 1% both, and 15% remained asymptomatic without medication. Quality of life did not change after step-down therapy [97]. Other studies have demonstrated that full-dose PPI step-down therapy is superior both to H2RA therapy and low-dose PPI step-up strategy in regard to efficacy in symptom relief and cost-effectiveness [108, 109]. A multicenter study demonstrated an 80% success rate of step down from omeprazole 20 mg for 8 weeks to omeprazole 10 mg for an additional 6 months [99].

It is reasonable to gradually taper therapy in patients on PPIs for longer than 6 months. Tapering occurs until the patient is on the lowest dose for 1 week, and then discontinuation can be recommended [97, 110].

Drug Interactions

PPIs are rapidly metabolized in the liver, primary by CYPC219 with contribution from CYP3A4. Genetic variation has led to rapid and slow metabolizers, which may explain some differences in the response to PPIs [111]. Overall, the clinical significance of most interactions with PPIs is low, with some notable exceptions. Mechanisms involved in potential drug interactions include decreased bioavailability of other drugs that require an acidic gastric pH for dissolution and effects on cytochrome function (Table 14.7).

There is a potential for adverse effects from other medications when taken concomitantly with PPIs including risedronate (gastrointestinal effects), HIV protease inhibitors (drug resistance), levothyroxine (decreased absorption), clozapine (neutropenia and agranulocytosis), and mycophenolate (decreased absorption) [111].

In 2009, the FDA issued a warning regarding adverse cardiovascular effects with use of clopidogrel and omeprazole. Clopidogrel requires activation by CYP2C19, leading to the concern of decreased platelet aggregation in the presence of omeprazole. Two randomized controlled trials studying all PPIs except for dexlansoprazole have shown no increased risk for adverse cardiovascular events with simultaneous clopidogrel use [4, 112, 113].

Complication of PPI Therapy

Although PPIs are effective at treating the symptoms and complications of GERD and are generally well tolerated by patients, growing concern has arisen about the safety of long-term PPI therapy. Large epidemiologic studies have demonstrated associations between PPI use and kidney disease, cerebrovascular disease, myocardial infarction, osteoporosis, fracture risk, nutrient deficiencies, gastrointestinal malignancies, and numerous infections [114]. However, the majority of studies suggesting associations between PPIs and adverse outcomes are observational and limited by confounding variables, making causal-

ity difficult to prove. Available evidence on the long-term complications of PPI use is reviewed below.

PPIs have been thought to affect bone metabolism via pH-dependent reduction in calcium absorption and hypergastrinemia-mediated secondary hyperparathyroidism in addition to direct inhibition of osteoclast activity [115–117]. Numerous studies have demonstrated an association between PPI use and risk of bone fracture [118–123]. Two large meta-analyses have demonstrated a modest association between PPI use and hip or vertebral fracture [117, 124, 125]. In 2010, the FDA issued a warning regarding the risk for wrist, hip, and spine fracture with PPI use. Despite the theoretical deleterious effects of PPIs on bone strength and metabolism, multiple studies have failed to demonstrate an association between PPI use and loss of measurable bone density [119, 126–128]. Although it is possible that PPIs could negatively impact bone integrity through an alternative unmeasured mechanism, the studies associating their use with bone fracture have all been observational, and a causal effect has not yet been demonstrated. Moreover, existing studies have demonstrated the significant role of confounders on an outcome as complex as fracture risk [120, 123]. It is not currently recommended to routinely screen long-term PPI users for osteoporosis [129].

PPI use has also been linked to the development of both acute and chronic kidney disease. Several large population-based studies have demonstrated an association between PPI use and increased risk of development of chronic kidney disease (CKD), acute kidney injury, end-stage renal disease (ESRD), and acute interstitial nephritis (AIN) [130–133]. Moreover, these studies demonstrated a dose response with increased risk of CKD among patients with higher PPI doses [130] or longer cumulative exposure [131, 133]. Although no mechanism by which PPIs could be contributing to CKD has been identified, one theory is that recurrent AIN could contribute to progressive injury. Studies have shown a modestly increased risk of AIN with PPI use, but the onset of injury is varied and often more insidious than a typical immune-mediated drug toxicity [114, 134–136]. Some data further suggests that the association between PPI use and CKD persists even after controlling for AKI, disputing the notion that chronic renal injury with PPI use is AIN mediated [131]. Despite compelling data from a number of large studies, the association between PPIs and kidney disease is entirely based on observational data which is highly subject to confounding effects of unmeasured comorbidities among PPI users, making it difficult to draw firm conclusions about the risk of kidney disease with PPI use. Routine monitoring of renal function in patients taking PPIs is not recommended [129].

The bactericidal activity of gastric acid serves as one of the body's defenses against bacterial proliferation and entry of pathogenic bacteria. By raising the gastric pH, PPIs can promote small intestinal bacterial overgrowth (SIBO), a condition characterized by excess bacterial fermentation, inflammation, and occasionally malabsorption in the small bowel [137–139]. A strong association between PPI use and SIBO has been shown in two prospective studies and a large meta-analysis [139–141]. Although PPI use has been shown to contribute to objective measures of increased small bowel bacterial colonization, the association with development of symptomatic SIBO remains less clear and warrants further study.

PPI-induced hypochlorhydria is also theorized to promote *Clostridium difficile* infection (CDI). Although *C. difficile* spores are resistant to gastric acid [142], reduced gastric acidity is thought to allow for enhanced survival of the toxin-producing vegetative form of the bacteria. Moreover, PPIs have been shown to alter the makeup of the intestinal flora in such a way that could favor development of CDI [143, 144]. SIBO and its associated increased intestinal bile acid deconjugation may also promote conversion of *C. difficile* spores to the vegetative form. Although several observational studies have demonstrated a modest association between PPI use and CDI [145–148], other studies have shown no association when controlling for presence of comorbid conditions or antibiotic use [149, 150]. Given these inconsistencies, a causative associa-

tion between PPIs and CDI has yet to be demonstrated.

PPIs have long been thought to be a risk factor for development of community-acquired pneumonia (CAP), possibly via hypochlorhydria-induced micro-aspiration of gastric anaerobic bacteria or even altered neutrophil function [151]. Although several studies have shown an association between PPI use and CAP [152–154], others have either failed to show an association [155, 156] or have demonstrated that this risk is highest within the first 30 days of PPI initiation [157–159], increasing the likelihood that any observed association is due to confounding rather than a causative association.

PPI use has also been associated with dementia. Increased accumulation of neurotoxic beta amyloid proteins is felt to be a key step in the pathogenesis of Alzheimer's disease. Beta-amyloid accumulation may be enhanced by PPIs through their inhibition of V-type ATPases in microglial cells, which are important mediators of beta amyloid degradation. Supporting this hypothesis is the finding that lansoprazole has been found to result in increased production of beta-amyloid in the brains of mice [160]. Two large prospective observational studies have found that PPIs were modestly associated with development of dementia in elderly populations [161, 162]. Subsequent prospective studies, however, showed no increased risk of development of cognitive decline or Alzheimer's disease with PPI use [163, 164], highlighting the difficulty of drawing conclusions about harm from PPI use from observational studies of elderly patients or those with dementia, in whom the burden of confounding variables such as comorbid illness or polypharmacy is higher.

By altering the biochemical and microbial environment of the stomach and small bowel, PPI use may contribute to the development of micronutrient deficiencies, most notably of vitamin B12, iron, and magnesium. Vitamin B12 is dependent on gastric acid for absorption. Cobalamin enters the stomach bound to dietary proteins, where hydrochloric acid and pepsin mediate its release and subsequent binding to R proteins and transfer to intrinsic factor. The cobalamin-intrinsic factor complex can then be absorbed by the terminal ileum. Large studies have shown a twofold increased risk of vitamin B12 deficiency with either PPI or H2 receptor antagonist use [165]. Gastric acid is also important for the absorption of nonheme iron, which requires a low-pH environment to facilitate reduction of ferric iron to the ferrous state [166]. Studies of the effects of PPI use on iron absorption have been inconsistent, however [167–171].

Magnesium absorption is not dependent on gastric acid and occurs mostly through passive absorption in the small intestine. Nonetheless, PPIs have been implicated in the development of potentially dangerous levels of hypomagnesemia [172, 173]. Although the mechanism of PPI-mediated hypomagnesemia is not known, treatment with H2 receptor antagonists does not seem to contribute to magnesium deficiency. The observation that hypomagnesemia persists despite supplementation and recovers promptly following PPI discontinuation [174] further supports an idiosyncratic causative drug effect. This data prompted the FDA to issue an alert about the association between PPI use and hypomagnesemia. There are currently no specific guideline recommendations, however, recommending routine monitoring or supplementation of micronutrients in patients on long-term PPI therapy [129].

Management of GERD in Pregnancy

The prevalence of GERD is increased in pregnancy, with 40–80% of patients experiencing symptoms of GERD at some point during their pregnancy [175, 176]. GERD can develop during any trimester [177], and symptoms tend to worsen over the course of a pregnancy [178]. Risk factors for GERD in pregnancy include pre-pregnancy GERD and multiparity, but not pre-pregnancy obesity or weight gain during pregnancy [178]. The combined action of increased estrogen and progesterone in pregnancy results in decreased LES tone and reduced response to normal physiologic stimuli that result in LES contraction [179, 180]. Increased intra-

abdominal pressure and altered gastric emptying have also been proposed to play a role [179].

Initial treatment of mild symptoms of GERD in pregnancy typically starts with employment of lifestyle modifications such as avoidance of late evening meals and trigger foods in addition to elevation of the head of bed [181]. Organogenesis occurs from 31 to 71 days after the last menstrual period, so pharmacologic therapy is generally avoided during this period of heightened teratogenicity if possible [182]. Antacids are generally considered first line given their lack of systemic absorption [183, 184]. However, compounds containing magnesium trisilicate and sodium bicarbonate are generally avoided due to potential side effects in the mother and fetus [181, 183]. Sucralfate, an aluminum salt of sulphated disaccharide, is also a nonabsorbable pharmacologic agent that facilitates mucosal protection via topical effect and has been demonstrated in an RCT to be more effective than placebo in controlling GERD symptoms in pregnant patients with no reported adverse maternal or fetal events [185]. Sucralfate has also been shown to be safe for the fetus in animal models [186]. Current guidelines do not support the use of sucralfate for management of GERD in nonpregnant patients. Antacids and sucralfate are minimally, if at all, secreted in breast milk and are considered safe during lactation [182].

H2 receptor antagonists are the most commonly used and safest systemically absorbed pharmacologic agents used for treatment of GERD in pregnant patients. Cimetidine and ranitidine have been used in this population with no evidence of increased risk of adverse pregnancy-related outcomes seen in observational studies [187, 188]. Ranitidine has even been shown to be safe and effective in an RCT of pregnant patients with GERD [189]. Ranitidine is favored by some due to data from animal models documenting a weak anti-androgen effect of cimetidine that was absent in ranitidine [190]. Although less well studied, famotidine has been found to be safe in animal [191] and human [186] studies. Animal studies of nizatidine have shown an increased risk of fetal complications [192], but no significant harm has been demonstrated in humans. H2RAs are secreted into breastmilk, but are all considered safe during lactation, except for nizatidine, which has been shown to promote growth retardation in animal studies [189, 192].

The efficacy and safety of PPIs in pregnancy are less well studied than H2 receptor antagonists. All PPIs are categorized as class B drugs in pregnancy by the FDA, except for omeprazole, which is categorized as class C due to increased embryonic and fetal mortality in animal studies [182]. Several large observational studies of PPI exposure among infants showed no increased risk of congenital malformations to any PPI or omeprazole specifically [193–199]. Little is known about the safety of PPIs during lactation or their excretion in breast milk [182]. Table 14.8 highlights the safety of GERD pharmacotherapy in pregnancy.

Table 14.8 Safety of GERD pharmacotherapy in pregnancy [182]

Drug	FDA class	Comments
Antacids		
Aluminum, calcium, or magnesium-containing antacids	None	Most are safe during pregnancy due to minimal systemic absorption
Magnesium trisilicates	None	Avoid long-term, high-dose therapy in pregnancy
Sodium bicarbonate	None	Not safe for use in pregnancy as can cause fluid overload or metabolic alkalosis in mother and fetus
Sucralfate	B	Human safety in pregnancy demonstrated in RCT Minimal excretion in breast milk
Histamine$_2$-receptor antagonists		
Cimetidine	B	Found to be safe in pregnancy in prospective human study. Possible anti-androgen effect in animal studies
Ranitidine	B	Only systemic pharmacologic therapy studied in RCT in pregnancy. No anti-androgen effect

(continued)

Table 14.8 (continued)

Drug	FDA class	Comments
Famotidine	B	Safe in animal studies. Paucity of robust human studies
Nizatidine	B	Animal studies with increased fetal complications. No significant complications shown in humans but large studies lacking. Possible growth retardation shown in animal studies of lactation
Proton-pump inhibitors		
Omeprazole	C	Increased embryonic and fetal loss in animal studies. Some case reports of congenital defects in humans. Has been shown to be excreted in breast milk. Animal studies of lactation show increased infant weight gain
Lansoprazole	B	No significant fetal complications or teratogenicity Little human data available
Rabeprazole	B	No significant fetal complications or teratogenicity Little human data available
Pantoprazole	B	No significant fetal complications or teratogenicity Little human data available
Esomeprazole	B	No significant fetal complications or teratogenicity Little human data available
Dexlansoprazole	B	No significant fetal complications or teratogenicity Little human data available

Adapted with permission © Wiley and Sons [182]

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Wolfe MM, Sachs G. Acid suppression: optimizing therapy for gastroduodenal ulcer healing, gastroesophageal reflux disease, and stress-related erosive syndrome. Gastroenterology. 2000;118(2): S9–S31.
2. Kroch DA, Madanick RD. Medical treatment of gastroesophageal reflux disease. World J Surg. 2017;41(7):1678–84.
3. Kahrilas PJ, Shaheen NJ, Vaezi MF, Institute AGA, Committee CPaQM. American Gastroenterological Association Institute technical review on the management of gastroesophageal reflux disease. Gastroenterology. 2008;135(4):1392–413, 413.e1–5
4. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol. 2013;108(3):308–28.. quiz 29
5. Kaltenbach T, Crockett S, Gerson LB. Are lifestyle measures effective in patients with gastroesophageal reflux disease? An evidence-based approach. Arch Intern Med. 2006;166(9):965–71.
6. Dua K, Bardan E, Ren J, Sui Z, Shaker R. Effect of chronic and acute cigarette smoking on the pharyngo-upper oesophageal sphincter contractile reflex and reflexive pharyngeal swallow. Gut. 1998;43(4):537–41.
7. Stanciu C, Bennett JR. Smoking and gastro-oesophageal reflux. Br Med J. 1972;3(5830):793–5.
8. Bujanda L. The effects of alcohol consumption upon the gastrointestinal tract. Am J Gastroenterol. 2000;95(12):3374–82.
9. Grande L, Monforte R, Ros E, Toledo-Pimentel V, Estruch R, Lacima G, et al. High amplitude contractions in the middle third of the oesophagus: a manometric marker of chronic alcoholism? Gut. 1996;38(5):655–62.
10. Cranley JP, Achkar E, Fleshler B. Abnormal lower esophageal sphincter pressure responses in patients with orange juice-induced heartburn. Am J Gastroenterol. 1986;81(2):104–6.
11. Thomas FB, Steinbaugh JT, Fromkes JJ, Mekhjian HS, Caldwell JH. Inhibitory effect of coffee on lower esophageal sphincter pressure. Gastroenterology. 1980;79(6):1262–6.
12. Wright LE, Castell DO. The adverse effect of chocolate on lower esophageal sphincter pressure. Am J Dig Dis. 1975;20(8):703–7.
13. Nebel OT, Castell DO. Inhibition of the lower oesophageal sphincter by fat–a mechanism for fatty food intolerance. Gut. 1973;14(4):270–4.
14. Kadakia SC, Kikendall JW, Maydonovitch C, Johnson LF. Effect of cigarette smoking on gastroesophageal reflux measured by 24-h ambulatory esophageal pH monitoring. Am J Gastroenterol. 1995;90(10):1785–90.
15. Pehl C, Pfeiffer A, Wendl B, Kaess H. The effect of decaffeination of coffee on gastro-oesophageal reflux in patients with reflux disease. Aliment Pharmacol Ther. 1997;11(3):483–6.

16. Wendl B, Pfeiffer A, Pehl C, Schmidt T, Kaess H. Effect of decaffeination of coffee or tea on gastro-oesophageal reflux. Aliment Pharmacol Ther. 1994;8(3):283–7.
17. Murphy DW, Castell DO. Chocolate and heartburn: evidence of increased esophageal acid exposure after chocolate ingestion. Am J Gastroenterol. 1988;83(6):633–6.
18. Allen ML, Mellow MH, Robinson MG, Orr WC. The effect of raw onions on acid reflux and reflux symptoms. Am J Gastroenterol. 1990;85(4):377–80.
19. Iwakiri K, Kobayashi M, Kotoyori M, Yamada H, Sugiura T, Nakagawa Y. Relationship between postprandial esophageal acid exposure and meal volume and fat content. Dig Dis Sci. 1996;41(5):926–30.
20. Hamilton JW, Boisen RJ, Yamamoto DT, Wagner JL, Reichelderfer M. Sleeping on a wedge diminishes exposure of the esophagus to refluxed acid. Dig Dis Sci. 1988;33(5):518–22.
21. Pollmann H, Zillessen E, Pohl J, Rosemeyer D, Abucar A, Armbrecht U, et al. Effect of elevated head position in bed in therapy of gastroesophageal reflux. Z Gastroenterol. 1996;34 Suppl 2:93–9.
22. Harvey RF, Gordon PC, Hadley N, Long DE, Gill TR, Macpherson RI, et al. Effects of sleeping with the bed-head raised and of ranitidine in patients with severe peptic oesophagitis. Lancet. 1987;2(8569):1200–3.
23. Duroux P, Bauerfeind P, Emde C, Koelz HR, Blum AL. Early dinner reduces nocturnal gastric acidity. Gut. 1989;30(8):1063–7.
24. Orr WC, Harnish MJ. Sleep-related gastro-oesophageal reflux: provocation with a late evening meal and treatment with acid suppression. Aliment Pharmacol Ther. 1998;12(10):1033–8.
25. Pandolfino JE, El-Serag HB, Zhang Q, Shah N, Ghosh SK, Kahrilas PJ. Obesity: a challenge to esophagogastric junction integrity. Gastroenterology. 2006;130(3):639–49.
26. Jacobson BC, Somers SC, Fuchs CS, Kelly CP, Camargo CA. Body-mass index and symptoms of gastroesophageal reflux in women. N Engl J Med. 2006;354(22):2340–8.
27. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. Ann Intern Med. 2005;143(3):199–211.
28. Ness-Jensen E, Lindam A, Lagergren J, Hveem K. Weight loss and reduction in gastroesophageal reflux. A prospective population-based cohort study: the HUNT study. Am J Gastroenterol. 2013;108(3):376–82.
29. Mathus-Vliegen LM, Tytgat GN. Twenty-four-hour pH measurements in morbid obesity: effects of massive overweight, weight loss and gastric distension. Eur J Gastroenterol Hepatol. 1996;8(7):635–40.
30. Mathus-Vliegen EM, Tygat GN. Gastro-oesophageal reflux in obese subjects: influence of overweight, weight loss and chronic gastric balloon distension. Scand J Gastroenterol. 2002;37(11):1246–52.
31. Mathus-Vliegen EM, van Weeren M, van Eerten PV. Los function and obesity: the impact of untreated obesity, weight loss, and chronic gastric balloon distension. Digestion. 2003;68(2–3):161–8.
32. Fraser-Moodie CA, Norton B, Gornall C, Magnago S, Weale AR, Holmes GK. Weight loss has an independent beneficial effect on symptoms of gastro-oesophageal reflux in patients who are overweight. Scand J Gastroenterol. 1999;34(4):337–40.
33. Kjellin A, Ramel S, Rössner S, Thor K. Gastroesophageal reflux in obese patients is not reduced by weight reduction. Scand J Gastroenterol. 1996;31(11):1047–51.
34. Singh M, Lee J, Gupta N, Gaddam S, Smith BK, Wani SB, et al. Weight loss can lead to resolution of gastroesophageal reflux disease symptoms: a prospective intervention trial. Obesity (Silver Spring). 2013;21(2):284–90.
35. Sontag SJ. The medical-management of reflux esophagitis – role of antacids and acid inhibition. Gastroenterol Clin N. 1990;19(3):683–712.
36. Decktor DL, Robinson M, Maton PN, Lanza FL, Gottlieb S. Effects of aluminum/magnesium hydroxide and calcium carbonate on esophageal and gastric pH in subjects with heartburn. Am J Ther. 1995;2(8):546–52.
37. Decktor DL, Robinson M, Gottlieb S. Comparative effects of liquid antacids on esophageal and gastric pH in patients with heartburn. Am J Ther. 1995;2(7):481–6.
38. McRorie JW Jr, Gibb RD, Miner PB Jr. Evidence-based treatment of frequent heartburn: the benefits and limitations of over-the-counter medications. J Am Assoc Nurse Pract. 2014;26(6):330–9.
39. Maton PN, Burton ME. Antacids revisited – a review of their clinical pharmacology and recommended therapeutic use. Drugs. 1999;57(6):855–70.
40. Collings KL, Rodriguez-Stanley S, Proskin HM, Robinson M, Miner PB. Clinical effectiveness of a new antacid chewing gum on heartburn and oesophageal pH control. Aliment Pharm Therap. 2002;16(12):2029–35.
41. Robinson M, Rodriguez-Stanley S, Miner PB, McGuire AJ, Fung K, Ciociola AA. Effects of antacid formulation on postprandial oesophageal acidity in patients with a history of episodic heartburn. Aliment Pharm Therap. 2002;16(3):435–43.
42. Grove O, Bekker C, Jeppe-Hansen MG, Karstoft E, Sanchez G, Axelsson CK, et al. Ranitidine and high-dose antacid in reflux oesophagitis. A randomized, placebo-controlled trial. Scand J Gastroenterol. 1985;20(4):457–61.
43. Weberg R, Berstad A. Symptomatic effect of a low-dose antacid regimen in reflux oesophagitis. Scand J Gastroenterol. 1989;24(4):401–6.
44. Graham DY, Patterson DJ. Double-blind comparison of liquid antacid and placebo in the treatment of symptomatic reflux esophagitis. Dig Dis Sci. 1983;28(6):559–63.

45. Petrokubi RJ, Jeffries GH. Cimetidine versus antacid in scleroderma with reflux esophagitis – randomized double-blind controlled-study. Gastroenterology. 1979;77(4):691–5.
46. Cucchiara S, Staiano A, Romaniello G, Capobianco S, Auricchio S. Antacids and cimetidine treatment for gastro-oesophageal reflux and peptic oesophagitis. Arch Dis Child. 1984;59(9):842–7.
47. Houcke P, Maffioli C, Corallo J, Bouxin-Sauzet A, Martin AL. Comparison of the effects of Rocgel and anti-H2 on the symptomatology of gastroesophageal reflux without esophagitis. Ann Gastroenterol Hepatol (Paris). 1995;31(4):264–7.
48. Leiman DA, Riff BP, Morgan S, Metz DC, Falk GW, French B, et al. Alginate therapy is effective treatment for GERD symptoms: a systematic review and meta-analysis. Dis Esophagus. 2017;30(5):1–9.
49. Manabe N, Haruma K, Ito M, Takahashi N, Takasugi H, Wada Y, et al. Efficacy of adding sodium alginate to omeprazole in patients with nonerosive reflux disease: a randomized clinical trial. Dis Esophagus. 2012;25(5):373–80.
50. Boeckxstaens GE, Smout A. Systematic review: role of acid, weakly acidic and weakly alkaline reflux in gastro-oesophageal reflux disease. Aliment Pharm Therap. 2010;32(3):334–43.
51. Kessing BF, Conchillo JM, Bredenoord AJ, Smout AJPM, Masclee AAM. Review article: the clinical relevance of transient lower oesophageal sphincter relaxations in gastro-oesophageal reflux disease. Aliment Pharm Therap. 2011;33(6):650–61.
52. Li S, Shi S, Chen F, Lin J. The effects of baclofen for the treatment of gastroesophageal reflux disease: a meta-analysis of randomized controlled trials. Gastroenterol Res Pract. 2014;2014:307805.
53. Koek GH, Sifrim D, Lerut T, Janssens J, Tack J. Effect of the GABA(B) agonist baclofen in patients with symptoms and duodeno-gastro-oesophageal reflux refractory to proton pump inhibitors. Gut. 2003;52(10):1397–402.
54. Huang JQ, Hunt RH. Pharmacological and pharmacodynamic essentials of H(2)-receptor antagonists and proton pump inhibitors for the practising physician. Best Pract Res Clin Gastroenterol. 2001;15(3):355–70.
55. Tutuian R, Katz PO, Castell DO. Nocturnal acid breakthrough: pH, drugs and bugs. Eur J Gastroenterol Hepatol. 2004;16(5):441–3.
56. Kung YM, Hsu WH, Wu MC, Wang JW, Liu CJ, Su YC, et al. Recent advances in the pharmacological management of gastroesophageal reflux disease. Dig Dis Sci. 2017;62(12):3298–316.
57. Wang Y, Pan T, Wang Q, Guo Z. Additional bedtime H2-receptor antagonist for the control of nocturnal gastric acid breakthrough. Cochrane Database Syst Rev. 2009;4:CD004275.
58. Rackoff A, Agrawal A, Hila A, Mainie I, Tutuian R, Castell DO. Histamine-2 receptor antagonists at night improve gastroesophageal reflux disease symptoms for patients on proton pump inhibitor therapy. Dis Esophagus. 2005;18(6):370–3.
59. Zhao F, Wang S, Liu L, Wang Y. Comparative effectiveness of histamine-2 receptor antagonists as short-term therapy for gastro-esophageal reflux disease: a network meta-analysis. Int J Clin Pharmacol Ther. 2016;54(10):761–70.
60. Gyawali CP. Proton pump inhibitors in gastroesophageal reflux disease: friend or foe. Curr Gastroenterol Rep. 2017;19(9):46.
61. Larsson H, Carlsson E, Junggren U, Olbe L, Sjostrand SE, Skanberg I, et al. Inhibition of gastric acid secretion by omeprazole in the dog and rat. Gastroenterology. 1983;85(4):900–7.
62. Olbe L, Carlsson E, Lindberg P. A proton-pump inhibitor expedition: the case histories of omeprazole and esomeprazole. Nat Rev Drug Discov. 2003;2(2):132–9.
63. Klinkenberg-Knol EC, Jansen JM, Festen HP, Meuwissen SG, Lamers CB. Double-blind multicentre comparison of omeprazole and ranitidine in the treatment of reflux oesophagitis. Lancet (London, England). 1987;1(8529):349–51.
64. Lauritsen K, Rune SJ, Bytzer P, Kelbaek H, Jensen KG, Rask-Madsen J, et al. Effect of omeprazole and cimetidine on duodenal ulcer. A double-blind comparative trial. N Engl J Med. 1985;312(15):958–61.
65. Walan A, Bader JP, Classen M, Lamers CB, Piper DW, Rutgersson K, et al. Effect of omeprazole and ranitidine on ulcer healing and relapse rates in patients with benign gastric ulcer. N Engl J Med. 1989;320(2):69–75.
66. Andersson T. Pharmacokinetics, metabolism and interactions of acid pump inhibitors. Focus on omeprazole, lansoprazole and pantoprazole. Clin Pharmacokinet. 1996;31(1):9–28.
67. Sigterman KE, van Pinxteren B, Bonis PA, Lau J, Numans ME. Short-term treatment with proton pump inhibitors, H2-receptor antagonists and prokinetics for gastro-oesophageal reflux disease-like symptoms and endoscopy negative reflux disease. Cochrane Database Syst Rev. 2013;5:CD002095.
68. Wang WH, Huang JQ, Zheng GF, Xia HH, Wong WM, Lam SK, et al. Head-to-head comparison of H2-receptor antagonists and proton pump inhibitors in the treatment of erosive esophagitis: a meta-analysis. World J Gastroenterol. 2005;11(26):4067–77.
69. Labenz J, Malfertheiner P. Treatment of uncomplicated reflux disease. World J Gastroenterol. 2005;11(28):4291–9.
70. Chiba N, De Gara CJ, Wilkinson JM, Hunt RH. Speed of healing and symptom relief in grade II to IV gastroesophageal reflux disease: a meta-analysis. Gastroenterology. 1997;112(6):1798–810.
71. Strand DS, Kim D, Peura DA. 25 years of proton pump inhibitors: a comprehensive review. Gut Liver. 2017;11(1):27–37.
72. De Graef J, Woussen-Colle MC. Influence of the stimulation state of the parietal cells on the inhibitory effect of omeprazole on gastric acid secretion in dogs. Gastroenterology. 1986;91(2):333–7.

73. Sachs G. Proton pump inhibitors and acid-related diseases. Pharmacotherapy. 1997;17(1):22–37.
74. Howden CW. Review article: immediate-release proton-pump inhibitor therapy–potential advantages. Aliment Pharmacol Ther. 2005;22(Suppl 3):25–30.
75. Castell D, Bagin R, Goldlust B, Major J, Hepburn B. Comparison of the effects of immediate-release omeprazole powder for oral suspension and pantoprazole delayed-release tablets on nocturnal acid breakthrough in patients with symptomatic gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2005;21(12):1467–74.
76. Howden CW, Ballard ED, Koch FK, Gautille TC, Bagin RG. Control of 24-hour intragastric acidity with morning dosing of immediate-release and delayed-release proton pump inhibitors in patients with GERD. J Clin Gastroenterol. 2009;43(4):323–6.
77. Walker D, Ng Kwet Shing R, Jones D, Gruss HJ, Regula J. Challenges of correlating pH change with relief of clinical symptoms in gastro esophageal reflux disease: a phase III, randomized study of Zegerid versus Losec. PLoS One. 2015;10(2):e0116308.
78. Gralnek IM, Dulai GS, Fennerty MB, Spiegel BM. Esomeprazole versus other proton pump inhibitors in erosive esophagitis: a meta-analysis of randomized clinical trials. Clin Gastroenterol Hepatol. 2006;4(12):1452–8.
79. Vakil N, Fennerty MB. Direct comparative trials of the efficacy of proton pump inhibitors in the management of gastro-oesophageal reflux disease and peptic ulcer disease. Aliment Pharmacol Ther. 2003;18(6):559–68.
80. Edwards SJ, Lind T, Lundell L. Systematic review of proton pump inhibitors for the acute treatment of reflux oesophagitis. Aliment Pharmacol Ther. 2001;15(11):1729–36.
81. Klok RM, Postma MJ, van Hout BA, Brouwers JR. Meta-analysis: comparing the efficacy of proton pump inhibitors in short-term use. Aliment Pharmacol Ther. 2003;17(10):1237–45.
82. Mathews S, Reid A, Tian C, Cai Q. An update on the use of pantoprazole as a treatment for gastro-esophageal reflux disease. Clin Exp Gastroenterol. 2010;3:11–6.
83. Cheer SM, Prakash A, Faulds D, Lamb HM. Pantoprazole: an update of its pharmacological properties and therapeutic use in the management of acid-related disorders. Drugs. 2003;63(1):101–33.
84. Simon B, Muller P, Pascu O, Gatz G, Sander P, Huber R, et al. Intra-oesophageal pH profiles and pharmacokinetics of pantoprazole and esomeprazole: a crossover study in patients with gastro-oesophageal reflux disease. Eur J Gastroenterol Hepatol. 2003;15(7):791–9.
85. Mulder CJJ, Westerveld BD, Smit JM, Pool MO, Otten MH, Tan TG, et al. A double-blind, randomized comparison of omeprazole Multiple Unit Pellet System (MUPS) 20 mg, lansoprazole 30 mg and pantoprazole 40 mg in symptomatic reflux oesophagitis followed by 3 months of omeprazole MUPS maintenance treatment: a Dutch multicentre trial. Eur J Gastroen Hepat. 2002;14(6):649–56.
86. Thomson A. Impact of PPIs on patient focused symptomatology in GERD. Ther Clin Risk Manag. 2008;4(6):1185–200.
87. Scholten T, Teutsch I, Bohuschke M, Gatz G. Pantoprazole on-demand effectively treats symptoms in patients with gastro-oesophageal reflux disease. Clin Drug Invest. 2007;27(4):287–96.
88. Morelli G, Chen H, Rossiter G, Rege B, Lu Y. An open-label, parallel, multiple-dose study comparing the pharmacokinetics and gastric acid suppression of rabeprazole extended-release with esomeprazole 40 mg and rabeprazole delayed-release 20 mg in healthy volunteers. Aliment Pharmacol Ther. 2011;33(7):845–54.
89. Laine L, Katz PO, Johnson DA, Ibegbu I, Goldstein MJ, Chou C, et al. Randomised clinical trial: a novel rabeprazole extended release 50 mg formulation vs. esomeprazole 40 mg in healing of moderate-to-severe erosive oesophagitis – the results of two double-blind studies. Aliment Pharmacol Ther. 2011;33(2):203–12.
90. Thoring M, Hedenstrom H, Eriksson LS. Rapid effect of lansoprazole on intragastric pH: a crossover comparison with omeprazole. Scand J Gastroenterol. 1999;34(4):341–5.
91. Baldi F, Malfertheiner P. Lansoprazole fast disintegrating tablet: a new formulation for an established proton pump inhibitor. Digestion. 2003;67(1–2):1–5.
92. Wu MS, Tan SC, Xiong T. Indirect comparison of randomised controlled trials: comparative efficacy of dexlansoprazole vs. esomeprazole in the treatment of gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2013;38(2):190–201.
93. Hershcovici T, Jha LK, Fass R. Dexlansoprazole MR: a review. Ann Med. 2011;43(5):366–74.
94. Lee RD, Vakily M, Mulford D, Wu J, Atkinson SN. Clinical trial: the effect and timing of food on the pharmacokinetics and pharmacodynamics of dexlansoprazole MR, a novel Dual Delayed Release formulation of a proton pump inhibitor–evidence for dosing flexibility. Aliment Pharmacol Ther. 2009;29(8):824–33.
95. Fass R, Johnson DA, Orr WC, Han C, Mody R, Stern KN, et al. The effect of dexlansoprazole MR on nocturnal heartburn and GERD-related sleep disturbances in patients with symptomatic GERD. Am J Gastroenterol. 2011;106(3):421–31.
96. Fass R, Inadomi J, Han C, Mody R, O'Neil J, Perez MC. Maintenance of heartburn relief after step-down from twice-daily proton pump inhibitor to once-daily dexlansoprazole modified release. Clin Gastroenterol Hepatol. 2012;10(3):247–53.
97. Inadomi JM, Jamal R, Murata GH, Hoffman RM, Lavezo LA, Vigil JM, et al. Step-down management of gastroesophageal reflux disease. Gastroenterology. 2001;121(5):1095–100.
98. Inadomi JM, McIntyre L, Bernard L, Fendrick AM. Step-down from multiple- to single-dose pro-

ton pump inhibitors (PPIs): a prospective study of patients with heartburn or acid regurgitation completely relieved with PPIs. Am J Gastroenterol. 2003;98(9):1940–4.
99. Tsuzuki T, Okada H, Kawahara Y, Takenaka R, Nasu J, Ishioka H, et al. Proton pump inhibitor step-down therapy for GERD: a multi-center study in Japan. World J Gastroenterol. 2011;17(11):1480–7.
100. Miner P Jr, Katz PO, Chen Y, Sostek M. Gastric acid control with esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole: a five-way crossover study. Am J Gastroenterol. 2003;98(12):2616–20.
101. Miner PB Jr, McKean LA, Gibb RD, Erasala GN, Ramsey DL, McRorie JW. Omeprazole-Mg 20.6 mg is superior to lansoprazole 15 mg for control of gastric acid: a comparison of over-the-counter doses of proton pump inhibitors. Aliment Pharmacol Ther. 2010;31(8):846–51.
102. Miehlke S, Lobe S, Madisch A, Kuhlisch E, Laass M, Grossmann D, et al. Intragastric acidity during administration of generic omeprazole or esomeprazole – a randomised, two-way crossover study including CYP2C19 genotyping. Aliment Pharm Therap. 2011;33(4):471–6.
103. Kushner PR, Peura DA. Review of proton pump inhibitors for the initial treatment of heartburn: is there a dose ceiling effect? Adv Ther. 2011;28(5):367–88.
104. Armstrong D, Talley NJ, Lauritsen K, Moum B, Lind T, Tunturi-Hihnala H, et al. The role of acid suppression in patients with endoscopy-negative reflux disease: the effect of treatment with esomeprazole or omeprazole. Aliment Pharmacol Ther. 2004;20(4):413–21.
105. Fass R, Sontag SJ, Traxler B, Sostek M. Treatment of patients with persistent heartburn symptoms: a double-blind, randomized trial. Clin Gastroenterol Hepatol. 2006;4(1):50–6.
106. Fass R, Murthy U, Hayden CW, Malagon IB, Pulliam G, Wendel C, et al. Omeprazole 40 mg once a day is equally effective as lansoprazole 30 mg twice a day in symptom control of patients with gastro-oesophageal reflux disease (GERD) who are resistant to conventional-dose lansoprazole therapy-a prospective, randomized, multi-centre study. Aliment Pharmacol Ther. 2000;14(12):1595–603.
107. Mainie I, Tutuian R, Shay S, Vela M, Zhang X, Sifrim D, et al. Acid and non-acid reflux in patients with persistent symptoms despite acid suppressive therapy: a multicentre study using combined ambulatory impedance-pH monitoring. Gut. 2006;55(10):1398–402.
108. Habu Y, Maeda K, Kusuda T, Yoshino T, Shio S, Yamazaki M, et al. "Proton-pump inhibitor-first" strategy versus "step-up" strategy for the acute treatment of reflux esophagitis: a cost-effectiveness analysis in Japan. J Gastroenterol. 2005;40(11):1029–35.
109. Mine S, Iida T, Tabata T, Kishikawa H, Tanaka Y. Management of symptoms in step-down therapy of gastroesophageal reflux disease. J Gastroenterol Hepatol. 2005;20(9):1365–70.
110. Bjornsson E, Abrahamsson H, Simren M, Mattsson N, Jensen C, Agerforz P, et al. Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial. Aliment Pharmacol Ther. 2006;24(6):945–54.
111. MacFarlane B. Management of gastroesophageal reflux disease in adults: a pharmacist's perspective. Integr Pharm Res Pract. 2018;7:41–52.
112. O'Donoghue ML, Braunwald E, Antman EM, Murphy SA, Bates ER, Rozenman Y, et al. Pharmacodynamic effect and clinical efficacy of clopidogrel and prasugrel with or without a proton-pump inhibitor: an analysis of two randomised trials. Lancet (London, England). 2009;374(9694):989–97.
113. Bhatt DL, Cryer BL, Contant CF, Cohen M, Lanas A, Schnitzer TJ, et al. Clopidogrel with or without omeprazole in coronary artery disease. N Engl J Med. 2010;363(20):1909–17.
114. Vaezi MF, Yang YX, Howden CW. Complications of proton pump inhibitor therapy. Gastroenterology. 2017;153(1):35–48.
115. Yang YX. Chronic proton pump inihibitor therapy and calcium metabolism. Curr Gastroenterol Rep. 2012;14(6):473–9.
116. O'Connell MB, Madden DM, Murray AM, Heaney RP, Kerzner LJ. Effects of proton pump inhibitors on calcium carbonate absorption in women: a randomized crossover trial. Am J Med. 2005;118(7):778–81.
117. Mizunashi K, Furukawa Y, Katano K, Abe K. Effect of omeprazole, an inhibitor of H+,K(+)-ATPase, on bone resorption in humans. Calcif Tissue Int. 1993;53(1):21–5.
118. Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. JAMA. 2006;296(24):2947–53.
119. Gray SL, LaCroix AZ, Larson J, Robbins J, Cauley JA, Manson JE, et al. Proton pump inhibitor use, hip fracture, and change in bone mineral density in postmenopausal women: results from the Women's Health Initiative. Arch Intern Med. 2010;170(9):765–71.
120. Corley DA, Kubo A, Zhao W, Quesenberry C. Proton pump inhibitors and histamine-2 receptor antagonists are associated with hip fractures among at-risk patients. Gastroenterology. 2010;139(1):93–101.
121. Targownik LE, Lix LM, Metge CJ, Prior HJ, Leung S, Leslie WD. Use of proton pump inhibitors and risk of osteoporosis-related fractures. CMAJ. 2008;179(4):319–26.
122. Fraser LA, Leslie WD, Targownik LE, Papaioannou A, Adachi JD, Group CR. The effect of proton pump inhibitors on fracture risk: report from the Canadian Multicenter Osteoporosis Study. Osteoporos Int. 2013;24(4):1161–8.
123. Khalili H, Huang ES, Jacobson BC, Camargo CA, Feskanich D, Chan AT. Use of proton pump inhibitors and risk of hip fracture in relation to dietary and

lifestyle factors: a prospective cohort study. BMJ. 2012;344:e372.
124. Ngamruengphong S, Leontiadis GI, Radhi S, Dentino A, Nugent K. Proton pump inhibitors and risk of fracture: a systematic review and meta-analysis of observational studies. Am J Gastroenterol. 2011;106(7):1209–18; quiz 19
125. Zhou B, Huang Y, Li H, Sun W, Liu J. Proton-pump inhibitors and risk of fractures: an update meta-analysis. Osteoporos Int. 2016;27(1):339–47.
126. Targownik LE, Lix LM, Leung S, Leslie WD. Proton-pump inhibitor use is not associated with osteoporosis or accelerated bone mineral density loss. Gastroenterology. 2010;138(3):896–904.
127. Targownik LE, Goertzen AL, Luo Y, Leslie WD. Long-term proton pump inhibitor use is not associated with changes in bone strength and structure. Am J Gastroenterol. 2017;112(1):95–101.
128. Targownik LE, Leslie WD, Davison KS, Goltzman D, Jamal SA, Kreiger N, et al. The relationship between proton pump inhibitor use and longitudinal change in bone mineral density: a population-based study [corrected] from the Canadian Multicentre Osteoporosis Study (CaMos). Am J Gastroenterol. 2012;107(9):1361–9.
129. Freedberg DE, Kim LS, Yang YX. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology. 2017;152(4):706–15.
130. Lazarus B, Chen Y, Wilson FP, Sang Y, Chang AR, Coresh J, et al. Proton pump inhibitor use and the risk of chronic kidney disease. JAMA Intern Med. 2016;176(2):238–46.
131. Xie Y, Bowe B, Li T, Xian H, Balasubramanian S, Al-Aly Z. Proton pump inhibitors and risk of incident CKD and progression to ESRD. J Am Soc Nephrol. 2016;27(10):3153–63.
132. Antoniou T, Macdonald EM, Hollands S, Gomes T, Mamdani MM, Garg AX, et al. Proton pump inhibitors and the risk of acute kidney injury in older patients: a population-based cohort study. CMAJ Open. 2015;3(2):E166–71.
133. Klatte DCF, Gasparini A, Xu H, de Deco P, Trevisan M, Johansson ALV, et al. Association between proton pump inhibitor use and risk of progression of chronic kidney disease. Gastroenterology. 2017;153(3):702–10.
134. Blank ML, Parkin L, Paul C, Herbison P. A nationwide nested case-control study indicates an increased risk of acute interstitial nephritis with proton pump inhibitor use. Kidney Int. 2014;86(4):837–44.
135. Simpson IJ, Marshall MR, Pilmore H, Manley P, Williams L, Thein H, et al. Proton pump inhibitors and acute interstitial nephritis: report and analysis of 15 cases. Nephrology (Carlton). 2006;11(5):381–5.
136. Sierra F, Suarez M, Rey M, Vela MF. Systematic review: proton pump inhibitor-associated acute interstitial nephritis. Aliment Pharmacol Ther. 2007;26(4):545–53.
137. Williams C. Occurrence and significance of gastric colonization during acid-inhibitory therapy. Best Pract Res Clin Gastroenterol. 2001;15(3):511–21.
138. Theisen J, Nehra D, Citron D, Johansson J, Hagen JA, Crookes PF, et al. Suppression of gastric acid secretion in patients with gastroesophageal reflux disease results in gastric bacterial overgrowth and deconjugation of bile acids. J Gastrointest Surg. 2000;4(1):50–4.
139. Pereira SP, Gainsborough N, Dowling RH. Drug-induced hypochlorhydria causes high duodenal bacterial counts in the elderly. Aliment Pharmacol Ther. 1998;12(1):99–104.
140. Lo WK, Chan WW. Proton pump inhibitor use and the risk of small intestinal bacterial overgrowth: a meta-analysis. Clin Gastroenterol Hepatol. 2013;11(5):483–90.
141. Lewis SJ, Franco S, Young G, O'Keefe SJ. Altered bowel function and duodenal bacterial overgrowth in patients treated with omeprazole. Aliment Pharmacol Ther. 1996;10(4):557–61.
142. Wilson KH, Sheagren JN, Freter R. Population dynamics of ingested Clostridium difficile in the gastrointestinal tract of the Syrian hamster. J Infect Dis. 1985;151(2):355–61.
143. Freedberg DE, Toussaint NC, Chen SP, Ratner AJ, Whittier S, Wang TC, et al. Proton pump inhibitors alter specific taxa in the human gastrointestinal microbiome: a Crossover Trial. Gastroenterology. 2015;149(4):883–5.e9.
144. Seto CT, Jeraldo P, Orenstein R, Chia N, DiBaise JK. Prolonged use of a proton pump inhibitor reduces microbial diversity: implications for Clostridium difficile susceptibility. Microbiome. 2014;2:42.
145. Janarthanan S, Ditah I, Adler DG, Ehrinpreis MN. Clostridium difficile-associated diarrhea and proton pump inhibitor therapy: a meta-analysis. Am J Gastroenterol. 2012;107(7):1001–10.
146. Kwok CS, Arthur AK, Anibueze CI, Singh S, Cavallazzi R, Loke YK. Risk of Clostridium difficile infection with acid suppressing drugs and antibiotics: meta-analysis. Am J Gastroenterol. 2012;107(7):1011–9.
147. Howell MD, Novack V, Grgurich P, Soulliard D, Novack L, Pencina M, et al. Iatrogenic gastric acid suppression and the risk of nosocomial Clostridium difficile infection. Arch Intern Med. 2010;170(9):784–90.
148. Tariq R, Singh S, Gupta A, Pardi DS, Khanna S. Association of gastric acid suppression with recurrent Clostridium difficile infection: a systematic review and meta-analysis. JAMA Intern Med. 2017;177(6):784–91.
149. Khanna S, Aronson SL, Kammer PP, Baddour LM, Pardi DS. Gastric acid suppression and outcomes in Clostridium difficile infection: a population-based study. Mayo Clin Proc. 2012;87(7):636–42.
150. Leonard AD, Ho KM, Flexman J. Proton pump inhibitors and diarrhoea related to Clostridium diffi-

cile infection in hospitalised patients: a case-control study. Intern Med J. 2012;42(5):591–4.
151. Wandall JH. Effects of omeprazole on neutrophil chemotaxis, super oxide production, degranulation, and translocation of cytochrome b-245. Gut. 1992;33(5):617–21.
152. Laheij RJ, Sturkenboom MC, Hassing RJ, Dieleman J, Stricker BH, Jansen JB. Risk of community-acquired pneumonia and use of gastric acid-suppressive drugs. JAMA. 2004;292(16):1955–60.
153. Gulmez SE, Holm A, Frederiksen H, Jensen TG, Pedersen C, Hallas J. Use of proton pump inhibitors and the risk of community-acquired pneumonia: a population-based case-control study. Arch Intern Med. 2007;167(9):950–5.
154. Herzig SJ, Howell MD, Ngo LH, Marcantonio ER. Acid-suppressive medication use and the risk for hospital-acquired pneumonia. JAMA. 2009;301(20):2120–8.
155. Filion KB, Chateau D, Targownik LE, Gershon A, Durand M, Tamim H, et al. Proton pump inhibitors and the risk of hospitalisation for community-acquired pneumonia: replicated cohort studies with meta-analysis. Gut. 2014;63(4):552–8.
156. Johnstone J, Nerenberg K, Loeb M. Meta-analysis: proton pump inhibitor use and the risk of community-acquired pneumonia. Aliment Pharmacol Ther. 2010;31(11):1165–77.
157. Giuliano C, Wilhelm SM, Kale-Pradhan PB. Are proton pump inhibitors associated with the development of community-acquired pneumonia? A meta-analysis. Expert Rev Clin Pharmacol. 2012;5(3):337–44.
158. Hermos JA, Young MM, Fonda JR, Gagnon DR, Fiore LD, Lawler EV. Risk of community-acquired pneumonia in veteran patients to whom proton pump inhibitors were dispensed. Clin Infect Dis. 2012;54(1):33–42.
159. Lambert AA, Lam JO, Paik JJ, Ugarte-Gil C, Drummond MB, Crowell TA. Risk of community-acquired pneumonia with outpatient proton-pump inhibitor therapy: a systematic review and meta-analysis. PLoS One. 2015;10(6):e0128004.
160. Badiola N, Alcalde V, Pujol A, Münter LM, Multhaup G, Lleó A, et al. The proton-pump inhibitor lansoprazole enhances amyloid beta production. PLoS One. 2013;8(3):e58837.
161. Haenisch B, von Holt K, Wiese B, Prokein J, Lange C, Ernst A, et al. Risk of dementia in elderly patients with the use of proton pump inhibitors. Eur Arch Psychiatry Clin Neurosci. 2015;265(5):419–28.
162. Gomm W, von Holt K, Thomé F, Broich K, Maier W, Fink A, et al. Association of proton pump inhibitors with risk of dementia: a pharmacoepidemiological claims data analysis. JAMA Neurol. 2016;73(4):410–6.
163. Taipale H, Tolppanen AM, Tiihonen M, Tanskanen A, Tiihonen J, Hartikainen S. No association between proton pump inhibitor use and risk of Alzheimer's disease. Am J Gastroenterol. 2017;112(12):1802–8.
164. Lochhead P, Hagan K, Joshi AD, Khalili H, Nguyen LH, Grodstein F, et al. Association between proton pump inhibitor use and cognitive function in women. Gastroenterology. 2017;153(4):971–9.e4.
165. Lam JR, Schneider JL, Zhao W, Corley DA. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. JAMA. 2013;310(22):2435–42.
166. Bezwoda W, Charlton R, Bothwell T, Torrance J, Mayet F. The importance of gastric hydrochloric acid in the absorption of nonheme food iron. J Lab Clin Med. 1978;92(1):108–16.
167. Stewart CA, Termanini B, Sutliff VE, Serrano J, Yu F, Gibril F, et al. Iron absorption in patients with Zollinger-Ellison syndrome treated with long-term gastric acid antisecretory therapy. Aliment Pharmacol Ther. 1998;12(1):83–98.
168. Hutchinson C, Geissler CA, Powell JJ, Bomford A. Proton pump inhibitors suppress absorption of dietary non-haem iron in hereditary haemochromatosis. Gut. 2007;56(9):1291–5.
169. Sarzynski E, Puttarajappa C, Xie Y, Grover M, Laird-Fick H. Association between proton pump inhibitor use and anemia: a retrospective cohort study. Dig Dis Sci. 2011;56(8):2349–53.
170. Lam JR, Schneider JL, Quesenberry CP, Corley DA. Proton pump inhibitor and histamine-2 receptor antagonist use and iron deficiency. Gastroenterology. 2017;152(4):821–9.e1.
171. Koop H, Bachem MG. Serum iron, ferritin, and vitamin B12 during prolonged omeprazole therapy. J Clin Gastroenterol. 1992;14(4):288–92.
172. Epstein M, McGrath S, Law F. Proton-pump inhibitors and hypomagnesemic hypoparathyroidism. N Engl J Med. 2006;355(17):1834–6.
173. Cheungpasitporn W, Thongprayoon C, Kittanamongkolchai W, Srivali N, Edmonds PJ, Ungprasert P, et al. Proton pump inhibitors linked to hypomagnesemia: a systematic review and meta-analysis of observational studies. Ren Fail. 2015;37(7):1237–41.
174. Hess MW, Hoenderop JG, Bindels RJ, Drenth JP. Systematic review: hypomagnesaemia induced by proton pump inhibition. Aliment Pharmacol Ther. 2012;36(5):405–13.
175. Bassey OO. Pregnancy heartburn in Nigerians and Caucasians with theories about aetiology based on manometric recordings from the oesophagus and stomach. Br J Obstet Gynaecol. 1977;84(6):439–43.
176. Isolauri J, Laippala P. Prevalence of symptoms suggestive of gastro-oesophageal reflux disease in an adult population. Ann Med. 1995;27(1):67–70.
177. Rey E, Rodriguez-Artalejo F, Herraiz MA, Sanchez P, Alvarez-Sanchez A, Escudero M, et al. Gastroesophageal reflux symptoms during and after pregnancy: a longitudinal study. Am J Gastroenterol. 2007;102(11):2395–400.
178. Marrero JM, Goggin PM, de Caestecker JS, Pearce JM, Maxwell JD. Determinants of pregnancy heartburn. Br J Obstet Gynaecol. 1992;99(9):731–4.

179. Richter JE. Gastroesophageal reflux disease during pregnancy. Gastroenterol Clin North Am. 2003;32(1):235–61.
180. Tsai CC, Tey SL, Chang LC, Su YT, Lin KJ, Huang SC. Estradiol mediates relaxation of porcine lower esophageal sphincter. Steroids. 2018;136:56–62.
181. Ali RA, Egan LJ. Gastroesophageal reflux disease in pregnancy. Best Pract Res Clin Gastroenterol. 2007;21(5):793–806.
182. Richter JE. Review article: the management of heartburn in pregnancy. Aliment Pharmacol Ther. 2005;22(9):749–57.
183. Richter JE. Heartburn, nausea, and vomiting during pregnancy. Pregnancy in gastrointestinal disorders, ACG Monograph American College of Physicians. 2007, p. 18–25.
184. Ching CK, Lam SK. Antacids. Indications and limitations. Drugs. 1994;47(2):305–17.
185. Phupong V, Hanprasertpong T. Interventions for heartburn in pregnancy. Cochrane Database Syst Rev. 2015;(9):CD011379.
186. Eltonsy S, Martin B, Ferreira E, Blais L. Systematic procedure for the classification of proven and potential teratogens for use in research. Birth Defects Res A Clin Mol Teratol. 2016;106(4):285–97.
187. Undeland KA, Hausken T, Svebak S, Aanderud S, Berstad A. Wide gastric antrum and low vagal tone in patients with diabetes mellitus type 1 compared to patients with functional dyspepsia and healthy individuals. Dig Dis Sci. 1996;41(1):9–16.
188. Ruigómez A, García Rodríguez LA, Cattaruzzi C, Troncon MG, Agostinis L, Wallander MA, et al. Use of cimetidine, omeprazole, and ranitidine in pregnant women and pregnancy outcomes. Am J Epidemiol. 1999;150(5):476–81.
189. Larson JD, Patatanian E, Miner PB, Rayburn WF, Robinson MG. Double-blind, placebo-controlled study of ranitidine for gastroesophageal reflux symptoms during pregnancy. Obstet Gynecol. 1997;90(1):83–7.
190. Parker S, Schade RR, Pohl CR, Gavaler JS, Van Thiel DH. Prenatal and neonatal exposure of male rat pups to cimetidine but not ranitidine adversely affects subsequent adult sexual functioning. Gastroenterology. 1984;86(4):675–80.
191. Savarino V, Giusti M, Scalabrini P, Bessarione D, Magnolia MR, Percario G, et al. Famotidine has no significant effect on gonadal function in man. Gastroenterol Clin Biol. 1988;12(1):19–22.
192. Morton DM. Pharmacology and toxicology of nizatidine. Scand J Gastroenterol Suppl. 1987;136:1–8.
193. Nikfar S, Abdollahi M, Moretti ME, Magee LA, Koren G. Use of proton pump inhibitors during pregnancy and rates of major malformations: a meta-analysis. Dig Dis Sci. 2002;47(7):1526–9.
194. Gill SK, O'Brien L, Einarson TR, Koren G. The safety of proton pump inhibitors (PPIs) in pregnancy: a meta-analysis. Am J Gastroenterol. 2009;104(6):1541–5; quiz 0, 6
195. Pasternak B, Hviid A. Use of proton-pump inhibitors in early pregnancy and the risk of birth defects. N Engl J Med. 2010;363(22):2114–23.
196. Feldman M, Burton ME. Histamine2-receptor antagonists. Standard therapy for acid-peptic diseases. N Engl J Med. 1990;323(24):1672–80.
197. Wedemeyer RS, Blume H. Pharmacokinetic drug interaction profiles of proton pump inhibitors: an update. Drug Saf. 2014;37(4):201–11.
198. Vakily M, Lee RD, Wu J, Gunawardhana L, Mulford D. Drug interaction studies with dexlansoprazole modified release (TAK-390MR), a proton pump inhibitor with a dual delayed-release formulation: results of four randomized, double-blind, crossover, placebo-controlled, single-centre studies. Clin Drug Investig. 2009;29(1):35–50.
199. Ogawa R, Echizen H. Drug-drug interaction profiles of proton pump inhibitors. Clin Pharmacokinet. 2010;49(8):509–33.

Laparoscopic Antireflux Surgery: Total Fundoplication

15

Francisco Schlottmann, Marco Di Corpo, and Marco G. Patti

Introduction

Approximately 20% of the population in the United States has gastroesophageal reflux disease (GERD), and its prevalence is increasing mostly due to the epidemic of obesity [1]. Most patients obtain adequate symptomatic control with lifestyle modifications and proton-pump inhibitor (PPI) therapy. Nevertheless, some patients will need surgical intervention because they only have partial control of symptoms, do not want to be on long-term medical treatment, or suffer complications related to PPI therapy [2].

The laparoscopic Nissen fundoplication (360°) was first reported in 1991 [3, 4] and has since become widely embraced for the surgical treatment of GERD. Nowadays, this procedure is the most commonly performed antireflux operation and has a long-term success in about 80–90% of patients [5, 6]. Similar to other procedures, antireflux surgery at high volume hospitals is associated with better outcomes such as less postoperative morbidity, shorter length of hospital stay, and lower costs for the health care system [7].

The goals of antireflux surgery are to control symptoms, improve patients' quality of life, and prevent GERD complications (bleeding, esophageal stenosis, Barrett's esophagus, and adenocarcinoma). A properly executed operation is critical to achieve these goals.

Laparoscopic Antireflux Surgery

Position of the Patient

After induction of general endotracheal anesthesia, an orogastric tube is inserted to keep the stomach decompressed. The patient is positioned supine in low lithotomy position with the lower extremities extended on stirrups, with knees flexed 20–30°. To avoid sliding due to the steep reverse Trendelenburg position used during the entire procedure, a bean-bag is inflated to create a "saddle" under the perineum. Pneumatic compression stockings are always used as prophylaxis against deep vein thrombosis along with subcutaneous heparin (high risk because the steep Trendelenburg position decreases venous return). The surgeon stands between the patient's legs, and the first and second

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_15

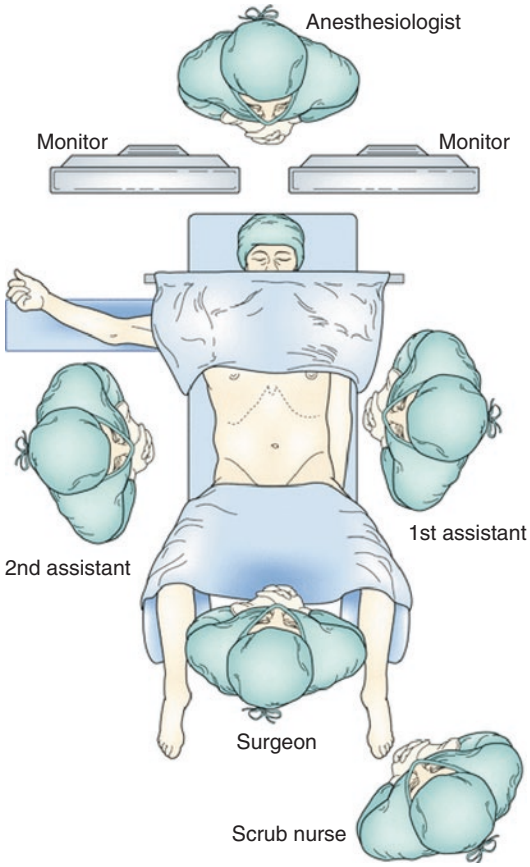


Fig. 15.1 Position of the patient

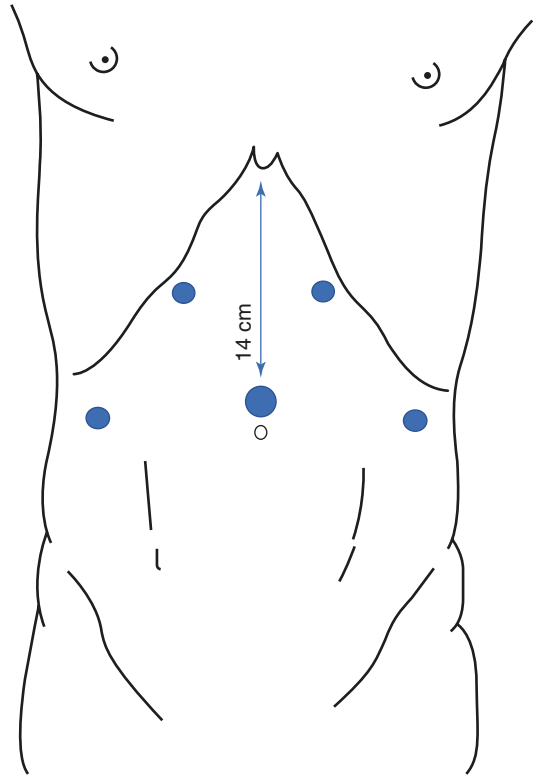


Fig. 15.2 Position of trocars for laparoscopic fundoplication

assistants on the left and right side of the operating table, respectively (Fig. 15.1).

Trocar Placement

We use five 10 mm ports for the procedure. The first port is placed in the mid-line about 14 cm below the xiphoid process; it can be also placed slightly (2–3 cm) to the left of the midline to be in line with the hiatus. This port is used for insertion of the scope. The second port is placed in the left midclavicular line at the same level of port 1, and it is used for the insertion of a Babcock clamp for traction, a grasper to hold the Penrose drain while surrounding the esophagus, or for devices used to divide the short gastric vessels. The third port is placed in the right midclavicular line at the same level of the other two ports, and it is used for the liver retractor. The fourth and fifth ports are placed under the right and left costal margins so that their axes and the camera form an angle of about 120°. These ports are used for the insertion of dissecting and suturing instruments (Fig. 15.2).

Key Note Trocars should not be placed too low. If this occurs, it might be difficult to take down the more proximal short gastric vessels or reach the gastroesophageal junction with the Babcock.

Division of Gastrohepatic Ligament and Identification of Right Crus of the Diaphragm and Posterior Vagus Nerve

The left lateral segment of the liver should be retracted to obtain an appropriate exposure of the gastroesophageal junction. The gastrohepatic

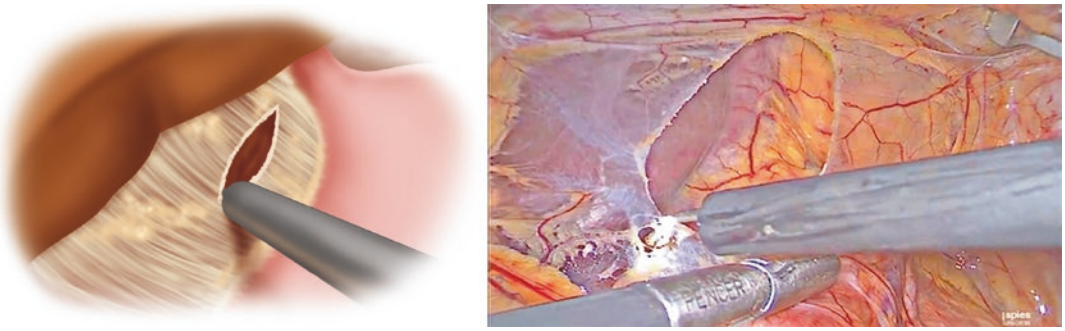


Fig. 15.3 Division of gastrohepatic ligament

ligament is then divided. The dissection begins above the caudate lobe of the liver and continues proximally until the right crus is identified. The crus is then separated from the right side of the esophagus by blunt dissection and the posterior vagus nerve is identified. The right crus is dissected inferiorly toward the junction with the left crus (Fig. 15.3).

Key Note If an accessory left hepatic artery originating from the left gastric artery is encountered, it can usually be safely divided. The electrocautery should be used with caution next to the right pillar of the crus because the lateral spread of the monopolar current may injury the posterior vagus nerve.

Division of Peritoneum and Phrenoesophageal Membrane Above the Esophagus and Identification of the Left Crus of the Diaphragm and Anterior Vagus Nerve

The peritoneum and the phrenoesophageal membrane above the esophagus are transected with the electrocautery, and the anterior vagus nerve is identified. The left pillar of the crus is separated from the esophagus and dissected bluntly downward toward the junction with the right crus (Fig. 15.4).

Key Note In order to avoid injury of the anterior vagus nerve or the esophageal wall during this step of the procedure, the nerve should be always left attached to the esophageal wall and the phrenoesophageal membrane should be lifted from the esophageal wall by blunt dissection before it is divided.

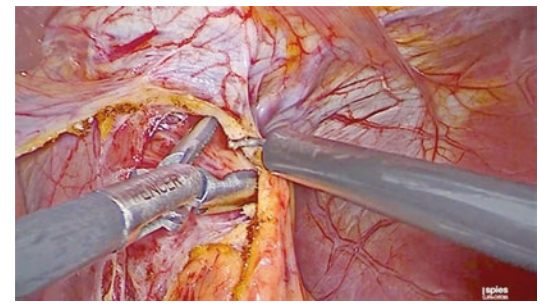


Fig. 15.4 Division of phrenoesophageal membrane

Division of Short Gastric Vessels

The short gastric vessels are divided all the way to the left pillar of the crus, starting from a point midway along the greater curvature of the stomach. The division of the short gastric vessels will ensure a tension-free wrap (Fig. 15.5).

Key Note Excessive traction of the gastric vessels can cause bleeding of the spleen. In addition, care must be taken to avoid damage of the gastric wall while sealing the short gastric vessels.

Placement of Penrose Drain Around the Esophagus

A Babcock clamp is applied at the level of the esophagogastric junction to retract upward the

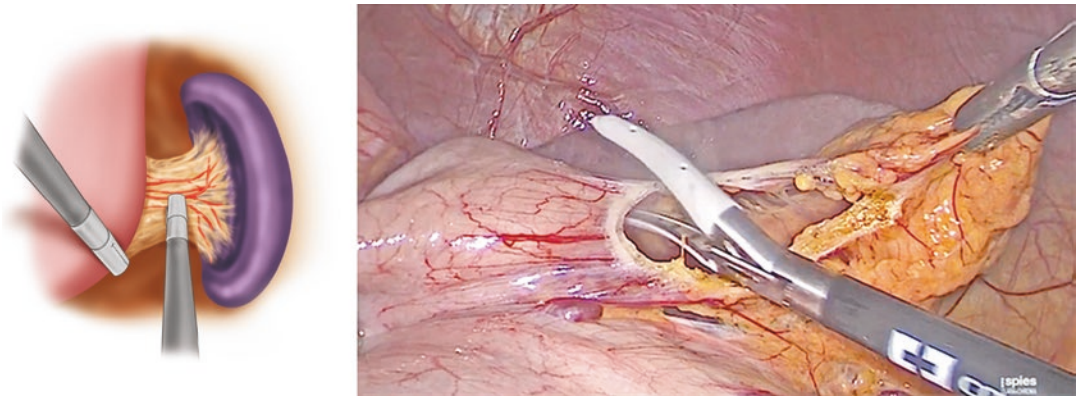


Fig. 15.5 Division of short gastric vessels

esophagus. A window is opened by blunt dissection under the esophagus between the gastric fundus, the esophagus, and the left pillar of the crus. The window is then enlarged and a Penrose drain is passed around the esophagus, incorporating both the anterior and posterior vagus nerves.

Key Note Dissection above the left pillar of the crus in the mediastinum, rather than between the crus and the gastric fundus, can cause a left pneumothorax. Perforation of the gastric fundus is also possible by pushing a blunt instrument under the esophagus.

Closure of the Crura

Proper exposure of the hiatus is obtained by retraction of the esophagus upward and toward the patient's left with the Penrose drain. The closure of the diaphragmatic crura is done with interrupted non-absorbable sutures (2-0 silk). The first stitch should be placed just above the junction of the two pillars. Additional stitches are placed 1 cm apart, and a space of about 1 cm is left between the uppermost stitch and the esophagus (Fig. 15.6).

Key Note While placing the stitches, care must be taken to avoid injury of the inferior vena cava and aorta. The crura should not be closed too tight (e.g., a close grasper should slide easily between the esophagus and the crura).

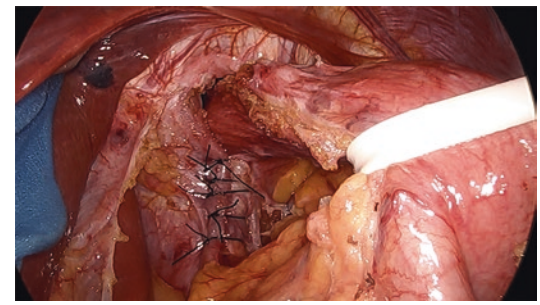


Fig. 15.6 Closure of the diaphragmatic crura

Insertion of the Bougie into the Esophagus and Through the Esophageal Junction

After the orogastric tube is removed, the anesthesiologist should insert a 56 French bougie down the esophagus through the esophagogastric junction. The use of a calibration bougie decreases the incidence of postoperative dysphagia [8].

Key Note The bougie should be properly lubricated to reduce the risk of esophageal perforation. In addition, the anesthesiologist should advance the bougie slowly, and stop if any resistance is encountered.

Nissen Fundoplication (360°)

The stomach is passed behind the esophagus, and a "shoe-shine maneuver" is performed to verify sufficient fundic mobilization and to avoid having part of the gastric fundus above the wrap. The left and right sides of the fundus are then wrapped above the esophagogastric junction. A Babcock clamp is used to hold the two sides of the fundus during the placement of the first stitch. A 360° fundoplication is created by placing 3 stitches of non-absorbable material (2-0 silk) at 1 cm intervals to approximate the right and left side of the fundoplication. The length of the anterior portion of the fundoplication should be approximately 2 cm (Fig. 15.7).

Key Note The wrap should not be under tension. If the wrap remains in the right side after pulling the fundus under the esophagus and does not retract back to the left, then it is floppy and suturing can be performed. If not, more posterior dissection is necessary. If tension is still present after these maneuvers, a partial fundoplication should be performed.

Postoperative Course

Patients are fed with clear liquids and then soft diet the morning of the first postoperative day. Most patients are discharged within 23 hours and are instructed to avoid meat, bread, and carbonated beverages for the following 2 weeks. Patients usually resume their regular activity within 2 weeks.

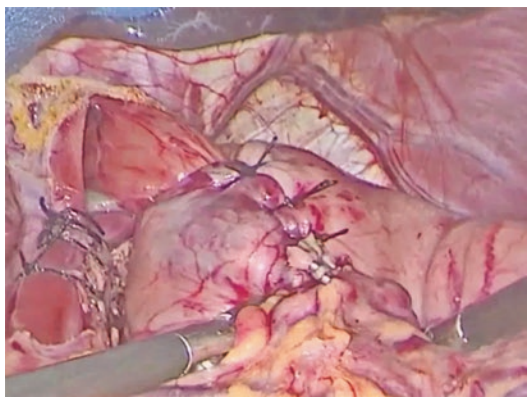


Fig. 15.7 Nissen (360°) fundoplication

Conclusions

A properly executed laparoscopic Nissen fundoplication can control patients' symptoms, improve patients' quality of life, and prevent GERD complications. Each step of the procedure should respect important technical elements to avoid troublesome side effects and obtain optimal postoperative outcomes.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. El-Serag HN, Sweet S, Winchester CC, et al. Update on the epidemiology of gastro-esophageal reflux disease: a systematic review. Gut. 2014;63:871–80.
2. Schlottmann F, Herbella FA, Allaix ME, et al. Surgical treatment of gastroesophageal reflux disease. World J Surg. 2017;41(7):1685–90.
3. Dallemagne B, Weerts JM, Jehaes C, et al. Laparoscopic Nissen fundoplication: preliminary report. Surg Laparosc Endosc. 1991;1(3):138–43.
4. Geagea T. Laparoscopic Nissen's fundoplication: preliminary report on ten cases. Surg Endosc. 1991;5(4):170–3.
5. Dallemagne B, Weerts J, Markiewicz S, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc. 2006;20(1):159–65.
6. Broeders JA, Rijnhart-de Jong HG, Draaisma WA, et al. Ten-year outcome of laparoscopic and conventional Nissen fundoplication: randomized clinical trial. Ann Surg. 2009;250(5):698–706.
7. Schlottmann F, Strassle PD, Patti MG. Antireflux surgery in the USA: influence of surgical volume on perioperative outcomes and costs-time for centralization? World J Surg. 2018;42(7):2183–9.
8. Patterson EJ, Herron DM, Hansen PD, et al. Effect of an esophageal bougie on the incidence of dysphagia following Nissen fundoplication: a prospective, blinded, randomized clinical trial. Arch Surg. 2000;135(9):1055–61.

Laparoscopic Partial Fundoplication

16

Salim Hosein, Sarah Samreen, and Dmitry Oleynikov

Introduction

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal problems, with population-based studies estimating the prevalence in North America to be between 18.1% and 22.7% [1]. The heartburn a patient feels is related to multiple factors. Fluctuations in LES pressure is the most important factor in heartburn. The diagnosis, treatment, and follow-up of these patients are a significant burden to our health-care system. This is evident from the fact that proton-pump inhibitors are some of the costliest and commonly prescribed medications in the United States.

The benefits of laparoscopic antireflux surgery (LARS) include a decrease in perioperative morbidity, hospital length of stay, and cost compared with open operations. The correct construction of a laparoscopic fundoplication requires significant operative experience and skills in complex laparoscopy. Compared with first-time operations, re-operative antireflux surgery is technically even more challenging, associated with a higher risk for perioperative complications, and results in less durable symptom improvement. Therefore, compared with first-time antireflux surgery, surgeons should have a higher threshold for offering patients reoperation, and operations should be performed by experienced, high-volume gastroesophageal surgeons.

Partial fundoplication is indicated for patients with esophageal dysmotility disorders [2]. As discussed later, the two most commonly performed types of partial fundoplication are the Toupet and the Dor. Many studies have published lower dysphagia rates after Toupet fundoplication compared with Nissen, with little difference in control of GERD after 1–5 years of follow-up [3]. An antireflux procedure, whether a Nissen or a partial fundoplication, is key to restoring the mechanical barrier to reflux and should be part of all laparoscopic paraesophageal hernia repairs. Other partial fundoplication procedures are less employed. One such procedure, the Belsey Mark IV, has fallen out of favor owing to the need for a thoracic approach and poor long-term antireflux outcomes. The Hill repair, though not truly a fundoplication but rather a plication of the gastroesophageal junction to the median arcuate ligament, is another uncommon procedure as results have been difficult to replicate.

S. Hosein · S. Samreen
Division of General Surgery, Section of GI/MIS, Department of Surgery, University of Nebraska Medical Center, Omaha, NE, USA

D. Oleynikov (✉)
Gastrointestinal, Minimally Invasive and Bariatric Surgery, Center for Advanced Surgical Technology, Omaha, NE, USA
e-mail: dmitry.oleynikov@unmc.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_16

Patient Selection/Role in GERD Algorithm

In patients who have a clinical history suggestive of gastroesophageal reflux disease, diagnostic testing should include upper gastrointestinal series, esophagogastroduodenoscopy, esophageal manometry, and ambulatory pH monitoring. For patients who exhibit elevated distal esophageal acid exposure and severe symptoms despite maximal medical therapy, antireflux surgery should be strongly considered. However, as some patients who do not experience improvement in their symptoms with PPI use may not have GERD, surgeons must carefully consider alternative causes and perform a complete workup before offering surgical treatment. Correct construction of the fundoplication reduces the risk of postoperative dysphagia caused by an inappropriately tight fundoplication, posterior herniation of gastric fundus, and slipped fundoplication.

Antireflux operations include partial posterior, partial anterior, and 360° fundoplications. In antireflux surgery, there has been a long-standing debate over which fundoplication provides superior control of GERD symptoms while mitigating postoperative side effects (e.g., dysphagia and gas bloat). Furthermore, studies have attempted to determine whether the type of fundoplication performed should be tailored to the patients' preoperative esophageal motility and symptoms. In patients with GERD and esophageal dysmotility, it has been suggested that partial fundoplication should be performed because of the concern that a Nissen fundoplication will lead to greater postoperative dysphagia. Booth and colleagues conducted a randomized controlled trial comparing laparoscopic Nissen fundoplication with Toupet fundoplication in patients stratified based on preoperative manometry [4]. At 1 year postoperatively, there were no differences between groups for heartburn and regurgitation, while dysphagia was more frequent in patients who underwent Nissen fundoplication. Similarly, the authors have previously shown that a Nissen fundoplication can be performed in patients with ineffective esophageal motility without an increase in development of dysphagia [5].

A review of nine randomized trials showed that an anterior fundoplication was associated with a greater risk of recurrent GERD symptoms when compared to other partial or total fundoplications. Even though Nissen was associated with more postoperative dysphagia, these patients required minimal treatment and no reoperations [6]. Another review of 32 studies, including randomized controlled trials, compared laparoscopic Nissen fundoplication with laparoscopic Toupet fundoplication [7]. No differences were noted between the groups concerning patient satisfaction with the operation or perioperative morbidity and mortality. Assessing postoperative dysphagia, no difference was noted between fundoplication types when esophageal motility was normal; however, in patients with abnormal esophageal motility, laparoscopic Nissen fundoplication was associated with greater rates of postoperative dysphagia. This review would suggest that a Toupet fundoplication is the treatment of choice in patients with impaired esophageal motility, as it determines effective GERD symptom control but less postoperative side effects. Interestingly, despite numerous randomized clinical trials and two meta-analyses, there still remains conflicting evidence regarding which fundoplication provides the most durable control of reflux and the best side-effect profile. The reasons for this finding probably is due to the heterogeneity of these studies in terms of patients' characteristics, patient's selection, and operative technique. For example, in the studies evaluated by Fein and Seyfried, there were four different bougie sizes used (34 F to 60 F); fixation of the stomach to the esophagus and hiatus was inconsistent; and division of the short gastric vessels was not always performed [6]. Currently, the only consistent finding in these studies is that anterior fundoplications provide less durable control of GERD than posterior partial and total fundoplications.

Preoperative Patient Preparation

The authors perform all laparoscopic antireflux operations with patients in the supine position in steep reverse Trendelenburg position, with a

footboard at the base of the bed and a belt strap at the waist and shoulders. The operating surgeon stands on the patient's right side and an assistant on the left. This allows for an unobstructed view of the esophageal hiatus. Patients are appropriately padded to prevent pressure ulcers and neuropathies, with arms tucked bilaterally. Since the procedure can take some time, consideration shoulder be given to Foley catheter placement for accurate measurement of urine output. An orogastric tube is inserted for gastric decompression. A video monitor is placed at the head of the bed so that both operators are able to view the screen. Preoperative antibiotics are administered to reduce the risk of surgical site infection, and subcutaneous heparin or Lovenox and sequential compression devices are used to reduce the risk of venous thromboembolic events.

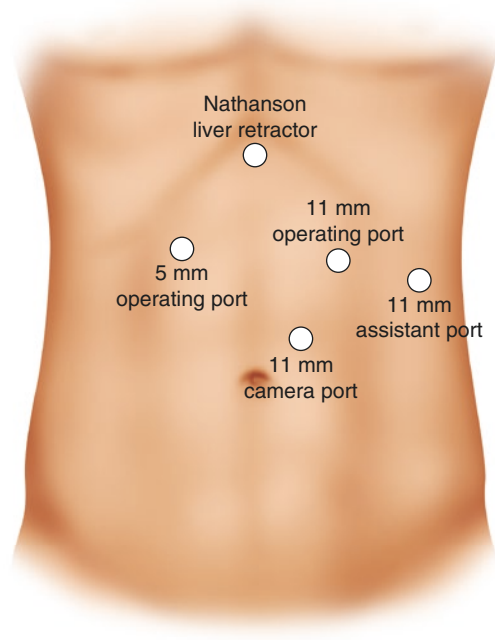


Fig. 16.1 Laparoscopic antireflux surgery port placement

The Procedure

Access to the abdomen is obtained using a 2 mm incision, and Veress needle is introduced at Palmer's point in the left upper quadrant. The appropriate laparoscopic port position for triangulation at the hiatus is shown in Fig. 16.1. It is important to ensure that the laparoscopic ports are placed high enough and slightly to the left on the patient's abdominal wall.

We use an 11 mm optical viewing trocar to obtain access to the peritoneal cavity and position this approximately 10 cm inferior to the xiphoid process and 2 cm lateral to midline (to the patient's left). Three additional working ports, 11 mm in the left upper quadrant right below the rib cage, 11 mm lateral in the left upper quadrant, and a 5 mm in right upper quadrant (which will go through the falciform ligament), and a Nathanson liver retractor are added through a 5 mm epigastric incision. The surgeon stands on the right side of the patient and operates through the two most cephalad ports. The assistant stands on the left side of the patient, running the camera and holding retraction through the left later port.

We begin the procedure at the level of the inferior edge of the spleen, by taking the short gastric vessels and entering the lesser sac. This allows for early transection of the short gastric vessels and mobilization of the gastric fundus. Dissection then is carried cephalad, and the left phreno-esophageal membrane is divided to expose the left crus. We then carry the dissection to the right crus. The gastro-hepatic ligament is divided, and the right phreno-esophageal membrane is opened to expose the right crus. A window is created behind the esophagus. Care is taken to preserve the anterior and posterior vagus nerves at all times during this mobilization. A Penrose drain is placed around the esophagus to facilitate the mediastinal dissection and assist with creation of the fundoplication.

The esophagus is mobilized in the mediastinum to obtain a minimum of 3 cm of intra-abdominal esophagus without any tension. The crura are approximated posteriorly with permanent sutures. In our practice we use 2-0 nonabsorbable V-lock to close the hiatus. Care must be taken to ensure straight orientation of the esophagus and a 54-56-Fr bougie in women, and a 56-60F bougie in men should easily pass beyond the esophageal hiatus into the stomach. At this point, the fundoplication is created.

Creation of a Partial Fundoplication

There are several types of partial fundoplications. The most commonly performed is the Toupet fundoplication. In this operation, the gastric and esophageal dissections, as well as the repair of the crura, are the same as for a 360° fundoplication. The fundoplication must be created with the fundus, and not the body, of the stomach.

The key difference between Toupet and Nissen fundoplication is that the stomach is positioned 180° to 270° in a Toupet fundoplication compared with 360° in a Nissen fundoplication around the posterior aspect of the esophagus. On both sides of the esophagus, the most cephalad sutures of the fundoplication incorporate the fundus and crus. The remaining sutures anchor the fundus to the esophagus.

If an anterior Dor fundoplication is to be performed, there is no need to disrupt the posterior attachments of the esophagus. We recreate the angle of His by approximating the medial fundus to the left crus and the esophagus on the left. Next the fundus is folded over the anterior aspect of the esophagus and anchored first to the right crus and then the esophagus.

Upon completion of the fundoplication, our standard practice is to perform an esophagogastroduodenoscopy (EGD) to evaluate the fundoplication. We ensure that the esophagus is straight, and the lower esophageal sphincter opens easily with insufflation. A retroflexion view is useful to evaluate the adequacy of the wrap and rule out presence of any redundant stomach above the wrap.

Postoperative Management

With the exception of patients with comorbid medical conditions requiring cardiac or pulmonary monitoring, postoperatively most patients are admitted to a general surgical floor for overnight observation. They are given a clear-liquid diet the evening of surgery, along with pain and nausea medications as needed. They are ambulated in the hallways with nursing assistance. The following morning, postoperative day 1, they are advanced to a full-liquid diet. Discharge requirements include tolerance of a diet to maintain hydration and nutrition, adequate pain control on oral analgesics, and ability to void without a Foley catheter. After discharge from the hospital, patients can gradually introduce soft, easy-to-swallow, and moist foods into their diet, avoiding difficult to swallow foods like bread, raw vegetables, and dry meats until their 2-week follow-up visit. We additionally advise all medications larger than a baby aspirin be in liquid form, crushed or opened during this time, and routinely have patients take simethicone with all meals to avoid troublesome gas bloat in the early postoperative period. Antacid therapy is held at discharge. Patients should expect to resume a diet without limitations in about 4 to 6 weeks.

Side Effects and Perioperative Complications

Laparoscopic antireflux surgery is a safe operation when performed by experienced surgeons. Thirty-day mortality rates are less than 1% [8]. Complication rates vary according to surgeon, technique, and extent of patient follow-up. Since 1993, using the National Inpatient Database, the rate of complications following surgery has fluctuated between 4.7% and 8.3% [9–11]. These complications are typically minor and not specific to antireflux procedures; these include urinary retention, wound infection, venous thrombosis, and ileus. Complications specific to antireflux surgery include capno-/pneumothorax, gastric/esophageal injury, splenic/liver injury, and bleeding. Additionally, antireflux surgery can result in postoperative side effects, including bloating and dysphagia.

Side Effects

It is not uncommon for patients to have mild, temporary dysphagia during the first 2 to 4 weeks postoperatively, thought to be a result of postoperative edema of the wrap and the closure of the esophageal hiatus. In the vast majority of these

patients, the dysphagia resolves spontaneously. A second, but less common, cause of dysphagia is a hematoma of the esophageal/gastric wall that develops as a result of the sutures used to create the fundoplication. Although this may create more severe dysphagia initially, patients are generally able to tolerate secretions and liquids; typically, dysphagia resolves over a few days. In either of these scenarios, surgeons should ensure that patients can maintain their nutrition and hydration on a liquid or soft diet, and additional interventions are rarely needed.

In the event of severe dysphagia and inability to tolerate liquids, a UGI should be obtained to ensure that no anatomic abnormality exists, such as an early hiatal hernia or obstruction at the esophagogastric junction. Assuming there is no early recurrent hiatal hernia or true obstruction and patients can tolerate liquids, an expectant management should be followed for 3 months. If patients cannot maintain hydration, or dysphagia persists beyond 3 months, another UGI should be obtained to ensure that there is no anatomic abnormality that could explain the dysphagia. If the UGI demonstrates an appropriately positioned fundoplication below the diaphragm, an EGD with dilation of the GEJ may provide relief.

Aerophagia – the normal swallowing of air – is the main factor leading to gastric distention, and the physiologic mechanism for venting this air is belching, occurring via vagal-mediated transient LES relaxation. Following antireflux surgery, patients have decreased belching due to fewer transient LES relaxations [12] and therefore can experience troublesome abdominal bloating. In a study on the impact of gas-related symptoms on the outcomes of both Nissen and Toupet fundoplications, Kessing and colleagues [13] found that preoperative belching and air swallowing were not predictive of postoperative gas-related symptoms, including bloating. They concluded gas-related symptoms to be caused by gastrointestinal hypersensitivity to gaseous distention. In this study, all patients experienced postoperative normalization of esophageal acid exposure. However, despite reflux resolution, patients who developed postoperative gas symptoms were less satisfied when compared with patients who did not experience these symptoms. We have found dietary and behavioral interventions such as the routine use of simethicone and avoiding chewing gum, straws, and carbonated beverages, particularly in the first few weeks after surgery, to be helpful.

During the early postoperative period, patients who report persistent nausea or demonstrate inadequate intake of a liquid diet should undergo an abdominal radiograph. If significant gastric distention is identified, a nasogastric tube can safely be placed to decompress the stomach for 24 hours. Few patients require further intervention for gastric bloating.

Perioperative Complications

Although capnothorax is one of the more common intraoperative complications, it is reported to occur in only approximately 2% of patients [14]. While postoperative chest radiographs are not routinely obtained, pleural violation should be identified intraoperatively, and the anesthesia team should be informed. The pleural violation results in intrathoracic infusion of carbon dioxide, which is absorbed rapidly. Because no underlying lung injury exists, the lung will re-expand without problems. When violation of the pleura is identified intraoperatively, the pleural should be reapproximated with a suture or endoloop if technically feasible, and a postoperative radiograph should be obtained. If a pneumothorax is identified on this radiograph, patients may be maintained on oxygen therapy to facilitate resolution. Unless patients experience shortness of breath or the need for persistent oxygen therapy to maintain oxygen saturation, no further radiographs are obtained.

Gastric and esophageal injuries rates in the literature are approximately 1% in patients undergoing minimally invasive antireflux surgeries [15–17]. These injuries tend to result from unnecessarily rough manipulation of these organs or during the passage of a bougie into the stomach: for these reasons we do not routinely use a bougie. Not surprisingly, injuries are more likely to occur in re-operative cases and should be rare

during initial operations. If identified at the time of operation, repair of these injuries can be performed with suture or stapled wedge resection, as appropriate, without sequelae. When the injury is not identified intraoperatively, patients commonly require a return to the operating room to repair the viscus, unless the leak is small and contained.

The incidence of splenic injury resulting in bleeding is about 2.3% in population-based studies, and major liver injury is rarely reported [17]. Although splenic bleeding is relatively uncommon and when it does occur, usually it is easily controlled with pressure and topical hemostatic agents, in rare cases, it can require splenectomy. Splenic parenchymal injury most commonly occurs during mobilization of the fundus and greater curvature of the stomach. This is one of the reasons we prefer to begin with the left crus approach, dividing the phreno-gastric ligament and the short gastric vessels early in the operation. Care must be taken during mobilization of the fundus to avoid excessive traction on the spleno-gastric ligament. Partial splenic infarction is another type of injury that can occur. This typically occurs during transection of the short gastric vessels and inadvertent coagulation of superior pole branch of the main splenic artery [18]. Partial splenic infarction rarely causes any symptoms, and it is generally well tolerated. Finally, lacerations and subcapsular hematomas of the left lateral section of the liver can be avoided by carefully retracting it out of the operative field using a fixed retractor.

Conclusions

Despite numerous randomized clinical trials and meta-analyses, there still remains controversy as to which fundoplication provides the most durable control of reflux and the best side-effect profile. A likely reason for this is that these studies vary in terms of patient characteristics, selection, and operative technique. The only consistent finding in these studies is that anterior fundoplications provide less durable control of GERD than posterior partial and total fundoplications. In our practice, we routinely use preoperative manometry to evaluate for esophageal dysmotility, and if present, we proceed with a Toupet fundoplication. In the presence of normal motility, we perform a Nissen fundoplication. An anterior (Dor) fundoplication is mostly used as an adjunct to a Heller myotomy. We follow all of our patients for the first 12 months and perform upper GI studies at their follow-up to better understand their individual outcomes. We also use postoperative symptom score questionnaires to help us better characterize our patients' outcomes.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. El-Serag HB, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut. 2014;63(6):871–80. https://doi.org/10.1136/gutjnl-2012-304269.
2. Soper NJ, Teitelbaum EN. Laparoscopic paraesophageal hernia repair: current controversies. Surg Laparosc Endosc Percutan Tech. 2013;23(5):442–5.
3. Stefanidis D, Hope WW, Kohn GP, Reardon PR, Richardson WS, Fanelli RD, et al. Guidelines for surgical treatment of gastroesophageal reflux disease. Surg Endosc. 2010;24(11):2647–69.
4. Booth MI, Stratford J, Jones L, et al. Randomized clinical trial of laparoscopic total (Nissen) versus posterior partial (Toupet) fundoplication for gastro-oesophageal reflux disease based on preoperative oesophageal manometry. Br J Surg. 2008;95(1):57–63.
5. Oleynikov D, Eubanks TR, Oelschlager BK, et al. Total fundoplication is the operation of choice for patients with gastroesophageal reflux and defective peristalsis. Surg Endosc. 2002;16(6):909–13.
6. Fein M, Seyfried F. Is there a role for anything other than a Nissen's operation? J Gastrointest Surg. 2010;14(Suppl 1):S67–74.
7. Shan CX, Zhang W, Zheng XM, et al. Evidence-based appraisal in laparoscopic Nissen and Toupet fundoplications for gastroesophageal reflux disease. World J Gastroenterol. 2010;16(24):3063–71.
8. Stefanidis D, Hope WW, Kohn GP, et al. Guidelines for surgical treatment of gastroesophageal reflux disease. Surg Endosc. 2010;24(11):2647–69.
9. Wang YR, Dempsey DT, Richter JE. Trends and perioperative outcomes of inpatient antireflux surgery in the United States, 1993–2006. Dis Esophagus. 2011;24(4):215–23.

10. Richter JE. Gastroesophageal reflux disease treatment: side effects and complications of fundoplication. Clin Gastroenterol Hepatol. 2013;11(5):465–71.
11. Cadiere GB, Himpens J, Rajan A, et al. Laparoscopic Nissen fundoplication: laparoscopic dissection technique and results. Hepato-Gastroenterology. 1997;44(13):4–10.
12. Bredenoord AJ, Draaisma WA, Weusten BL, et al. Mechanisms of acid, weakly acidic and gas reflux after anti-reflux surgery. Gut. 2008;57(2):161–6.
13. Kessing BF, Broeders JAJL, Vinke N, et al. Gas-related symptoms after antireflux surgery. Surg Endosc. 2013;27(10):3739–47.
14. Bizekis C, Kent M, Luketich J. Complications after surgery for gastroesophageal reflux disease. Thorac Surg Clin. 2006;16(1):99–108.
15. Collet D, Cadie're GB. Conversions and complications of laparoscopic treatment of gastroesophageal reflux disease. Formation for the Development of Laparoscopic Surgery for Gastroesophageal Reflux Disease Group. Am J Surg. 1995;169(6):622–6.
16. Hunter JG, Smith CD, Branum GD, et al. Laparoscopic fundoplication failures: patterns of failure and response to fundoplication revision. Ann Surg. 1999;230(4):595–604; (discussion: 604–6)
17. Watson DI, de Beaux AC. Complications of laparoscopic antireflux surgery. Surg Endosc. 2001;15(4):344–52.
18. Odabasi M, Abuoglu HH, Arslan C, et al. Asymptomatic partial splenic infarction in laparoscopic floppy Nissen fundoplication and brief literature review. Int Surg. 2014;99(3):291–4.

Management of Paraesophageal Hernia

17

Francisco Schlottmann, Marco Di Corpo, and Marco G. Patti

Introduction

Hiatal hernias (HH) are a common finding in the general population, and due to the progressive aging of patients, the number of HH is expected to increase in the future [1]. Interestingly, the real incidence of these hernias is unclear because many patients are asymptomatic, and the HH is diagnosed incidentally in the context of chest or abdominal imaging for unrelated conditions.

Hiatal hernias occur due to a progressive widening of the diaphragmatic esophageal hiatus and weakening of the phrenoesophageal membrane. Consequently, the stomach and other intra-abdominal organs may herniate through the diaphragmatic hiatus into the mediastinum.

Hiatal hernias are classified into four types (Fig. 17.1):

- *Type I* "sliding hernia": The esophagogastric junction (EGJ) herniates above the diaphragm into the mediastinum.
- *Type II*: A portion of the stomach is herniated into the mediastinum alongside a normally positioned (i.e., intra-abdominal) EGJ.
- *Type III*: The EGJ is above the hiatus, and a portion of the stomach is folded alongside the esophagus.
- *Type IV*: An intra-abdominal organ other than the stomach is additionally herniated through the hiatus.

Type I hernias are the most common and account for up to 95% of the total prevalence. Type II, III, and IV hernias are together termed paraesophageal hernias (PEH) and combined account for the remaining 5% of hiatal hernias.

Clinical Findings

As mentioned above, many patients remain asymptomatic, and their hernias are diagnosed accidentally. Large PEH, on the other hand, may cause a wide variety of symptoms such as epigastric discomfort, chest pain, postprandial bloating, dysphagia, or respiratory problems

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_17

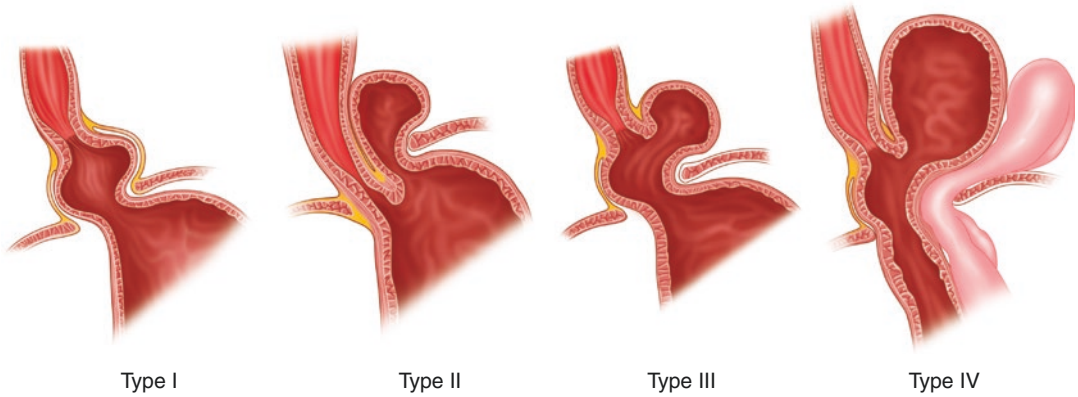


Fig. 17.1 Hiatal hernia classification

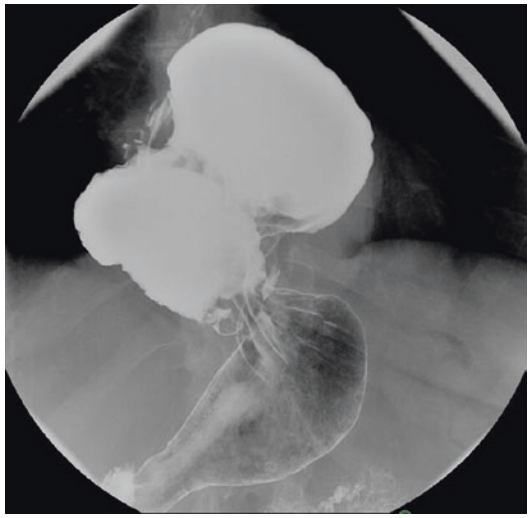


Fig. 17.2 Gastric volvulus

(asthma, cough, or dyspnea caused by chronic aspiration). In addition, patients may experience symptoms due to gastroesophageal reflux (heartburn or regurgitation). Anemia secondary to gastric erosions can also be present.

Rarely, patients may present with acute severe symptoms and potentially lethal complications such as volvulus, strangulation, incarceration, and perforation (Fig. 17.2).

Diagnosis

Several tests are needed preoperatively to determine the anatomy and physiology of the esophagus and stomach.

Barium Swallow

This study is critical in order to delineate the anatomy and the type of hiatal hernia. The ability to distinguish between different hernia types helps in determining the complexity of the operation (Fig. 17.3).

Upper Endoscopy

An upper endoscopy is also useful to determine if gastric or esophageal inflammation is present and to rule out cancer. Cameron ulcers are ulcerations of the mucosal folds lining the stomach due to extrinsic compression of the diaphragm on the distal neck of a hiatal hernia. Though typically asymptomatic, they may present as acute and severe upper gastrointestinal bleeding.

Abdominal and Chest CT Scan

This test is particularly important if the presence of a Type IV hernia is suspected (Fig. 17.4).

Esophageal Manometry

Abnormal esophageal motility is common in these patients. A partial fundoplication is preferred if there is severely impaired peristalsis. If the manometry is technically unfeasible or the

patient cannot tolerate the catheter, a partial fundoplication should also be performed**.**

Although patients with PEH usually have pathologic reflux, performing a pH monitoring study does not add relevant information preoperatively. The operation will alter the physiology of the EGJ, and a fundoplication to prevent reflux will be performed regardless of the results of the study.

Cardiac- and pulmonary-related tests are performed on a case-by-case basis, particularly because these patients are often elderly.

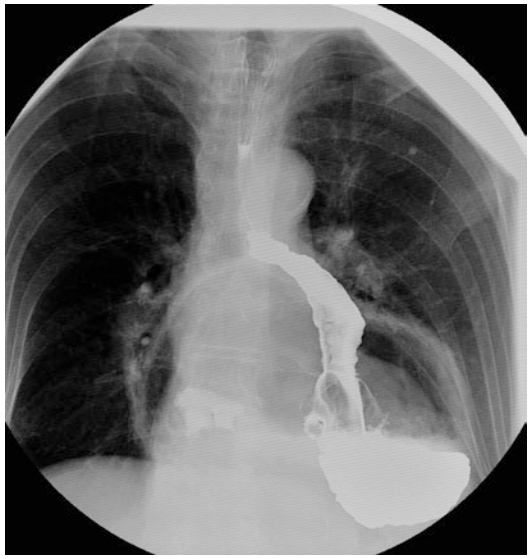


Fig. 17.3 Barium swallow showing a large paraesophageal hernia

Surgical Repair of PEH

Historically, surgical repair has been advocated in all patients with PEH, even when asymptomatic, due to the considerable mortality associated with acute hernia incarceration and strangulation. Currently, nonsurgical management is considered a better alternative in asymptomatic or minimally symptomatic patients because the risk of strangulation is lower than the risk of morbidity associated with the operation. Therefore, surgical repair is indicated mainly for symptomatic PEH [2].

Traditionally, PEH repair required either a laparotomy or thoracotomy, and these approaches were associated with high morbidity. Since its introduction in 1992, the laparoscopic approach has been increasingly embraced due to its improved postoperative outcomes [3, 4]. Nowadays, the vast majority of patients with PEH are managed with a laparoscopic approach.

Laparoscopic PEH Repair

Positioning of the Patient

After induction of general endotracheal anesthesia, an orogastric tube is inserted to keep the stomach decompressed. The patient is positioned supine in low lithotomy position with the lower extremities extended on stirrups, with knees flexed 20–30°. To avoid sliding due to the steep reverse Trendelenburg position used during the

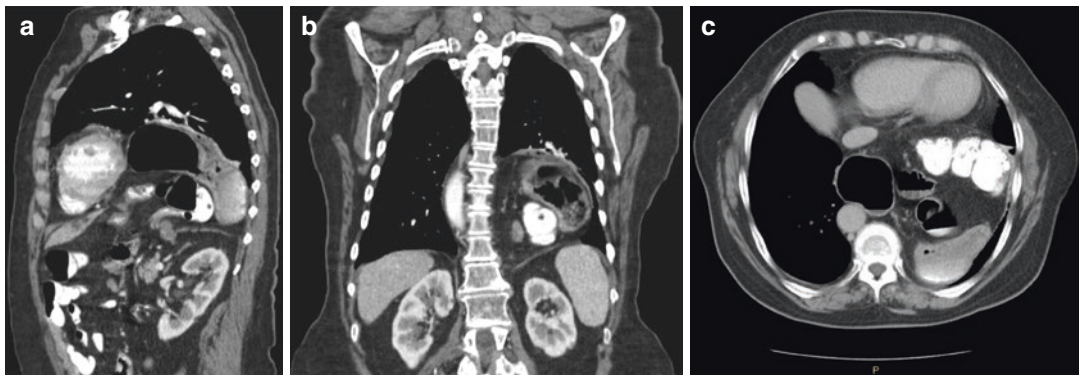


Fig. 17.4 Computed tomography showing a Type IV paraesophageal hernia; (**a**) sagittal plane; (**b**) coronal plane; (**c**) axial plane

entire procedure, a bean bag is inflated to create a "saddle" under the perineum. Pneumatic compression stockings and subcutaneous heparin are always used as prophylaxis against deep vein thrombosis (particularly important as the increased abdominal pressure secondary to the pneumoperitoneum and the steep Trendelenburg position decrease venous return). The surgeon stands between the patient's legs and the first and second assistants on the left and right side of the operating table, respectively.

Trocar Placement

Five 10-mm ports are used for the procedure: one for the camera, two for the operating surgeon, one for the assistant, and one for the liver retractor. The first port is usually placed in the midline about 14 cm below the xiphoid process; it can be also placed slightly to the left of the midline to be in line with the esophagus. This port is used for insertion of the scope. The second port is placed in the left midclavicular line at the same level of port 1, and it is used for the insertion of a Babcock clamp for traction, a grasper to hold the Penrose drain while surrounding the esophagus, or for devices used to divide the short gastric vessels. The third port is placed in the right midclavicular line at the same level of the other two ports, and it is used for the liver retractor. The fourth and fifth ports are placed under the right and left costal margins so that their axes and the camera form an angle of about 120°. These ports are used for the insertion of dissecting and suturing instruments (Fig. 17.5).

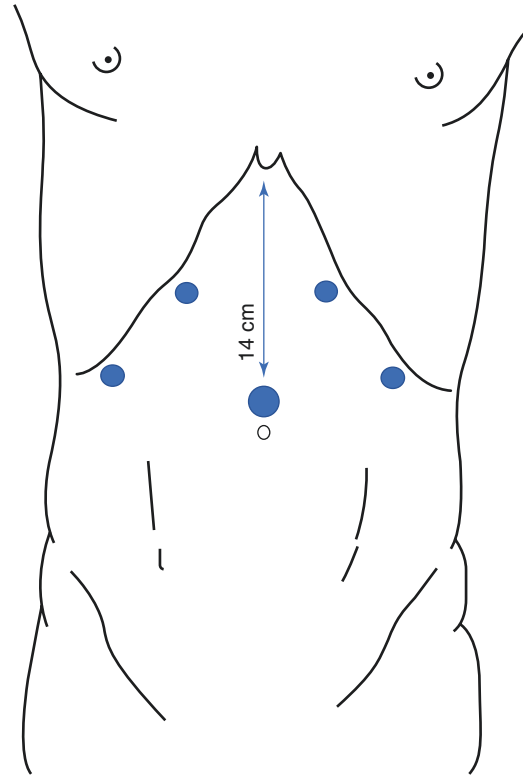


Fig. 17.5 Ports placement for laparoscopic paraesophageal hernia repair

Dissection and Reduction of Hernia Sac

Reduction of the stomach into the abdominal cavity is done by gently pulling the herniated stomach out of the posterior mediastinum down into the abdomen using a Babcock clamp. The dissection is started along the greater curvature, the short gastric vessels are divided, and the left pillar of the crus is reached. The hernia sac is then incised at the junction with the left crus, and an anterior and lateral mobilization of the esophagus is performed. Once the initial dissection from the left has been completed and more stomach is reduced, the gastrohepatic ligament is opened toward the right pillar of the crus, and the esophagus is further dissected in the posterior mediastinum. A posterior window behind the esophagus is created and a Penrose drain is placed around the esophagus incorporating both the anterior and posterior vagus nerves. The hernia sac is then freed from mediastinal adhesions by blunt dissection (Fig. 17.6).

Key Note Excessive force should be avoided during the reduction of the stomach to prevent gastric injury or perforation. Starting the dissection along the greater curvature of the stomach by dividing the short gastric vessels reduces the risk of injury of an accessory left hepatic artery that can occur if the dissection is started over the gastrohepatic ligament (can be challenging to control the resultant bleeding if the arterial stump retracts above the diaphragm into the mediastinum). During the dissection of the hernia sac, the pleura can be injured in both sides. The anesthesiologist should be informed in case of pleural opening, and in case of capnothorax that results in hypotension or increased airways pressure, the

reduction in insufflation pressure usually corrects these abnormalities.

Esophageal Mobilization

The mediastinal dissection is extended proximally to have at least 3 cm of the esophagus below the diaphragm without tension. This limits the risk of recurrence and returns the EGJ to its most physiologic location.

Key Note After extended mobilization of the esophagus in the posterior mediastinum, the presence of a short esophagus is rare. Therefore, esophageal lengthening procedures (e.g., stapled-wedge gastroplasty) are rarely needed.

Closure of the Esophageal Hiatus

Proper exposure of the hiatus is obtained by retraction of the esophagus upward and toward the patient's left with the Penrose drain (Fig. 17.7). The closure of the diaphragmatic crura is done with interrupted nonabsorbable sutures (2-0 silk). This first stitch is placed about 1 cm posterior to the esophagus. Subsequent stitches are placed below the first one. Usually only posterior sutures are necessary, but sometimes one or two additional stitches anterior to the esophagus are needed to further narrow the hiatus (Fig. 17.8).

As the hiatus is often very large, the closure of the crura can be under tension. If there is considerable tension placed on the closure, a relaxing incision on the right hemidiaphragm (incision just lateral to the right crus) can help to approximate the right crus with the left one. If this is performed, a mesh patch over the resulting diaphragmatic defect is needed (Fig. 17.8).

Key Note To mesh or not to mesh? The use of a nonabsorbable mesh is not recommended due to serious complications such as mesh erosion into the esophagus or the aorta. Biological meshes with absorbable material are a safer alternative. In 2006, a randomized trial showed a significant reduction of the 6-month recurrence rate with the use of a biologic prosthesis as compared to cruroplasty alone (9 vs. 24%) [5]. The same study group, however, reported later a similar 5-year recurrence rate between the two groups (54 vs. 59%) [6]. Therefore, we do not recommend the routine use of mesh, and its use should rather be reserved for selected patients (e.g., patients in whom a tension-free cruroplasty cannot be achieved or redo PEH repair).

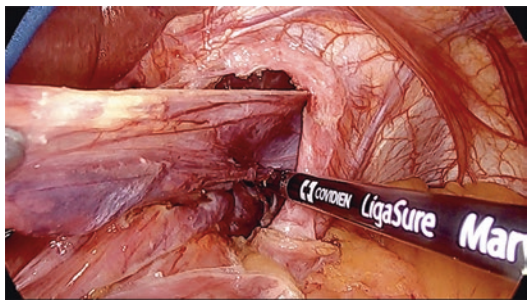


Fig. 17.6 Dissection and reduction of the hernia sac

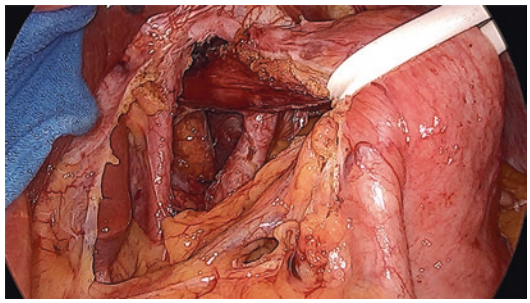


Fig. 17.7 Exposure of the hiatus

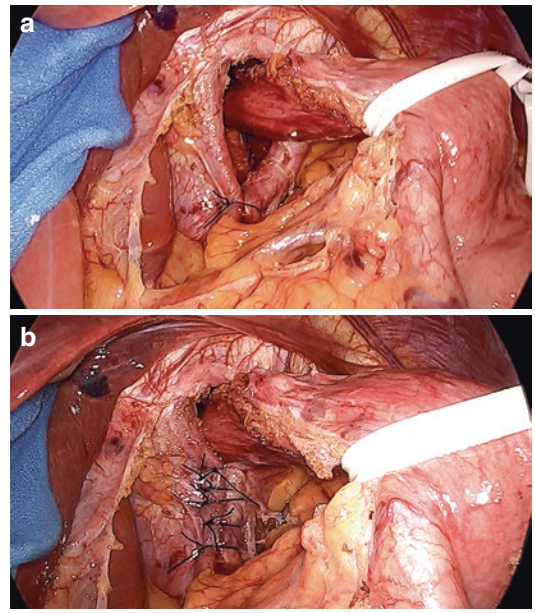


Fig. 17.8 (**a**, **b**) Closure of the esophageal hiatus

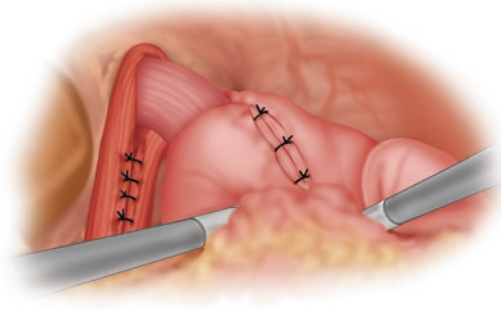


Fig. 17.9 Total 360° fundoplication

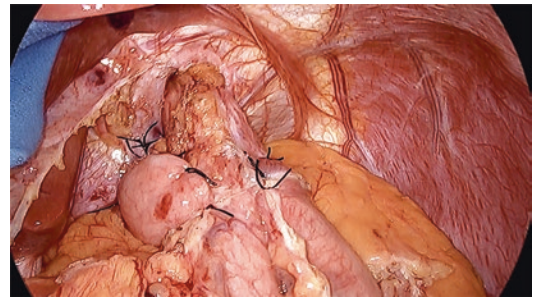


Fig. 17.10 Toupet fundoplication

Fundoplication

The fundoplication is key to either treat gastroesophageal reflux present preoperatively or prevent the development of postoperative reflux secondary to the extensive dissection of the gastroesophageal junction. In addition, the fundoplication helps anchoring the stomach below the diaphragm.

The stomach is passed behind the esophagus and a shoeshine maneuver is performed to verify sufficient fundic mobilization and to avoid having part of the gastric fundus above the wrap. For a total 360° fundoplication, a 56 French bougie is inserted down the esophagus into the stomach to prevent postoperative dysphagia. Then, the gastric fundus is pulled under the esophagus with two graspers, and the left and right sides of the fundus are wrapped above the esophagogastric junction. A Babcock clamp is used to hold the two sides of the fundus during the placement of the first stitch. A 360° fundoplication is created by placing three stitches of nonabsorbable material at 1-cm intervals to approximate the right and left side of the fundoplication. The length of the anterior portion of the fundoplication should be approximately 2 cm (Fig. 17.9).

The partial posterior 240° fundoplication (Toupet fundoplication) is created by placing six stitches of nonabsorbable material. The right and left sides of the fundus are separately sutured to the right and left side of the esophagus, leaving 120° of the anterior esophageal wall uncovered (Fig. 17.10).

Key Note Care must be taken to avoid having a wrap under tension. For instance, if the wrap does not remain in the right side after pulling the fundus under the esophagus and retracts back to the left, a partial fundoplication is preferred.

Postoperative Care

Patients start with clear liquids and then soft diet the morning after the procedure. They are usually discharged after 24 to 48 hours, and they are instructed to avoid meat, bread, and carbonated beverages for the following 2 weeks. The time to full recovery ranges between 2 and 3 weeks.

References

1. Davis SS Jr. Current controversies in paraesophageal hernia repair. Surg Clin North Am. 2008;88(5):959–78.
2. Dallemagne B, Quero G, Lapergola A, et al. Treatment of giant paraesophageal hernia: pro laparoscopic approach. Hernia. 2018;22(6):909–19.
3. Cuschieri A, Shimi S, Nathanson LK. Laparoscopic reduction, crural repair, and fundoplication of large hiatal hernia. Am J Surg. 1992;163(4):425–30.
4. Schlottmann F, Strassle PD, Farrell TM, et al. Minimally invasive surgery should be the standard of care for paraesophageal hernia repair. J Gastrointest Surg. 2017;21(5):778–84.
5. Oelschlager BK, Pellegrini CA, Hunter J, et al. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. Ann Surg. 2006;244(4):481–90.
6. Oelschlager BK, Pellegrini CA, Hunter JG, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. J Am Coll Surg. 2011;213(4):461–8.

18

Surgery in the Morbidly Obese Patient with Gastroesophageal Reflux Disease (GERD)

Marco Di Corpo, Francisco Schlottmann, and Marco G. Patti

Introduction

Gastroesophageal reflux disease (GERD) is described as symptoms and mucosal injury that are caused by the reflux of gastric contents into the esophagus. Its prevalence has been increasing in the Western world, estimated to be today between 10 and 20%, with a lower prevalence in Asia [1]. An important risk factor for GERD is obesity, which is associated with adverse metabolic, cardiovascular, chronic inflammatory, and malignant problems. Bariatric surgery has been used more often during the last 10 years as it has been shown to be safe and effective in determining weight loss and decreasing or resolving comorbidities [2].

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

F. Schlottmann
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti (✉)
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA
e-mail: marco_patti@med.unc.edu

The American Medical Association now recognizes obesity, defined as a body mass index (BMI) of 30 or higher, as a chronic multisystem disease which is associated with multiple anatomical, physiological, and psychological consequences [3]. It has been shown that a high BMI increases the risk of GERD symptoms, erosive esophagitis, Barrett's esophagus, and adenocarcinoma and that there is a dose-response relationship between increasing BMI and prevalence and severity of GERD and its complications [4, 5]. Therefore, unlike nonobese patients with GERD, bariatric surgery still remains the recommended treatment for GERD in the morbidly obese population [6]. Proper understanding of the pathophysiological mechanisms underlying GERD in obese patients is essential for planning the correct operation and achieving a successful outcome [7, 8].

This chapter reviews the surgical management of morbidly obese patients with GERD.

GERD in Obese Patients

The global pandemic of obesity and its associated comorbidities has become a major public health concern. Over the last four decades, worldwide prevalence of obesity has increased from 3 to 10% in men and from 6 to 15% in women [9]. In 2016, the prevalence of obesity in the United States increased from 33.7 to 39.6%, particularly among women and individuals 40 years or older [10].

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_18

Obesity is a well-established risk factor for developing GERD and its related complications (esophagitis, Barrett's esophagus, and esophageal adenocarcinoma). Thus, GERD is present in a large number of patients who are considered for bariatric surgery [7]. Interestingly, the pathophysiology of GERD in morbidly obese patients is multifactorial and different from that of lean individuals (Table 18.1). Data from 24-hour pH monitoring studies show that an increase of 5 kg/m^2 in the BMI leads to a 3-point increase in the DeMeester score [5]. Moreover, El-Serag et al. showed that for each 1-point increase in the BMI, the gastric/abdominal pressure (AP) is expected to increase 10% [11]. This increase in intra-abdominal pressure determines and increase gradient between the abdomen and the chest, the so-called transdiaphragmatic pressure gradient (TDPG). The difference in pressure between the positive gastric pressure and the negative esophageal/thoracic pressure (TP) may exceed the pressure of the esophagogastric barrier represented by the lower esophageal sphincter (LES) and the diaphragm. As a consequence, obese patients have a higher risk of developing GERD [12]. In addition, about 70% of patients have obstructive sleep apnea, which determines a more negative intrathoracic pressure, therefore increasing the TDPG and promoting reflux [13]. This increased intra-abdominal pressure also disrupts the integrity of the gastroesophageal junction, determining the presence of a hiatal hernia (present in about 40% of morbidity obese patients), which contributes to the presence and severity of reflux [12, 14, 15].

Table 18.1 Pathophysiology of GERD in obese and lean patients

Pathophysiology of GERD	
Lean patients	Obese patients
TLESR	Worse esophageal clearance (hyposalivation)
Hiatal hernia	Lower TP (obstructive sleep apnea)
	Higher AP (increased waist circumference and BMI)
	Higher TDPG
	Acid pocket (postprandial reflux)
	Altered esophageal motility
	Overfeeding gastric distention and increased number of TLESR

LES lower esophageal sphincter, *TLESR* transient lower esophageal relaxation, *TP* thoracic pressure, *AP* abdominal pressure, *TDPG* transdiaphragmatic pressure gradient

Diagnosis and Workup

A proper workup of patients with symptoms suggestive of GERD is essential for a correct diagnosis and for planning treatment. The goal of the evaluation is to confirm the presence of reflux, to correlate the reflux episodes with symptoms, to identify anatomical and functional abnormalities, and lastly to recognize complications due to reflux.

Surgical Options

Laparoscopic Antireflux Surgery (LARS)

A laparoscopic Nissen fundoplication (360°) is a durable and effective operation that controls the abnormal reflux in most patients [16]. It is considered today the procedure of choice because it increases the resting pressure and length of the LES, decreases the number of transient LES relaxations, and improves the quality of esophageal peristalsis. However, outcomes in morbidly obese patients may be not as good as in non-obese patients because this procedure does not induce weight loss, does not decrease the transdiaphragmatic pressure gradient, and does not improve the comorbid conditions [17, 18]. In addition, many studies have shown that LARS in obese patients results in longer operative times, longer length of stay [19–21], and is associated with a higher incidence of postoperative complications (i.e., recurrence of reflux and hiatal hernia [20, 22]). Performing a bariatric procedure after a previous fundoplication is more challenging and often associated to complications (morbidity for a laparoscopic gastric bypass performed after a fundoplication can reach 43%) [18]. In addition, it may have detrimental effects on the overall

well-being of obese patients, as their comorbidities will not improve over time if a gastric bypass is not performed [23].

Overall, while LARS addresses most of the pathophysiological mechanisms of GERD, it does not affect the increased intra-abdominal pressure found in morbidly obese patients (whose weight promotes retrograde flow of gastric contents into the esophagus) leading to worse outcomes. Hence, if a fundoplication is chosen, behavioral modification and significant weight loss are essential before the operation in order to minimize poor outcomes [24].

Bariatric Surgery

The most frequently used bariatric procedures include the sleeve gastrectomy (SG) and the Roux-en-Y gastric bypass (RYGB). These procedures have been shown to be effective in achieving significant weight loss (the primary goal) and improving associated comorbidities [25, 26].

Sleeve Gastrectomy

Sleeve gastrectomy is becoming the most frequently used restrictive bariatric procedure. The stapling of the stomach from the prepyloric area to the angle of His creates a tubular stomach with decreased reservoir function. In addition, removal of a large part of the gastric fundus leads to decreased levels of ghrelin (Fig. 18.1) [27].

In 2011, Miguel et al. [28] reported the results of a nonrandomized, prospective, controlled clinical study including 65 patients with a 1-year follow-up, analyzing the influence of SG and RYGB on erosive esophagitis. At baseline, 6 of 33 (18%) patients in the SG group and 9 of 32 (28%) patients in the RYGB group had endoscopically visible esophageal erosions (P = NS). One year following the bariatric intervention, the percentage of patients with erosive esophagitis rose in the SG group to 14 of 31 (45%) and decreased in the gastric bypass group to 2 of 32 (6%) ($p < 0.001$). Based on these findings, the authors concluded that SG increases the incidence of erosive esophagitis, whereas RYGB improves the mucosal damage.

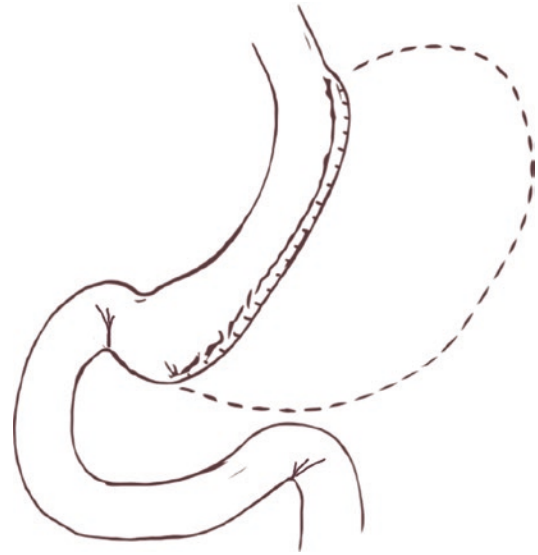


Fig. 18.1 Sleeve gastrectomy

There is evidence that the SG not only worsens symptoms and esophagitis in patients with pre-existing GERD, but it also induces "de novo" GERD in many patients [29–32]. Probably, this is due to the effect that a SG has on the antireflux mechanism: development of a hypotensive LES (by damaging the sling fibers and angle of His), decreasing the gastric compliance, and increasing the intragastric pressure (secondary to creation of a narrow gastric tube). Mandeville et al. [29] analyzed 100 consecutive patients who underwent SG between 2005 and 2009, with a mean follow-up of 8.5 years. At the end of the study period, they noted that 52% of patients experienced reflux symptoms, 47% were using proton pump inhibitors, and 7 patients underwent secondary bariatric surgery (RYGB) due to GERD refractory to treatment, achieving complete resolution of symptoms. Gorodner et al. [30] analyzed 118 patients who underwent SG between 2012 and 2013. At 1-year follow-up, the DeMeester score increased from 12.6 in the preoperative period to 28.4 postoperatively ($p < 0.05$), 5 (36%) patients had de novo GERD, and in 3 patients (21%), GERD worsened. Genco et al. [31], in a large study with a 5-year follow-up, showed that the mean BMI decreased from 46 to 29, but postoperatively erosive esophagitis

(Los Angeles [LA] grade C and D) developed in 21% of patients and Barrett's metaplasia in 17%. Interestingly, GERD symptoms were experienced only by 33% of patients with LA grade C esophagitis and by 57% of patients with LA grade D esophagitis. Hence, as symptoms are not reliable to evaluate the presence/absence of GERD, SG patients should have a closer follow-up, including esophagogastroduodenoscopy (EGD) surveillance due to the risk of developing Barrett's esophagus [32].

Recently, two randomized multicenter trials performed in Finland and in Switzerland, with 5-year follow-up, have confirmed that the RYGB and the SG are equivalent in terms of weight loss [33, 34]. Both trials highlighted that the most common reason for an operation after a SG was severe gastroesophageal reflux refractory to medical treatment, requiring conversion to a RYGB.

In summary, currently available data indicate an increased prevalence of esophageal erosions and de novo GERD in patients undergoing SG. Thus, morbidly obese patients with GERD should not undergo SG. In addition, SG patients with documented GERD should be considered for conversion to a RYGB if symptoms are poorly controlled by proton pump inhibitors and if esophagitis is present.

Roux-en-Y Gastric Bypass

RYGB involves creating a small gastric pouch, followed by a gastrojejunostomy between this pouch and a 100–150-cm-long Roux loop. The procedure is highly effective for weight loss [33, 34], as documented by initial studies in the mid-1970s (Fig. 18.2) [35].

RYGB is considered the preferred bariatric procedure to treat GERD in morbidly obese patients [36] because this operation does not disrupt the natural antireflux mechanism, creates a small gastric pouch with few parietal cells (decreasing acid output), and diverts bile from the stomach. In addition, gastric emptying seems to be accelerated after RYGB [37] and esophageal motility not altered, independent of weight loss occurrence [38, 39]. Braghetto et al. showed

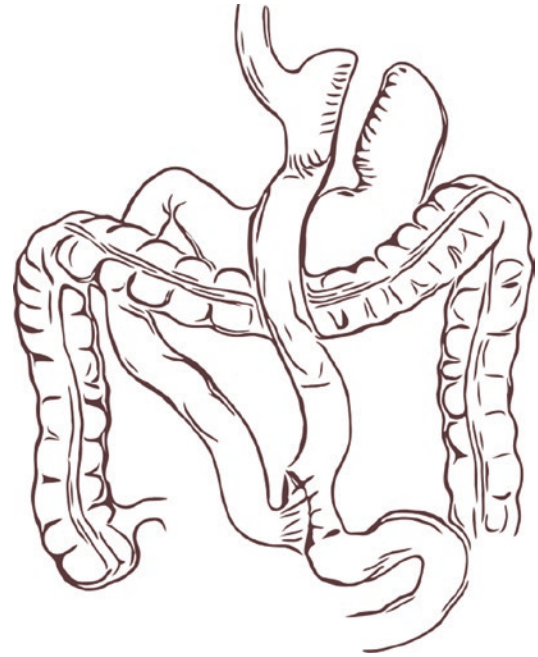


Fig. 18.2 Roux-en-Y gastric bypass

that RYGB reduces body weight and improves GERD and Barrett's esophagus when compared to antireflux surgery [40].

Langer et al. [41] published a report on conversion from SG to RYGP. Eight of 73 (11%) patients with SG underwent conversion to RYGP because of severe reflux ($N = 3$) confirmed by pH monitoring or because of weight loss failure ($N = 5$) about 3 years after laparoscopic SG. At a median follow-up of 14 months, conversion led to a significant weight reduction (15 ± 8 kg) in patients reoperated for weight loss failure and improved reflux in the three patients who had severe reflux. Patients with reflux symptoms after SG were able to discontinue acid-suppressive medication after conversion to RYGP.

Mejia-Rivas et al. [42] investigated the effect of RYGB on GERD in 20 patients using manometry and 24-h pH monitoring, and they observed resolution of symptoms in 90% of the patients. On esophageal manometry, LES pressure was slightly increased postoperatively, being 18 ± 11 and 20.1 ± 5.6 mmHg before and after the RYGBP, respectively (p = NS). On pH monitoring,

the DeMeester score significantly decreased from 48.3 to 7.7 ($p < 0.001$). Only one patient (5%) had persistent heartburn and abnormal esophageal acid. They concluded that weight reduction after a RYGBP improves reflux symptoms and esophageal exposure to acid.

Furthermore, Csendes et al. [43] performed preoperative and postoperative EGDs on 130 patients undergoing RYGB. Before surgery, distal erosive esophagitis was present in 23.8% of patients. Postoperative, at a mean follow-up of 92 months, EGDs showed that esophagitis had healed in 93% of these patients.

In summary, studies investigating gastroesophageal reflux in patients undergoing RYGB show significant improvement of erosive esophagitis and reflux symptoms. In addition, evidence suggest that conversion of SG to RYGB is successful in treating newly developed reflux symptoms and weight loss failure.

Hiatal Hernia and Bariatric Surgery

If a hiatal hernia is present, it should be addressed as this does not add morbidity or increase operative time significantly [44]. Hiatal hernia repair may help in controlling regurgitation in patients with this symptom preoperatively [45, 46].

Conclusion

The choice of the procedure should be tailored to the results of a methodical workup and should not be left to patient's or surgeon's preference. LARS may be more difficult and has worse outcomes in morbidly obese patients. Among the bariatric operations, SG is not the optimal operation for obese patients when GERD is present preoperatively. Follow-up after SG should focus not only on weight loss and comorbidities resolution, but also on detection and treatment of GERD. The preferred treatment modality for morbidly obese patients with GERD nonresponsive to medications is the Roux-en-Y gastric bypass [47].

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. Am J Gastroenterol. 2013;108:308–28; quiz 329.
2. Schlottmann F, Herbella FAM, Patti MG. Bariatric surgery and gastroesophageal reflux. J Laparoendosc Adv Surg Tech A. 2018;28(8):953–5.
3. American Medical Association House of Delegates. Recognition of obesity as a disease. 2013. Accessible at http://www.npr.org/documents/2013/jun/ama-resolution-obesity.pdf.
4. Hampel HH, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. Ann Intern Med. 2005;143:199–211.
5. Herbella FA, Sweet MP, Tedesco P, et al. Gastroesophageal reflux disease and obesity. Pathophysiology and implications for treatment. J Gastrointest Surg. 2007;11:286–90.
6. Fisichella PM, Patti MG. Gastroesophageal reflux disease and morbid obesity: is there a relation? World J Surg. 2009;33(10):2034–8.
7. Nadaleto BF, Herbella FA, Patti MG. Gastroesophageal reflux disease in the obese: pathophysiology and treatment. Surgery. 2016;159(2):475–86.
8. Andolfi C, Fisichella PM. Epidemiology of obesity and associated comorbidities. J Laparoendosc Adv Surg Tech A. 2018;28(8):919–24.
9. NCD Risk Factor Collaboration (NCD-RisC). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016;387:1377–96.
10. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007–2008 to 2015–2016. JAMA. 2018;319(16):1723–5.
11. El-Serag HB, Tran T, Richardson P, Ergun G. Anthropometric correlates of intragastric pressure. Scand J Gastroenterol. 2006;41:887–91.
12. Del Grande LM, Herbella FAM, Katayama RC, Schlottmann F, Patti MG. The role of the Transdiaphragmatic pressure gradient in the pathophysiology of gastroesophageal reflux disease. Arq Gastroenterol. 2018;55Suppl 1:13–7. pii: S0004-28032018005002102.
13. Frey WC, Pilcher J. Obstructive sleep-related breathing disorders in patients evaluated for bariatric surgery. Obes Surg. 2003;13:676–83.
14. Che F, Nguyen B, Cohen A, Nguyen NT. Prevalence of hiatal hernia in the morbidly obese. Surg Obes Relat Dis. 2013;9:920–5.
15. Patti MG, Goldberg HI, Arcerito M, et al. Hiatal hernia size affects the lower esophageal sphincter function, esophageal acid exposure, and the degree of mucosal injury. Am J Surg. 1996;171:182–6.

16. Bello B, Herbella FA, Allaix ME, Patti MG. Impact of minimally invasive surgery on the treatment of benign esophageal disorders. World J Gastroenterol. 2012;18:6764–70.
17. Morgenthal CB, Lin E, Shane MD, Hunter JG, Smith CD. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. Surg Endosc. 2007;21:1978–84.
18. Perez AR, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. Surg Endosc. 2001;15:986–9.
19. Tandon A, Rao R, Hotouras A, Nunes QM, Hartley M, Gunasekera R, Howes N. Safety and effectiveness of antireflux surgery in obese patients. Ann R Coll Surg Engl. 2017;99(7):515–23.
20. Tekin K, Toydemir T, Yerdel MA. Is laparoscopic antireflux surgery safe and effective in obese patients? Surg Endosc. 2012;26:86–95.
21. Schietroma M, Piccione F, Clementi M, et al. short- and long-term, 11–22 years, results after laparoscopic nissen fundoplication in obese versus nonobese patients. J Obes. 2017;2017:7589408.
22. Abdelrahman T, Latif A, Chan DS, Jones H, Farag M, Lewis WG, Havard T, Escofet X. Outcomes after laparoscopic anti-reflux surgery related to obesity: a systematic review and meta-analysis. Int J Surg. 2018;51:76–82.
23. Fisichella PM, Patti MG. GERD procedures: when and what? J Gastrointest Surg. 2014;18(11):2047–53.
24. Khan A, Kim A, Sanossian C, Francois F. Impact of obesity treatment on gastroesophageal reflux disease. World J Gastroenterol. 2016;22(4):1627–38.
25. Hariri K, Guevara D, Dong M, Kini SU, Herron DM, Fernandez-Ranvier G. Is bariatric surgery effective for co-morbidity resolution in the super-obese patients? Surg Obes Relat Dis. 2018;14:1261–8.
26. Wong AM, Barnes HN, Joosten SA, Landry SA, Dabscheck E, Mansfield DR, Dharmage SC, Senaratna CV, Edwards BA, Hamilton GS. The effect of surgical weight loss on obstructive sleep apnoea: a systematic review and meta-analysis. Sleep Med Rev. 2018;42:85–99.
27. Langer FB, Reza Hoda MA, Bohdjalian A, et al. Sleeve gastrectomy and gastric banding: effects on plasma ghrelin levels. Obes Surg. 2005;15:1024–9.
28. Miguel GP, Azevedo JL, de Souza PH, et al. Erosive esophagitis after bariatric surgery: banded vertical gastrectomy versus banded Roux-en-Y gastric bypass. Obes Surg. 2011;21:167–72.
29. Mandeville Y, Van Looveren R, Vancoillie PJ, et al. Moderating the enthusiasm of sleeve gastrectomy: up to fifty percent of reflux symptoms ten years in a consecutive series of 100 laparoscopic sleeve gastrectomies. Obes Surg. 2017;27:1797–803.
30. Gorodner V, Buxhoeveden R, Clemente G, Solé L, Caro L, Grigaites A. Does laparoscopic sleeve gastrectomy have any influence on gastroesophageal reflux disease? Preliminary results. Surg Endosc. 2015;29(7):1760–8.
31. Genco A, Soricelli E, Casella G, et al. Gastroesophageal reflux disease and Barrett's esophagus after laparoscopic sleeve gastrectomy: a possible, underestimated long-term complication. Surg Obes Relat Dis. 2017;13:568–74.
32. Gorodner V, Viscido G, Signorini F, Obeide L, Moser F. Gastroesophageal reflux disease and morbid obesity: evaluation and treatment. Updates Surg. 2018;70:331–7.
33. Salminen P, Helmio M, Ovaska J, et al. Effect of laparo- scopic sleeve gastrectomy vs laparoscopic Roux-en-Y gas- tric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. JAMA. 2018;319:241–54.
34. Peterli R, Wolnerhanssen BK, Peters T, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en- Y gastric bypass on weight loss at 5 years among patients with morbid obesity: the SM-BOSS randomized clinical trial. JAMA. 2018;319:255–65.
35. Mason EE, Printen KJ, Hartford CE, Boyd WC. Optimizing results of gastric bypass. Ann Surg. 1975;182:405–14.
36. Pagé MP, Kastenmeier A, Goldblatt M, et al. Medically refractory gastro- esophageal reflux disease in the obese: what is the best surgical approach? Surg Endosc. 2014;28:1500–4.
37. Wang G, Agenor K, Pizot J, Kotler DP, Harel Y, Van Der Schueren BJ, et al. Accelerated gastric emptying but no carbohydrate malabsorption 1 year after gastric bypass surgery (GBP). Obes Surg. 2012;22:1263–7.
38. Valezi AC, Herbella FA, Junior JM, de Almeida Menezes M. Esophageal motility after laparoscopic Roux-en-Y gastric bypass: the manometry should be preoperative examina- tion routine? Obes Surg. 2012;22:1050–4.
39. Tutuian R. Obesity and GERD: pathophysiology and effect of bariatric surgery. Curr Gastroenterol Rep. 2011;13(3):205–12.
40. Braghetto I, Korn O, Csendes A, et al. Laparoscopic treatment of obese patients with gastroesophageal reflux disease and Barrett's esophagus: a prospective study. Obes Surg. 2012;22(5):764–72.
41. Langer FB, Bohdjalian A, Shakeri-Leidenmühler S, et al. Conversion from sleeve gastrectomy to Roux-en-Y gastric bypass–indications and outcome. Obes Surg. 2010;20:835–40.
42. Mejia-Rivas MA, Herrera-Lopez A, Hernandez-Calleros J, Herrera MF, Valdovinos MA. Gastroesophageal reflux disease in morbid obesity: the effect of Roux-en-Y gastric bypass. Obes Surg. 2008;18(10):1217–24.
43. Csendes A, Smok G, Burgos AM, Canobra M. Prospective sequential endoscopic and histologic studies of the gastric pouch in 130 morbidly obese patients submitted to Roux-en-Y gastric bypass. Arq Bras Cir Dig. 2012;25(4):245–9.
44. Soricelli E, Iossa A, Casella G, Abbatini F, Calı B, Basso N. Sleeve gastrectomy and crural repair in obese patients with gastroesophageal reflux disease and/or hiatal hernia. Surg Obes Relat Dis. 2013;9:356–61.

45. Oliveira DR. Incidence of regurgitation after the banded gastric bypass. Obes Surg. 2005;15:1408–17.
46. Mahawar KK, Carr WR, Jennings N, Balupuri S, Small PK. Simultaneous sleeve gastrectomy and hiatus hernia repair: a systematic review. Obes Surg. 2015;25:156–66.
47. Madalosso CA, Gurski RR, Callegari-Jacques SM, Navarini D, Thiesen V, Fornari F. The impact of gastric bypass on gastroesophageal reflux disease in patients with morbid obesity: a prospective study based on the Montreal Consensus. Ann Surg. 2010;251:244–8.

GERD: Other Treatment Modalities

19

Amelia Dorsey and Mary Hawn

Introduction

The treatment of gastroesophageal reflux disease (GERD) has historically been dominated by diet and lifestyle modifications in concert with two therapeutic options: medications or surgery. Medications such as antacids, histamine receptor (H2) blockers, and proton pump inhibitors (PPIs) are the mainstay of treatment; however, studies have shown that as many as 30–40% of patients fail to completely respond to medical therapy for GERD [1]. Of the nonresponders, only approximately 5% pursue surgical intervention for their disease. For all patients with GERD, less than 1% undergo surgical treatment [2]. Of the surgical options for GERD, the laparoscopic Nissen fundoplication (NF) is the gold standard [3–5] as it restores the anti-reflux barrier [6] with documented long-term success [7, 8]. Despite the efficacy of the NF, with >90% of patients achieving symptom relief [1, 3, 4], many patients are reluctant to undergo this operation. Barriers to surgery include fear of the perceived invasiveness of the operation itself and reservations about side effects including dysphagia, inability to burp, bloating, flatulence, diarrhea, and possible recurrence of symptoms requiring re-intervention [9–13]. Additionally, the operation requires general anesthesia and a 1–2-day hospital stay, which pose additional considerations to those who are contemplating surgical intervention for GERD. Complicating lifelong medical management of GERD are the emerging concerns regarding long-term use of PPIs including risks of bone fracture, malabsorption (of calcium, vitamin B12, iron, and magnesium), bacterial overgrowth and infection including diarrhea secondary to *Clostridium difficile*, and hospitalization with community-acquired pneumonia [14–18]. Due to the substantial percentage of refractory GERD despite high-dose PPIs, emerging concerns regarding the long-term use of PPIs, and the small percentage of patients pursuing surgical interventions, there remains a GERD treatment gap with many patients not achieving symptomatic relief [19, 20].

There are a variety of novel endoscopic and laparoscopic minimally invasive techniques that strive to fill the treatment gap between PPIs and NF for GERD patients. The ideal technique to bridge this gap should be more effective than medications while also being less invasive and easier to perform than NF with fewer side effects [6]. These innovative techniques include, but are not limited to, Stretta® Endoscopic Radiofrequency Ablation System, transoral incisionless fundoplication (TIF) devices including Esophyx® and MUSE™, the LINX® Reflux

A. Dorsey
Department of Surgery, Metrowest Hospital, Cleveland, OH, USA

M. Hawn (✉)
Department of Surgery, Stanford University, Stanford, CA, USA
e-mail: mhawn@stanford.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_19

Management System, and EndoStim® LES Stimulation System. The outcome measures for these technologies are broad but considerations include healing of esophagitis, symptom improvement, GERD-related quality of life, reduction or discontinuation of PPIs, esophageal pH, esophageal manometry, and intrinsic LES pressure. These parameters are used to define the results of traditional and novel treatment modalities for GERD [19].

A proposed treatment algorithm for the management of GERD includes the following: patients diagnosed with GERD should have initial treatment of PPI of at least 3 months with twice-daily dosing. If patient fails PPI treatment, further workup should include manometry, 24 pH testing, and endoscopy. If patients have hiatal hernia >3 cm or severe esophagitis, they should undergo laparoscopic NF. If patients have mild to moderate esophagitis and/or small hiatal hernia, they should consider endoscopic therapies (Stretta, EsophyX, MUSE) [21].

Stretta® Endoscopic Radiofrequency Ablation System

The Stretta® system (Mederi Therapeutics Inc., Norwalk CT, USA) is a transoral endoscopic device approved by the FDA in 2000 that delivers radiofrequency (RF) energy to the lower esophageal sphincter and gastric cardia [22]. The FDA granted an updated clearance on the RF generator in 2011. The Stretta® procedure has the longest market exposure for endoscopic techniques approved by the FDA and has received strong recommendations for use in the SAGES 2013 and 2017 guidelines [22, 23]. The target patient population for Stretta® are adult patients (18 years or older) with symptoms of heartburn and/or regurgitation for 6 months or more who have partially or completely responded to antisecretory medications and who do not wish to undergo laparoscopic NF [23, 24]. Stretta® can be used in patients with prior surgical interventions. Stretta® should not be applied in patients with severe esophagitis, hiatal hernias greater than 2 cm, dysphagia, long-segment Barrett's, or those with autoimmune disease, collagen vascular disease, or clotting disorders [23]. Patients with obesity and esophageal dysmotility are often excluded as well [24].

The device includes a four-channel RF generator and a balloon catheter system with four needles that deliver radiofrequency energy of 60–300 J to each needle (465 kHz, 2–5 W per channel, 80 V max at 100–800 Ω) to achieve a desired target temperature of 85 °C to the esophageal musculature during sequential 1-minute treatment cycles (Fig. 19.1) [19]. The system has advanced thermocouples at each needle base (at mucosa level) and each needle tip (at muscular level) which causes cessation of power if mucosal temperatures exceed a preset value of 50 °C. The thermocouples in conjunction with continuous irrigation of the overlying mucosa assure tight temperature control to avoid mucosal damage and stricture formation [25].

This procedure is typically performed under conscious sedation in the endoscopy suite. The recommended treatments for Stretta® are four treatment levels in and around the LES, 5 mm apart from each other, and two treatment levels in

Fig. 19.1 Stretta device used for radiofrequency energy delivery to LES and gastric cardia for endoluminal treatment of GERD (Reused with permission © 2019 Restech | Mederi-RF)

the gastric cardia [22] totaling six treatment levels. The squamocolumnar junction (Z line) serves as a reference level for the treatments using the Stretta® catheter. Initial endoscopy is used to identify and measure the distance to the squamocolumnar junction. The catheter is then positioned 1.0–1.5 cm proximal to the Z line, and the balloon is inflated. The system is then activated, and ablation occurs at the four needle tips that project out at 90° angles from the balloon. The balloon is then deflated, and the catheter is rotated 45°, and ablation is then performed in this orthogonal position at the same level. The ablations continue in a sequential fashion progressing distally until the gastric cardia is reached (Fig. 19.2) [21, 24]. The treatment has a small learning curve with reductions in time occurring after three procedures [26]. The first three procedures took approximately 76 min, while the subsequent procedures took approximately 50 min in one published series [26]. Patients can usually return home a few hours after the procedure and return to work and normal activities within 24 h [21]. The patient is placed on a liquid diet following the endoluminal treatment, and advanced to regular diet as tolerated.

The proposed mechanism of action of radiofrequency ablation of the esophageal musculature is multifactorial and includes decreased compliance and distensibility of the lower esophageal sphincter (LES) without fibrosis, lengthening of the LES, and restoration of a physiologic anti-reflux barrier [27–29]. A double-blind sham-controlled study of the effect of radiofrequency energy on symptoms and distensibility of the gastroesophageal junction (GEJ) by Arts et al. showed that Stretta® patients did not have any change in esophageal acid exposure or pressure at the LES. However, they did have significantly improved symptom scores and decreased GEJ compliance. The administration of sildenafil, a smooth muscle relaxant, showed normalization of GEJ compliance to a pre-Stretta® level, thus discerning that fibrosis is not the mechanism of decreased distensibility of the LES [28].

Furthermore, nerve alteration, decreased sensitivity to acid, increased wall thickness, and decreased relaxations of the LES result in symptomatic improvements for GERD patients [30–32]. Increased frequency of transient lower esophageal sphincter relaxations (TLESRs) has been demonstrated as a contributing factor to GERD, and the Stretta® procedure has been shown to decrease these transient LES relaxations. The therapy is believed to alter vagal efferent fibers thus inhibiting the motor component of TLESRs and decreasing this mechanism of reflux episodes [24, 33–35].

Results

Stretta® has been on the market since FDA approval in 2000 and has many published papers citing its safety and efficacy. Studies show that it is effective in reducing symptoms of GERD, improving quality-of-life scores, and decreasing compliance of the LES [13]. Safety data, short-term and long-term results from many studies including randomized trials, are available and show good outcomes in symptom-

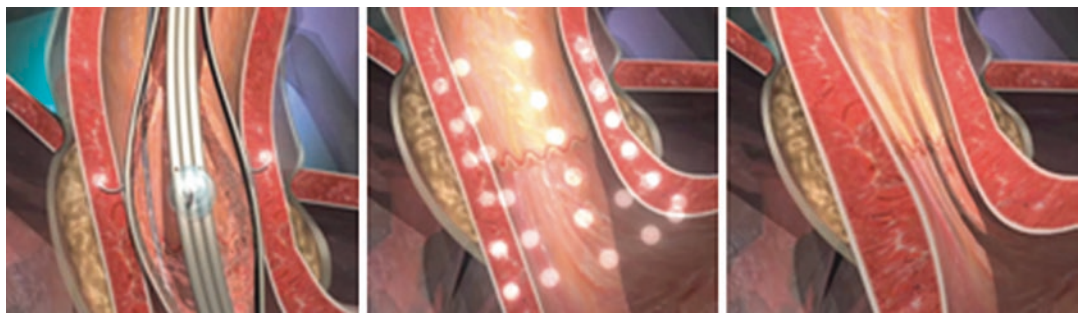


Fig. 19.2 Stretta procedure (Reused with permission © 2019 Restech | Mederi-RF)

atic improvement and medication reduction for GERD. The initial US open-label trial investigating the Stretta® procedure for the treatment of GERD showed 6- and 12-month data. At both 6 and 12 months, there were improvements in median heartburn score, GERD score, satisfaction, and mental and physical SF-36 quality-of-life scores. Additionally, PPI requirement went from 88% of patients to 30% of patients. This study showed a significant improvement in esophageal acid exposure and had a low complication rate of 8.6% [36]. An early randomized, sham-controlled trial by Corley et al. in 2003 showed 6-month data improvements in heartburn symptoms and quality of life but did not show decrease in esophageal acid exposure [32]. These initial studies along with a multitude of subsequent investigations emerged showing Stretta® as a new option for select symptomatic GERD patients and as an alternative to PPI therapy or surgical interventions.

The first published meta-analysis by Perry, Banerjee, and Melvin included a review of 18 publications and 2 RCTs with a total of 1441 patients who underwent Stretta® from 2001 to 2010. They were evaluated post-procedure and analysis compared symptoms, validated GERD-HQRS survey results, LES pressure, and esophageal acid exposure. Meta-analysis showed statistically significant GERD symptom improvement, GERD-HQRS score, and esophageal acid exposure, though it did not normalize. LES pressure improvement did not reach statistical significance [37, 38]. Long-term follow-up was then established with 8-year and 10-year follow-up data [39]. Noar et al. studied a group of 99 patients who were nonresponsive to PPIs and followed them for 10 years. Results showed that the GERD-HQRS normalized in 72% of patients, 41% of patients were able to stop PPI therapy, and 54% were satisfied at 10 years. There were 11 patients that required re-intervention with Stretta®, and 85% of patients who had Barrett's esophagus on biopsy had regression of their disease, and there were no reported adverse events or side effects from the procedure [39]. These studies helped establish Stretta® as an effective, safe, and durable treatment option for select GERD patients. The most recent published meta-analysis by Fass et al. included 24 published observational studies and 4 RCTs with 2468 patients followed for over 2 years. Results showed a statistically significant improvement GERD-HRQL, heartburn standardized score, and esophageal acid exposure. Overall, 51% of patients were able to stop PPI use. The treatment reduced the incidence of erosive esophagitis by 24%, and LES basal pressure increased slightly but did not reach statistical significance [40]. Data since inception and availability of Stretta® in 2000 have consistently shown improvement in subjective symptoms but have not shown significant improvement in objective measures such as LES pressure and normalization of esophageal acid exposure. Treatment with Stretta has been shown to be safe, effective, durable, and feasible and may help fill the treatment gap between PPI therapy and surgical therapy for GERD.

The procedure has very low complication rates, however; they include perforation, bleeding, and recurrence of symptoms. Esophageal injury with mucosal injury requires close observation, whereas full-thickness injury and perforation require definitive repair. Endoluminal stenting of such injuries is a potential option. Endoluminal bleeding is caused by penetration of submucosal vessels and can usually be controlled endoscopically with pressure, injection, cautery, or clipping. Esophageal varices are a contraindication to Stretta® [13]. In patients who fail to have improvement in GERD after Stretta®, antireflux surgery can still be performed. [35]

Additional Considerations

The role of Stretta® in the treatment of GERD may be broad. There is an established use in patients with hiatal hernia <2 cm who are refractory to maximal PPI therapy, those who are concerned about long-term risk of PPI therapy, and those who are averse to surgery. Additionally, Stretta® can be used in the LES of patients with prior gastric bypass [41] or subtotal gastrectomy [13] or with prior Nissen [42]. The Stretta® procedure was shown to be safe and effective in

improving satisfaction scores and quality of life and reducing PPI use in 18 patients with refractory GERD after laparoscopic NF [42]. Stretta® can therefore be used in patients with prior gastric surgery, but gastric surgery can also be done after Stretta®. Nissen or other laparoscopic anti-reflux operations can be safely performed after Stretta® [35, 43]. The therapy has also shown efficacy in reflux related childhood-to-adult persistent asthma [44] and is suggested as an initial anti-reflux procedure in children [45] and as treatment of recurrent reflux in pediatric patients [46].

Transoral Incisionless Fundoplication (TIF)

Transoral incisionless fundoplication (TIF) describes an endoluminal procedure that is another endoscopic option for the treatment of GERD. The procedure relies on restoring the angle of His to recreate and reinforce the gastroesophageal valve function, mimicking the anatomic principle of laparoscopic NF [5]. Incisionless fundoplication is performed using either the EsophyX™ device to create a 270° fundoplication or the Medigus Ultrasonic Surgical Endostapler (MUSE™) to create a partial anterior 180° fundoplication [6].

The EsophyX™ device, developed by Endogastric Solutions (Redwood City, WA), was initially approved by the FDA in 2007 [22] and is an endoscopic surgical stapling instrument that is single use and goes over the endoscope to create a partial fundoplication that is approximately 3-cm-long and 270° [47]. The TIF 2.0 technique is a plication formed by full-thickness apposition of the gastric fundus to the distal portion of the esophagus. The plication is fixed in place with H-shaped 3-0 polypropylene fasteners that measure 7.5 mm in length (Fig. 19.3) and are placed on the far anterior and far posterior sides of the lesser curve. The device is in its third iteration with the EsophyXZ® which was approved by the FDA in 2016 and boasts more efficient device use and stapler-style trigger device for fastener deployment and improved operative times. The procedure is performed under general anesthesia, requires less than 1 h to complete, and a surgeon operates the device while an assistant operates the gastroscope [22]. Patients can typically return to work within a few days of the procedure. Thus, the procedure may serve as an intermediate option to fill the treatment gap between PPI therapy and laparoscopic NF [22].

The initial phase I trial examined the histology of the procedure and demonstrated serosal fusion of full-thickness tissue plications. The procedure

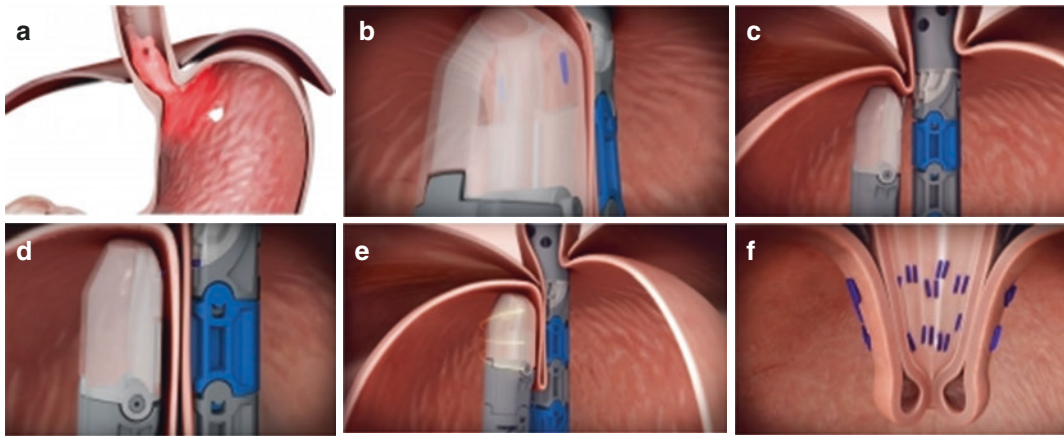


Fig. 19.3 Transoral incisionless fundoplication with EsophyX® device. (**a**) GE junction with poor valve function. (**b**) Fastener delivery system. (**c**) Helical retractor for tissue grasping and repair. (**d**) Tissue approximation to recreate valve. (**e**) Repaired tissue with initial tissue approximation for wrap. (**f**) Fundoplication complete with H-shaped fasteners (Reused with permission © EndoGastric Solutions, Inc.)

was shown to reduce the circumference of the gastric cardia and improve the Hill classification grade. The phase II trial showed normalization of distal esophageal acid exposure, increased LES pressure and length, and a valve appearance and location that appeared similar to the laparoscopic NF [48]. The procedure not only recreates the flap valve at the angle of His but also reduces the number of postprandial TLESRs, reduces EGJ distensibility, reduces the proximal extent of acid exposure, and reduces the number of reflux episodes [49].

Results

The randomized control trial by Hunter et al. in 2015 included patients with regurgitation and daily PPI use and evaluated the efficacy of transoral fundoplication versus omeprazole for treatment of regurgitation. Initially 696 patients were screened, and patients with troublesome regurgitation/GERD and hiatal hernias <2 cm were assigned to TIF followed by 6 months of placebo or sham surgery and 6 months of PPI (either once or twice daily). Results showed TIF eliminated troublesome regurgitation in 67% of patients, while PPIs did so in 45% of patients. There were 36% of patients who had no response at 3 months in the control group versus only 11% in the TIF group. Esophageal acid exposure improved, but did normalize, after TIF but not after sham surgery. Subjects in both groups reported similar improvements in GERD symptom scores. The complication rate was low with 3/87 in TIF group and 1/42 in the control group. This study showed that TIF was an effective treatment for GERD at 6 months and had a low complication rate [49].

The TEMPO RCT in 2015 compared TIF versus PPIs in 63 randomized patients with regurgitation and atypical symptoms and found at 6-month follow-up troublesome GERD was eliminated in 97% of TIF patients versus 50% of PPI patients. Regurgitation and extraesophageal symptoms were eliminated in 62% of TIF patients versus 5% of PPI patients. Esophageal acid exposure normalized in 54% of TIF patients and 52% of PPI patients, while 90% of TIF patients were off PPIs at 6-month follow-up [50]. The 3 and 5 year data from the TEMPO trial provide data on the long-term results of TIF. Of 63 patients who underwent TIF, 60 were available for 1-year follow-up, 52 for 3 years, and 44 patients at 5-year follow-up. At 3 years 90% of TIF patients had absence of regurgitation, while 88% had absence of atypical symptoms. Additionally, 71% of TIF patients no longer used PPIs, and 86% of patients had a full recovery of esophagitis [51]. This 3-year data showed that TIF offers durable symptom control for chronic GERD. At 5 years, the TEMPO trial showed that TIF is safe, durable, and cost-effective [52]. Troublesome regurgitation was eliminated in 86% of patients at 5 years, while resolution of troublesome atypical symptoms occurred in 80% of patients. No serious adverse events occurred, and only 34% of patients were on daily PPIs at 5 years compared to 100% of these patients prior to intervention. The GERD-HRQL score improved from 22.2 to 6.8 at 5 years showing sustained symptom improvement at 5 years.

Further long-term data at 6 and 8 years were published. The 6-year data by Testoni et al. showed elimination of daily dependence on PPIs in over 75% of patients, while 30% of patients were off PPIs altogether at 6 years [53]. Symptom scores off PPI were lower at 6, 12, 24, and 36 months. Factors predicting good outcome included absence of hiatal hernia or hernia <2 cm, effective esophageal motility, and increased number of fasteners deployed [53]. A retrospective cohort study by Chimakangara et al. provided 8-year data regarding reflux symptoms and quality of life after TIF in a patient group who were all taking PPI at least daily. At median follow-up of 97 months, 12 of 57 patients underwent subsequent laparoscopic anti-reflux surgery, and of the remaining patients who did not, 23 patients completed long-term follow-up. Of these patients, 73% reported daily acid-reducing medication use. The Median GERD-HRQL scores improved from 24 at baseline to 10 at long-term follow-

up. Of these patients available for long-term follow-up, 78% were either satisfied or neutral regarding their GERD management. The majority of patients in this study resumed daily PPI therapy; however, they did demonstrate significantly improve GERD-HRQL scores compared to baseline and increased satisfaction regarding their GERD management [54].

There have been two recent meta-analyses examining the efficacy of TIF. The first by Huang et al. in 2017 analyzed 18 studies comprised of 5 RCTs and 13 prospective observational studies totaling 963 patients. An intention-to-treat analysis of the pooled data of 5 RCTs showed that the relative risk of response rate to TIF versus PPI or sham was 2.44 and the total number of reflux events was decreased after TIF compared to the PPI or sham groups. The studies showed an improvement in typical and atypical GERD symptoms and a trend toward reduction of esophageal acid exposure that did not reach statistical significance. The majority of patients decreased PPI dose compared to pre-procedure, but PPI use increased with time following the TIF procedure. After TIF, the total satisfaction rate at 6 months was about 69%. This meta-analysis showed that TIF is an alternative intervention to control GERD-related symptoms and that short-term patient satisfaction is good but long-term results showed decreased efficacy with time [55]. Additional meta-analysis by Gerson et al. in 2018 analyzed RCTs of the TIF 2.0 procedure versus controls in patients with long-term chronic, refractory GERD on maximal PPI therapy. Data from 233 patients was included at 3-year follow-up and showed statistically significant improvement in esophageal pH, a decrease in PPI utilization, and improvement in quality of life [56]. Overall, TIF with the EsophyX™ device has been shown to be effective in improving GERD-related symptoms, PPI use, and quality of life and received a strong recommendation from the SAGES guidelines committee in 2017; however, the effectiveness of laparoscopic NF on GERD outcomes remained superior to PPIs and TIF [22].

Complications and Additional Considerations

The complication rate for the Esophyx™ device is low; however, severe adverse events occurred at a rate of 2.4% and consisted of gastrointestinal perforation and bleeding [55]. A total of 781 patients were evaluated in a meta-analysis including 4 RCTs and 12 prospective observational trials, and severe adverse events occurred in 19 patients. There were seven perforations, five complications of bleeding, four patients with pneumothorax and one patient, with severe post-procedure epigastric pain. There was one death reported which was 20 months after the procedure; however, the relationship to the prior TIF procedure was unknown.

The use of Esophyx as salvage for recurrent GERD after failed fundoplication has been described by Bell et al. and was shown in this study to be safe and effective [57, 58]. Additionally, Perry et al. showed that prior TIF does not significantly increase the morbidity of a subsequent laparoscopic NF [59]. Upon laparoscopic evaluation after TIF, reasons for failure were fundoplication breakdown or presence of hiatal hernia [58, 59].

Another proposed use of TIF described in one small retrospective cohort study is neurologically impaired children with GERD. In this small study, TIF was shown to resolve GERD in 10 out of 11 of these children [60]; however, TIF is not FDA approved in children, and the use of a 54Fr diameter delivery system limits its application in pediatrics. Areas for future investigation include comparisons of TIF to laparoscopic NF and evaluation of TIF effects on long-term GERD complications such as Barrett's esophagus, esophageal cancer, and stricture formation [20].

Medigus Ultrasonic Surgical Endostapler (MUSE™)

The Medigus Ultrasonic Surgical Endostapler (MUSE™ Medigus Ltd, Omer, Israel) is an endoscope that has an ultrasound transducer, a video

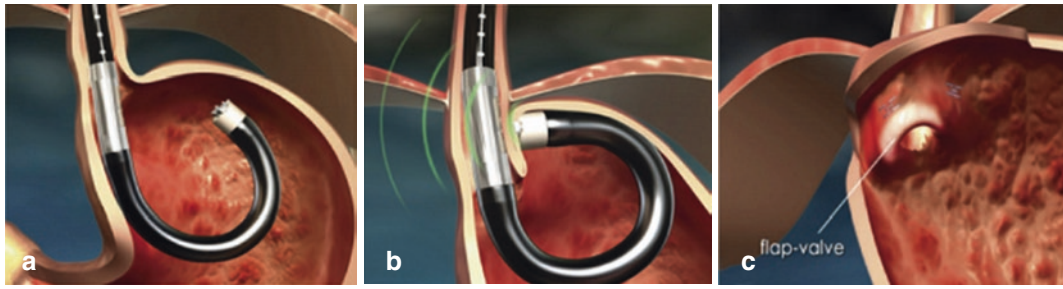


Fig. 19.4 Transoral incisionless fundoplication with MUSE™ endostapler. (**a**) MUSE™ endoscopic stapler. (**b**) Ultrasound guidance, device in retroflexion, and ready to begin creation of partial fundoplication. (**c**) Flap valve after endoscopic stapling (Reused with permission © Medigus)

camera, and an endostapler that deploys five 4.8-mm titanium surgical staples proximal to the Z line to create a partial anterior fundoplication (Fig. 19.4) [6]. The patient is placed under general anesthesia with endotracheal (ET) intubation, and the endoscope is inserted through an overtube, advanced and retroflexed in the stomach. The ideal site above the EGJ to create the partial fundoplication is detected using ultrasound and video images, and then the tissue is clamped and stapled endoscopically. The procedure is repeated to form a flap, creating a partial anterior 180° fundoplication [19, 61].

The MUSE™ device and procedure are the newest (FDA approval 2014) for the endoscopic treatment of GERD and, as a result, has the least amount of data supporting its use. The first preclinical trial was completed in 2008 on 12 study animals. All animals had a successful partial fundoplication with no short-term post-procedure complications [62]. An international multicenter, prospective trial evaluated 69 patients who underwent endoscopic anterior fundoplication and 6-month follow-up data for 66 patients showed GERD-HRQL score improved by >50% while patients were off PPIs in 73% of patients. Additionally, 64.6% of patients were no longer using daily PPIs at 6 months. The remaining patients who continued PPIs post-procedure reported ≥50% reduction in dose, and the mean percent of time with esophageal pH <4.0 decreased from baseline at 6 months. Adverse effects were periprocedural chest discomfort and sore throat, fever, and one patient with pneumomediastinum and pneumothorax. There were 2 severely adverse events that occurred in the first 24 patients (1patient with pneumothorax, pleural effusion, and esophageal leak; 1 patient with GI bleed), which prompted protocol and device changes. Subsequently, there were no further severe events that occurred in the remaining 48 enrolled patients [61].

A study with 5-year follow-up data, published in 2015, followed 13 patients initially in a MUSE™ pilot study for 6 weeks and then to 5 years. At 6 weeks the mean total acid exposure was significantly reduced, and 12/13 patients had reduced GERD-HRQL severity scores by ≥50% and were able to stop daily GERD medications. At 5 years, 11 of 13 patients were available for follow-up. GERD-HRQL scores were normal in 10/11 patients, and all patients would agree to do the procedure again with a median satisfaction score of 8/10. At 4–5 years no patients had dysphagia, 54% (7/13) patients eliminated PPI use, while another 23% (3/13) reduced PPI use by ≥50% [63]. Additional long-term data with 4-year follow-up was reported by Kim et al. in 2016. A multicenter, prospective study using the MUSE™ endoscopic stapling device evaluated 37 patients at baseline, 6 months, and annually up to 4 years post-procedure. At 6 months 83.8% of patients remained off daily PPIs, and at 4 years 69.4% were off of daily PPIs. The GERD-HRQL scores off PPIs were significantly decreased from baseline at both 6 months and 4 years post-procedure, and for those who were on GERD medications, the daily dose decreased at both time points [64, 65]. Overall, initial data for the MUSE™ endoscopic stapling device is promising for symptom relief and decreased PPI use with an acceptable safety profile; however, further study is needed. Future investigations

with larger randomized groups of patients, longer follow-up, presence of sham or control, and comparison to other endoscopic treatments for GERD along with ongoing safety and efficacy studies are warranted prior to widespread use of the device.

The endoscopic treatments for GERD discussed above represent new options to potentially fill the treatment gap between medications and traditional surgical techniques of fundoplication; however, patient selection remains paramount. In addition to endoscopic treatments for GERD, emerging laparoscopic therapies aside from NF pose additional options and these include LINX® magnetic LES augmentation, EndoStim® LES stimulation, and laparoscopic RYGB, particularly in patients with BMI >35 kg/m^2. These laparoscopic operations still allow for repair of hiatal hernias but eliminate fundoplication, and its side effects, and attempt to improve inefficient LES function [6].

Laparoscopic Modalities for Treatment of GERD

Magnetic Sphincter Augmentation (MSA) Using the LINX® Device

Magnetic sphincter augmentation (MSA) using the LINX® reflux management system (Torax Medical, Shoreview, MN) was approved in the USA in 2012 and is now an established laparoscopic procedure for reflux with published efficacy [6]. The device consists of a string of titanium beads (MRI safe to 1.5 T) with a magnetized core that are connected with independent titanium wires to form a ring that is placed circumferentially around the EGJ (Fig. 19.5) [66]. The beads are attracted to each other by magnetic forces and increase the pressure of the LES circumferentially to help restore the anti-reflux barrier and eliminate transient esophageal relaxations thought to contribute to reflux. The beads

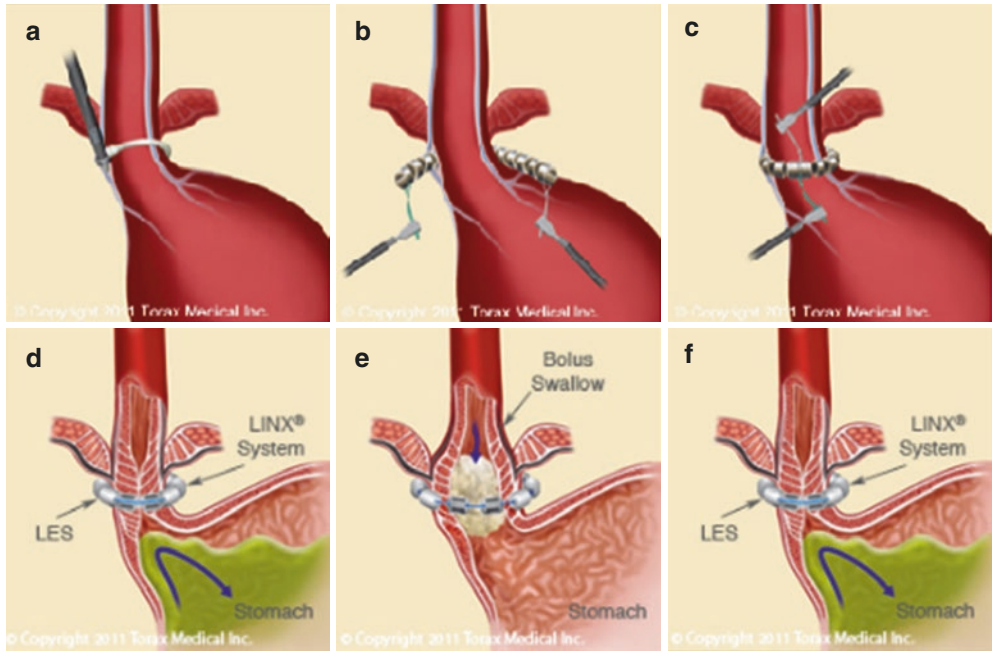


Fig. 19.5 LINX® Magnetic Sphincter Augmentation device placement and function. (**a**) Sizing tool for LINX® device measurement. (**b**) Positioning of LINX® around LES. (**c**) Closure and fastening of LINX® device using pre-attached sutures. (**d**) Device positioned at LES to resist opening gastric pressure and reflux. (**e**) Device opening during swallowing of food bolus. (**f**) Device returned to closed position to augment LES. © Ethicon Endosurgery

rest on each other when the device is in the closed position to prevent esophageal compression. The wire connecting the beads allows adjacent beads to be displaced relative to each other to reach a maximal fixed diameter of 3.6 mm [67]. The mechanism of action is dynamic augmentation; the magnets help keep the LES closed to minimize reflux yet temporarily open to allow a food bolus and liquid to pass through during swallowing. When adequate pressure is reached, 27 mm Hg, the magnetic attraction is overcome and the LES is allowed to open, allowing patients to eat, drink, belch, or vomit [6, 19, 67]. Peristaltic contractions of the esophagus produce pressure of 40–100 mmHg which is sufficient for the food bolus to overcome the force of the device and pass through the esophagogastric junction normally. Gastric contents will not generate enough pressure to overcome the barrier, hence, minimizing reflux. Emesis will generate enough force to allow patients to vomit if needed [66].

Pre-procedure workup includes EGD, GERD-HRQL score, pH study, and esophageal manometry. Selection criteria include patients 18–75 years of age, >6 months of reflux, a partial response to daily PPIs, and increased esophageal acid confirmed with esophageal pH study. Exclusion criteria are LA grade C or D esophagitis, Barrett's esophagus, esophageal motility disorder, dysphagia >3 times per week, BMI >35, allergy to components of the device (titanium, stainless steel, nickel, or ferrous materials), and traditionally, large hiatal hernia (≥3 cm) [68].

The procedure is a minimally invasive laparoscopic procedure during which the device is placed around the LES to augment its function [19]. The median time required to place the device, in the initial multicenter FDA trial, from time of last port insertion to first port removal was 36 min (range 7–125 min) [68]. The operation includes careful dissection of the GE junction fat pad away from the GE junction, opening the phrenoesophageal ligament along the anterior border of the left crus, and then dissection on the right side of the hiatus. The gastrohepatic ligament is incised, hepatic branch of the vagus nerve preserved, and the gastroesophageal junction is identified. The peritoneum along the anterior border of the right crus is opened above the crural decussation, and the posterior vagus nerve is identified. A retroesophageal window between the vagus nerve and the esophagus is created bluntly and then a Penrose or vessel loop is placed around the esophagus, excluding the posterior vagus nerve. The esophageal sizing tool is placed circumferentially, assuring that the underlying esophagus and musculature are not indented or compressed, to determine the appropriately sized device. The device is then placed encircling the esophagus, excluding the posterior vagus nerve, and the two ends of the device are approximated anteriorly and fastened into place using the pre-attached traction sutures. If there is a hiatal hernia present, it should be formally repaired prior to device measurement and placement. Patients can typically go home within 24 h on a solid diet [67–70].

Additional discussion exists around minimal versus obligatory dissection of the diaphragmatic hiatus during MSA surgery. At the inception of the device, minimal hiatal dissection (MHD) was recommended as the best surgical approach for MSA placement due to concern for device migration into the hiatus. However, in late 2015 the recommendation changed to obligatory dissection (OD) of the hiatus with concurrent hiatal hernia repair, if identified. A study published in 2018 showed that there was no difference in early dysphagia between the two groups. Delayed-onset dysphagia, recurrent GERD, recurrent hiatal hernia, and repeat surgery for hiatal hernia repair were less frequent in the OD group; hence obligatory hiatal dissection is now recommended [71].

Results

Results of the LINX® magnetic sphincter augmentation (MSA) device have been published starting with the feasibility trial in 2010 to establish safety and efficacy of the treatment. The pilot study included 44 patients with abnormal acid exposure on 24-hour pH monitoring and persistent GERD symptoms despite PPIs. The study showed improvement in GERD-HRQL scores from baseline of 25.7 to 3.8 at 1 year (80% reduction) and 2.4 (90% reduction) at 2-year follow-

up. At 1- and 2-year follow-up, 90 and 86% of patients were able to stop PPI use, respectively. The most common side effect was early dysphagia, occurring in 43% of patients, which resolved without intervention within 90 days in all but one patient, who had the device explanted due to persistent dysphagia. There were no reported device migrations or erosions. At 1 and 2 years, 77 and 90% of patients had normal esophageal acid exposure, respectively, and the mean percentage of time the pH was <4 decreased from 11.9 to 3.1% at 1 year and 2.4% at 2 years. Patient satisfaction was ≥86% at both follow-up periods. This initial study showed efficacy and safety at 1- and 2-year follow-up [70]. The 5-year results of this pilot study were subsequently published in 2015, and 33 of the 44 initial patients were available for follow-up. At 5 years esophageal acid exposure was 4.6% from 11.9%, 85% of patients had ≥50% reduction in esophageal pH, and 93.9% of patients had ≥50% reduction in total GERD-HRQL score with a mean score of 2.9 from 25.7 at baseline. Additionally, 87.8% of patients were able to stop PPIs, and no erosions or device migrations were observed [72].

A multicenter FDA trial involving 100 patients was published including 1-year, 3-year, and 5-year follow-up. The 1- and 3-year follow-up was published first, and the primary outcome of normalization or ≥50% acid reduction was achieved in 64% of patients with success of the device defined as achievement of the primary endpoint in ≥60% of patients. For the secondary outcomes, 93% of patients had ≥50% reduction in PPIs, and 92% of patients had ≥50% reduction in GERD-HRQL scores. Esophagitis was decreased from 40% at baseline to 12% at follow-up. Satisfaction with the reflux condition improved to 95% at 1 year, 90% at 2 years, and 93% at 3 years follow-up compared to 12% at baseline on PPI therapy. The most common adverse event was dysphagia in 68% of patients postoperatively, 11% of patients at 1-year follow-up, and 4% of patients at 3-year follow-up. Esophageal dilation for dysphagia was done on 19 patients, 16 of which reported improvement in symptoms. Of note, cruroplasty was performed in 34% of patients who underwent the procedure, thus confounding dysphagia analysis based on device or cruroplasty [66, 68].

Serious adverse events occurred in six patients, requiring device removal in four of the six (three patients for persistent dysphagia, one patient due to intermittent vomiting of unknown etiology with no relief after removal). The remaining two patients had rehospitalization for nausea and vomiting 2 days after surgery with resolution of symptoms without reoperation. Two additional devices were removed, one for persistent reflux symptoms and one for persistent chest pain. Three of the six patients who underwent device removal underwent subsequent NF with no complications. At 3-year follow-up only two patients complained of inability to belch or vomit. Based on chest radiography and endoscopy at 1-year and 2-year follow-up, there was no evidence of device migration or erosion [68].

The 5-year results of the FDA trial study were published in 2016, and the GERD-HRQL scores decreased to 4, from 27 at baseline (off PPIs) and 11 (on PPIs). At baseline, all study patients required PPIs, while only 15.3% of patients required them at 5 years post-LINX® and 89.4% of patients had ≥50% reduction in dose at 5 years versus 93% at 1 year. At baseline, 57% of study patients had moderate to severe regurgitation, while only 1.2% of patients experienced this at 5 years. At baseline, 40 patients had esophagitis, and of these patients 34 underwent follow-up endoscopy at 5 years, and 8 were shown to have esophagitis versus 12 at the 1-year mark, while 5 patients developed new esophagitis (grade A or B) during this period. All patients were able to belch and vomit. Troublesome dysphagia occurred in 5% of patients at baseline and 6% of patients at 5 years. Troublesome gas bloat was reported in 52% of patients at baseline and was decreased to 8.3% of patients at 5 years. There were no device erosions, malfunctions, or migrations reported [73].

The continued assessment of safety and efficacy post-FDA approval has been studied and published in 2018. A multicenter prospective study included 200 patients treated with MSA. At 1 year the mean total acid exposure time decreased from 10% to 3.6% and 74.4% of patients had nor-

mal esophageal acid exposure time. Additionally, GERD-HRQL scores improved from 26 to 4 (lower is better). The device removal rate was 2.5% with one erosion and no serious adverse events [74], thus confirming LINX® MSA as a safe and effective therapy for GERD outside of the initial investigational setting.

The most feared complication of implanting a device around the mobile LES remains to be erosion. A safety analysis of the first 1000 patients (from 82 institutions across the USA and Europe) treated with LINX® MSA over a 6-year period was performed and results published in 2015. The median implant duration at the time of analysis was 274 days. Various safety parameters were analyzed, and for intra- or peri-\operative complications, the event rate was 0.1% (one patient with respiratory arrest postop, considered unrelated to device, successfully resuscitated), 1.3% for hospital readmissions (dysphagia, pain, nausea, vomiting), 5.6% for endoscopic dilations due to dysphagia, and 3.4% for reoperations for device removal. Dysphagia rate of 5.6% of patients is similar to the reported rate of 6.4% after NF, both of which typically improved after dilation. Notably, many patients are able to overcome the early post-LINX® dysphagia by persistent swallowing of food boluses forcing the device to open and close to minimize constriction by the scar tissue around the device. All reoperations were nonemergent, primarily for dysphagia, and none had complications or required conversion to an open operation. Following removal, 10 of the 36 patients had subsequent NF, though this rate is likely underestimated as not all post-removal data was available. Erosion rate was 0.1% as it occurred in one patient, and no migrations or malfunctions were reported [75].

A similar study assessing 3283 patients undergoing MSA at 191 institutions with a median implant duration of 1.4 years and >1000 patients with the device in place >2 years showed an overall device removal rate of 2.7% (89/3283) with 57% removed within 1 year after implantation. The reasons for removal included dysphagia (52/89), persistent reflux symptoms (19/89), and erosion in 0.15% (5/3283), and no migrations or perforations were noted [76]. Worldwide experience with erosion was published in 2018 using manufacturer and user databases, and from 2007 to 2017, a total of 9453 devices were placed worldwide, and there were 29 reported cases of erosions. The median time to presentation was 26 months, and the risk of erosion at 4 years was 0.3% with the most commonly presenting symptom of new-onset dysphagia. The devices were successfully removed in all patients. The most commonly employed technique for removal was endoscopic removal of the eroded portion of the device followed by delayed laparoscopic removal of the remaining beads. At a median follow-up of 58 days, no long-term complications were reported after device removal [77]. A noted limitation of these studies is the reliance on providers for reporting of events outside of the clinical study to the FDA and manufacturer, which is likely not complete, raising the concern of underreporting of complications in the post-FDA approval period [75]. An additional study focusing on device removal had a high follow-up rate and evaluated 164 patients for 4 years during which 6.7% (11 devices) required removal and 1.2% (2 patients) had esophageal erosion (at 12 and 19 months post-placement) requiring removal [78]. The data supports the conclusion that MSA with the LINX® device is highly effective and safe for the treatment of GERD that should be considered as a tool to help fill the GERD treatment gap.

Additional Considerations

The efficacy of MSA in patients with GERD has been evaluated; however, the outcomes in comparison to NF remain unclear. A meta-analysis published in 2017 pooled results of 4 trials including 624 patients. MSA had shorter operative time than NF and length of stay. Rates of PPI use, GERD-HRQL scores, symptoms, complications, and severe dysphagia requiring dilation were similar among the groups. The number of adverse events was similar between groups; however, there was statistically significant increased gas bloating in the NF group while there was not a statistically significant difference in the ability to belch or vomit [79]. Another meta-analysis compared MSA to NF and evaluated 688 patients

with approximately 1-year follow-up and found that MSA was statistically superior to NF in preserving ability to belch and vomit, while there was no difference between the two operations in gas, bloating, postoperative dysphagia, or PPI elimination [80]. The data comparing MSA to NF is short term and inconsistent in its findings; hence further investigation is required, including long-term studies and RCTs to further elucidate these differences.

A multicenter, randomized trial comparing MSA to double-dose PPI for the management of GERD despite once-daily PPI therapy evaluated 152 patients from 21 institutions followed for 6 months. Patients were randomized 2:1 to treatment with twice-daily PPOs versus laparoscopic MSA. Relief of regurgitation symptoms was achieved in 89% of patients who underwent MSA versus 10% of patients in the twice-daily PPI group, while 81% of MSA patients had ≥50% improvement in GERD-HRQL scores versus 8% in the twice-daily PPI group. Of MSA patients, 91% were off PPI therapy, 91% had normal number of reflux episodes (versus 58% in PPI group), and 89% of MSA patients had normal number of acid exposures (versus 75% in PPI group). No significant safety events were observed; however, 28% of MSA patients reported transient dysphagia, and 4% reported ongoing dysphagia. The results of this study suggest that MSA is more effective than increasing PPI dose for controlling GERD in patients with moderate to severe regurgitation despite once-daily PPI [81].

Laparoscopic MSA has efficacy in the aforementioned populations; however, its use is being explored in additional patient populations. Reflux after sleeve gastrectomy is typically managed by conversion to RYGB; however, the LINX® device may have a potential use in these patients. In a recent case report, the device was placed for severe reflux after sleeve gastrectomy after which the postoperative UGI showed no reflux, the 10-day postop and the quality of life score improved, and at 1 year postop, the patient remained off antacid medication with no report of reflux [82].

The efficacy of the device in patients with large hiatal hernias, defined as ≥3 cm, was studied retrospectively and results published in 2017. There were 52 patients identified with large hiatal hernias, and they showed that mean GERD-HRQL score decreased from 20.5 to 3.6 and had decreased postop PPI requirement when compared to those with smaller hiatal hernias. The percentage of patients needing intervention for dysphagia was similar to those with small hiatal hernias at 13.5 versus 17.9% ($p = 0.52$), respectively, and the symptom improvement and resolution rates were similar in both groups at 98.1 and 91.3% ($p = 0.118$), respectively [83]. An additional study published in 2018 prospectively reviewed 200 patients treated with MSA with the LINX® device along with repair of hiatal hernias >3 cm, 78% of which had hiatal hernia ≥5 cm. Of note, nonpermanent mesh reinforcement of the hiatal repair was performed in 83% of patients. There were 156 patients available for follow-up with a median of 8.6 months and shown to have improvement in GERD-HRQL scores from 26 to 2, no explants, erosions or migrations; however, 19 patients did require dilation for dysphagia, showing overall favorable outcomes at 9-month follow-up [84]. This opens another potential door for the use of LINX® in GERD patients with large hiatal hernias.

Electrical Stimulation of the Lower Esophageal Sphincter (EndoStim®)

Electrical stimulation of the lower esophageal sphincter with the EndoStim® device (EndoStim, St. Louis, MO, USA) is an implantable electrical stimulator that delivers energy to the LES [6, 66]. The device has three components including a bipolar stimulation lead with two stitch electrodes, a pulse generator, and an external programmer [6]. The device received CE mark in Europe in 2012, and multiple FDA trials are ongoing in the USA. The device is placed laparoscopically during which the two electrodes are implanted anteriorly along the esophagus spanning the LES in a staggered position (Fig. 19.6) with approximately 1-cm distance between the two electrodes. The Z line is identified endoscopically, and transillumination is used to guide placement

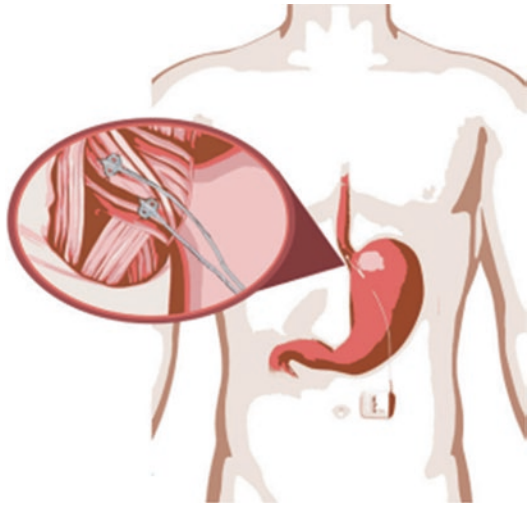


Fig. 19.6 EndoStim® Device implantation for stimulation of the LES (Reused with permission © Endostim)

of the electrodes. A superficial longitudinal seromuscular bite measuring 15 mm along the axis of the esophagus is performed, with care taken not to incorporate esophageal mucosa. The second electrode is placed in the same fashion. The generator is implanted in a subcutaneous pocket in the abdominal wall [66, 69]. The device settings can be modified with a wireless programmer; the battery lasts 7–10 years, and it can be exchanged as an outpatient surgical procedure [85].

The proposed mechanism of action is electrical stimulation delivered to the LES to increase the resting pressure and help control reflux [66, 86]. The device gives 30-minute stimulation cycles, 6–12 times per day, with intensity and duration that can be modified for each patient [6, 19]. The cycles are usually scheduled pre-meal and pre-reflux event based on the patient's 24-hour pH study. The device also has a sensor that detects upright versus supine position and allows modification in the programming based on patient position and reflux characteristics [19, 86].

Results

The EndoStim device does not currently have US FDA approval, but multicenter clinical trials are ongoing [87]. A study published in 2014 reported 3-year follow-up of 19 patients with electrical stimulation of the LES for treatment of proximal GERD. The 24-hour distal esophageal acid exposure improved from 10.2 to 3.4%; pH improved, and there was a significant improvement in GERD-HRQL at 12 months. There were no GI side effects including dysphagia, gas bloat, or diarrhea. There were no reported procedure-related serious adverse events [88].

A multicenter international trial was published in 2015 which followed 41 patients for 6 months. Hiatal hernia repair was required in 16 patients, and 3 severe adverse events were reported (1 device-related lead erosion through the esophagus, 1 procedure-related trocar perforation of the small bowel, and 1 unrelated AVNRT arrhythmia). Esophageal acid exposure improved at 3 and 6 months; GERD-HRQL improved from 31 at baseline off PPI, 16.5 on PPI, 4 at 3 months post-procedure, and 5 at 6 months follow-up. There was a reduction in regurgitation and no increase in dysphagia [89]. These studies showed an acceptable safety profile and good short-term efficacy in the study population. Another study evaluated 25 patients with 21 patients available at 2-year follow-up and showed improvement in regurgitation, symptoms of GERD, median GERD-HRQL, median 24-hour acid exposure, and 16/21 patients had cessation of PPI use. At baseline, 92% of patients unsatisfied with their condition off PPIs, 71% of patients were unsatisfied on PPIs, and 0% of patients unsatisfied at 2-year follow-up after device placement. There were no reported GI side effects or adverse events [90].

A multicenter international trial began as a 2-year open-label study which was extended to attain 3-year follow-up in a multicenter registry trial. The initial 2-year data included 23 patients, and the median 24-hour pH improved, GERD-HRQL improved, and PPI use improved or was eliminated completely [91]. Additionally, 15 patients completed the 3-year follow-up and were shown to have significant improvement in median GERD-HRQL, median 24-hour distal esophageal acid exposure, and 11/15 reported cessation of regular PPI use. During the 3-year follow-up period, there were no adverse GI side effects and no device- or procedure-related adverse events further demonstrating safety and

efficacy of the device and procedure for a longer follow-up period [92].

The Lower Esophageal Sphincter Stimulation for GERD (LESS GERD) trial is underway and is a multicenter trial with 16 participating sites worldwide with a goal of 110 patients. Enrollment starts May 2016 with planned primary completion August 2019 with a study completion date of December 2021. The trial is multicenter, randomized, double-blind, sham-controlled, and will evaluate the safety and efficacy of the EndoStim® LES Stimulation System in patients ages 22–75 with GERD who have persistent symptoms despite high-dose PPI. Outcome measures include rate of device and/or procedure-related serious adverse events, esophageal acid exposure, GERD symptoms, ability to avoid dependence on PPIs, and effect on quality of life. Patients with prior esophageal surgery, severe esophagitis (Grade C or D), hiatal hernia >3 cm, history of gastroparesis, Barrett's esophagus, esophageal varices, BMI >35, uncontrolled DM, and severely impaired esophageal motility are excluded. The patients all undergo laparoscopic device implantation and are randomized at 2 weeks postoperatively to either the Treatment Group (immediate stimulation) or Control Group (delayed stimulation) for 6 months followed by an open-label phase during which all study patients receive electrical LES stimulation with planned 5-year follow-up [87].

Additional Considerations

The use of the EndoStim® in patients with GERD after laparoscopic sleeve gastrectomy (LSG) was evaluated using a prospective, international, multicenter registry, and 17 patients were treated at 6 centers with a median follow-up of 12 months. All patients had reduction or cessation of PPI therapy after device placement, improvement in esophageal pH, and median GERD-HRQL scores improved from 34 at baseline (on PPIs) to 9 at follow-up (off PPIs) demonstrating LES stimulation as a potential therapy for patients with GERD after LSG [93].

The EndoStim® device for stimulation of the LES and management of GERD is early in its inception, and data for long-term follow-up, larger patient populations, and the results of the ongoing RCT are yet to be evaluated. Additionally, the device still requires FDA approval in the USA. It is unclear what the role of LES stimulation will be in the overall treatment of GERD, but initial data supports a good safety profile and efficacy with potential expansion to additional patient populations such as those with previously sleeve gastrectomy or those with impaired motility.

The role of novel endoscopic and laparoscopic techniques for the treatment of GERD is to be determined. There is certainly a need for additional options to fill the GERD treatment gap between medications and NF. The discussed techniques show promise to help fill this gap, while their durability, safety, efficacy, and frequency of use in patients with GERD will continue to evolve over the coming years.

Conflict of Interest The authors have no conflict of interest to declare

References

1. Peters JH, DeMeester TR, Crookes P, et al. The treatment of gastroesophageal reflux disease with laparoscopic Nissen fundoplication: prospective evaluation of 100 patients with "typical" symptoms. Ann Surg. 1998;228(1):40–50.
2. Funk LM, Kanji A, Scott Melvin W, Perry KA. Elective antireflux surgery in the US: an analysis of national trends in utilization and inpatient outcomes from 2005 to 2010. Surg Endosc. 2014;28(5):1712–9.
3. Streets CG, DeMeester SR, DeMeester TR, et al. Excellent quality of life after Nissen fundoplication depends on successful elimination of reflux symptoms and not the invasiveness of the surgical approach. Ann Thorac Surg. 2002;74(4):1019–25.
4. DeMeester TR, Bonavina L, Albertucci M. Nissen fundoplication for gastroesophageal reflux disease. Evaluation of primary repair in 100 consecutive patients. Ann Surg. 1986;201(1):9–20.
5. DeMeester TR. Surgical options for the treatment of gastroesophageal reflux disease. Gastroenterol Hepatol. 2017;23(2):128–9.
6. Nicolau AE, Lobontiu A, Constantinoiu S. New minimally invasive endoscopic and surgical therapies for gastroesophageal reflux disease (GERD). Chirurgia. 2018;113(1):70–82.
7. Papasavas PK, Keenan RJ, Yeaney WW, Caushaj PF, Gagne DJ, Landreneau RJ. Effectiveness of laparoscopic fundoplication in relieving the symptoms of gastroesophageal reflux disease (GERD) and eliminating antireflux medical therapy. Surg Endosc. 2003;17:1200–5.

8. Dallemagne B, Weerts J, Markiewicz S, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc. 2006;20:159–65.
9. Dallemagne B, Perretta S. Twenty years of laparoscopic fundoplication for GERD. World J Surg. 2011;35(7):1428–35.
10. Hunter JG, Swanstrom L, Waring JP. Dysphagia after laparoscopic antireflux surgery. The impact of operative technique. Ann Surg. 1996;224(1):51–7.
11. Robinson B, Dunst CM, Cassera MA, et al. 20 years later: laparoscopic fundoplication durability. Surg Endosc. 2015;29(9):2520–4.
12. Rantanen TK, Salo JA, Salminen JT. Functional outcome after laparoscopic or open Nissen fundoplication: a follow-up study. Arch Surg. 1999;134(3):240–4.
13. Reavis KM, Nguyen AK. Endolumenal approaches to gastroesophageal reflux disease. SAGES Manual. 2012;2(3):247–60.
14. Wai-Kit L, Mashimo H. Critical assessment of endoscopic techniques for gastroesophageal reflux disease. J Clin Gastroenterol. 2015;49(9):720–4.
15. Ito T, Jensen RT. Association of long-term proton pump inhibitor therapy with bone fractures and effects on absorption of calcium, vitamin B12, iron and magnesium. Curr Gastroenterol Rep. 2010;12:448–57.
16. Janarthanan S, Ditah I, Adler DG, et al. *Clostridium Difficile*-associated diarrhea and proton pump inhibitor therapy: a meta-analysis. Am J Gastroenterol. 2012;107:1001–10.
17. Filion KB, Chateau D, Targownik LE, et al. Proton pump inhibitors and the risk of hospitalization for community-acquired pneumonia: replicated cohort studies with meta-analysis. Gut. 2014;63:552–8.
18. Lo W-K, Chan WW. Proton pump inhibitor use and the risk of mall intestinal bacterial overgrowth: a meta-analysis. Clin Gastroenterol Hepatol. 2013;11:483–90.
19. Azagury DE. Triadafilopoulos. Minimally invasive GERD therapies. In: Diagnosis and treatment of gastroesophageal reflux disease, vol. 7. Cham: Springer International Publishing; 2016. p. 117–44.
20. Triadafilopoulos G, Azagury D. How can we deal with the GERD treatment gap? Ann N Y Acad Sci. 2016;138(1):14–20.
21. Mayor MA, Fernando HC. Endoluminal approaches to gastroesophageal reflux disease. Thorac Surg Clin. 2018;28:527–32.
22. Pearl J, Pauli E, Dunkin B, Stefanidis D. SAGES endoluminal treatments for GERD. Surg Endosc. 2017;31:3783–90.
23. Auyang ED, Carter P, Rauth T, Fanelli RD, SAGES Guidelines Committee. SAGES clinical spotlight review: endoluminal treatments for gastroesophageal reflux disease (GERD). Surg Endosc. 2013;27(8):2658–72.
24. Hummel K, Richards W. Endoscopic treatment of gastroesophageal reflux disease. Surg Clin N Am. 2015;95:653–67.
25. Triadafilopoulos G. Stretta: a valuable endoscopic treatment modality for gastroesophageal reflux disease. World J Gastroenterol. 2014;20:7730–8.
26. Richards WO, Scholz S, Khiatan L, et al. Initial experience with the Stretta procedure for the treatment of gastroesophageal reflux disease. J Laparoendosc Adv Surg Tech A. 2001;11(5):267–73.
27. Arts J, Sifrim D, Rutgeerts P, Lerut A, et al. Influence of radiofrequency energy delivery at the gastroesophageal junction (the Stretta procedure) on symptoms, acid exposure, and esophageal sensitivity to acid perfusion in gastroesophageal reflux disease. Dig Dis Sci. 2007;52(9):2170–7.
28. Arts J, Bisschops R, Blondeau K, et al. A double-blind sham-controlled study of the effect of radiofrequency energy on symptoms and distensibility of the gastroesophageal junction in GERD. Am J Gastroenterol. 2012;107(2):222–30.
29. Aziz AM, El-Khayat HR, Sadek A, Mattar SG, et al. A prospective randomized trial of sham, single-dose Stretta, and double-dose Stretta for the treatment of gastroesophageal reflux disease. Surg Endosc. 2010;24(4):818–25.
30. Kim MS, Holloway RH, Dent J, et al. Radiofrequency energy delivery to the gastric cardia inhibits triggering of transient lower esophageal sphincter relaxation and gastroesophageal reflux in dogs. Gastrointest Endosc. 2003;57(1):17–22.
31. Tam WCE. Delivery of radiofrequency energy to the lower oesophageal sphincter and gastric cardia inhibits transient lower oesophageal sphincter relaxations and gastro-oesophageal sphincter relaxations and gastro-oesophageal reflux in patients with reflux disease. Gut. 2003;52(4):479–85.
32. Corley DA, Katz P, Wo JM, et al. Improvement of gastroesophageal reflux symptoms after radiofrequency energy: a randomized, sham-controlled trial. Gastroenterology. 2003;52(4):479–85.
33. Galmich JP, des Varannes SB. Endoluminal therapies for gastroesophageal reflux disease. Lancet. 2003;361:1119–21.
34. DiBaise JK, Brand RE, Quigley EM. Endoluminal delivery of radiofrequency energy to the gastroesophageal junction in uncomplicated GERD: efficacy and potential mechanism of action. Am J Gastroenterol. 2002;97:833–42.
35. Yeh RW, Triadafilopoulos G. Endoscopic antireflux therapy: the Stretta procedure. Thorac Surg Clin. 2005;15:395–403.
36. Triadafilopoulos G, DiBaise JK, Nostrant TT, Stollman NH, et al. The Stretta procedure for the treatment of GERD: 6 and 12 month follow-up of the U.S. open label trial. Gastrointest Endosc. 2002;55(2):149–56.
37. Velanovich V. The development of the GERD-HRQL symptom severity instrument. Dis Esophagus. 2007;20(2):130–4.
38. Perry KA, Banerjee A, Melvin WS. Radiofrequency energy delivery to the lower esophageal sphincter reduces esophageal acid exposure and improves GERD symptoms: a systematic review and meta-analysis. Surg Laparosc Endosc Percutan Tech. 2012;22(4):283–8.

39. Noar M, Squires P, Noara E, Lee M. Long-term maintenance effect of radiofrequency energy delivery for refractory GERD: a decade later. Surg Endosc. 2014;28(8):2323–33.
40. Fass R, Cahn F, Scotti DJ, Gregory DA. Systematic review and meta-analysis of controlled and prospective cohort efficacy studies of endoscopic radiofrequency for treatment of gastroesophageal reflux disease. Surg Endosc. 2017;31(12):4865–82.
41. Mattar SG, Qureshi F, Taylor D, Schauer PR. Treatment of refractory gastroesophageal reflux disease with radiofrequency energy (Stretta) in patients after Roux-en-Y gastric bypass. Surg Endosc. 2006;20(6):850–4.
42. Noar M, Squires P, Khan S. Radiofrequency energy delivery to the lower esophageal sphincter improves gastroesophageal reflux patient-reported outcomes in failed laparoscopic Nissen fundoplication cohort. Surg Endosc. 2017;31(7):2854–62.
43. McClusky DA, Khaitan L, Swafford VA, Smith CD. Radiofrequency energy delivery to the lower esophageal sphincter (Stretta procedure) in patients with recurrent reflux after antireflux surgery: can surgery be avoided? Surg Endosc. 2007;21(7): 1207–11.
44. Hu ZW, Wang ZG, Shang Y, et al. A preliminary investigation of anti-reflux intervention for gastroesophageal reflux related childhood-to-adult persistent asthma. Ann Surg Innov Res. 2014;8:3.
45. Liu DC, Somme S, Mavrelis PG, et al. Stretta as the initial antireflux procedure in children. J Pediatr Surg. 2005;40(1):1448–51.
46. Islam S, Geiger JD, Coran AG, Teitelbaum DH. Use of radiofrequency ablation of the lower esophageal sphincter to treat recurrent gastroesophageal reflux disease. J Pediatr Surg. 2004;39(3):282–6.
47. Nicolau AE, Lobontiu A, Constantinescu G. Endoluminal fundoplication (ELF) with EsophyX2 for gastroesophageal reflux disease (GERD). Chirurgia. 2009;104(4):381–7.
48. Jobe BA, O'Rourke RW, McMahon BP, et al. Transoral endoscopic fundoplication the the treatment of gastroesophageal reflux disease. The anatomic and physiologic basis for reconstruction of the esophagogastric junction using a novel device. Ann Surg. 2008;248(1):69–76.
49. Hunter JG, Kahrilas PJ, Bell RC, Wilson EB, et al. Efficacy of transoral fundoplication vs omeprazole for the treatment of regurgitation in a randomized controlled trial. Gastroenterology. 2015;148(2):324–33.
50. Trad KS, Barnes WE, Simoni G, et al. Transoral incisionless fundoplication effective in eliminating GERD symptoms in partial responders to proton pump inhibitor therapy at 6 months: the TEMPO randomized clinical trial. Surg Innov. 2015;22(1):26–40.
51. Trad KS, Fox MA, Simoni G, et al. Transoral fundoplication offers durable symptom control for chronic GERD: 3 year report from the TEMPO randomized trial with crossover arm. Surg Endosc. 2017;31(6):2498–508.
52. Trad KS, Barnes WE, Prevou ER, Simoni G, et al. The TEMPO trial at 5 years: Transoral fundoplication (TIF 2.0) is safe, durable, and cost-effective. Surg Innov. 2018;25(2):149–57.
53. Testoni PA, Testoni S, Mazzoleni G, et al. Long term efficacy of transoral incisionless fundoplication with EsophyX (TIF 2.0) and factors affecting outcomes in GERD patients followed for up to 6 years: a prospective single-center study. Surg Endosc. 2015;29(9):2770–80.
54. Chimukangara M, Jalilvand AD, Melvin WS, Perry KA. Long-term reported outcomes of transoral incisionless fundoplication: an 8-year cohort study. Surg Endosc. 2019;33:1304–9.
55. Huang X, Chen S, Zhao H, et al. Efficacy of transoral incisionless fundoplication (TIF) for the treatment of GERD: a systematic review with meta-analysis. Surg Endosc. 2017;31(3):1032–44.
56. Gerson L, Stouch B, Lobontiu A. Transoral incisionless fundoplication (TIF 2.0): a meta-analysis of three randomized controlled clinical trials. Chirurgia. 2018;113(2):173–84.
57. Bell RC, Kurian AA, Freeman KD. Revision of failed traditional fundoplication using EsophyX transoral fundoplication. Surg Endosc. 2013;27(3):761–7.
58. Bell RC, Kurian AA, Freeman KD. Laparoscopic anti-reflux revision surgery after transoral incisionless fundoplication is safe and effective. Surg Endosc. 2015;29(7):1746–52.
59. Perry KA, Linn JG, Eakin JL, Onders RP, Velanovich V, Melvin WS. Transoral incisionless fundoplication does not significantly increase morbidity of subsequent laparoscopic Nissen fundoplication. J Laparoendosc Adv Surg Tech A. 2013;23(5):456–8.
60. Chen S, Jarobe MD, Teitelbaum DH. Effectiveness of transluminal endoscopic fundoplication for the treatment of pediatric gastroesophageal reflux disease. Pediatr Surg Int. 2012;28(3):229–34.
61. Zacherl J, Roy-Shapira A, Bonavina L, et al. Endoscopic anterior fundoplication with the Medigus Ultrasonic Surgical Stapler (MUSE™) for gastroesophageal reflux disease: 6 month results form a multi-center prospective trial. Surg Endosc. 2015;29:220–9.
62. Kauer WK, Roy-Shapira A, Watson D, et al. Preclinical trial of a modified gastroscope that performs a true anterior fundoplication for the endoluminal treatment of gastroesophageal reflux disease. Surg Endosc. 2009;23(12):2728–31.
63. Roy-Shapira A, Bapaye A, Date S, et al. Tran-oral anterior fundoplication: 5-year follow-up of pilot study. Surg Endosc. 2015;29(12):3717–21.
64. Kim HJ, Kown CI, Kessler WR, et al. Long-term follow-up results of endoscopic treatment of gastroesophageal reflux disease with the MUSE™ endoscopic stapling device. Surg Endosc. 2016;30:3402–8.
65. Testoni PA, Mazzoleni G, Testoni SG. Transoral incisionless fundoplication for gastro-esophageal reflux disease: techniques and outcomes. World J Gastrointest Pharmacol Ther. 2016;7(2):179–89.

66. Azagury D, Morton J. Surgical anti-reflux options beyond fundoplication. Curr Gastroenterol Rep. 2017;19(7):35, 1–4.
67. Zak Y, Rattner DW. The use of LINX for gastroesophagel reflux. Adv Surg. 2016;50:41–8.
68. Ganz RA, Peters JH, Horgan S, et al. Esophageal sphincter device for gastroesophageal reflux disease. N Engl J Med. 2013;368(8):719–27.
69. Kethman W, Hawn M. New approaches to gastroesophageal reflux disease. J Gastrointest Surg. 2017;21(9):1544–52.
70. Bonavina L, DeMeester T, Fockens P, et al. Laparoscopic sphincter augmentation device eliminates reflux symptoms and normalizes esophageal acid exposure: one and 2-year results of a feasibility trial. Ann Surg. 2010;252(5):857–62.
71. Tatum JM, Alicuben E, Bildzukewicz N, Samakar K, Houghton CC, Lipham JC. Minimal versus obligatory dissection of the diaphragmatic hiatus during magnetic sphincter augmentation surgery. Surg Endosc. 2019;33:782–8.
72. Saino G, Bonavina L, Lipham JC, Dunn D, Ganz RA. Magnetic sphincter augmentation for gastroesophageal reflux at 5 years: final results of a pilot study show long-term acid reduction and symptom improvement. J Laparoendosc Adv Surg Tech A. 2015;25(10):787–92.
73. Ganz RA, Edmundowicz SA, Taiganides PA, Lipham JC, Smith CD, et al. Long-term outcomes of patients receiving a magnetic sphincter augmentation device for gastroesophageal reflux. Clin Gastroenterol Hepatol. 2016;14(5):671–7.
74. Louie BE, Smith CD, Smith CC, et al. Objective evidence of reflux control after magnetic sphincter augmentation: one year results from a post approval study. Ann Surg. 2019;270:302–8.
75. Lipham JC, Taiganides PA, Louie BE, Ganz RA, DeMeester TR. Safety analysis of the first 1000 patients treated with magnetic sphincter augmentation for gastroesophageal reflux disease. Dis Esophagus. 2015;28(4):305–11.
76. Smith CD, Ganz RA, Lipham JC, Bell RC, Rattner DW. Lower esophageal sphincter augmentation for gastroesophageal reflux disease: the safety of a modern implant. J Laparoendosc Adv Surg Tech A. 2017;27(6):586–91.
77. Alicuben ET, Bell RCW, Jobe BA, Buckley FB 3rd, Daniel Smith C, Graybeal CJ, Lipham JC. Worldwide experience with erosion of the magnetic sphincter augmentation device. J Gastrointest Surg. 2018;22(8):1442–7.
78. Asti E, Siboni S, Lazzari V, Boniita G, Sironi A, Bonavina L. Removal of the magnetic sphincter augmentation device. Ann Surg. 2016;265:941–5.
79. Chen MY, Huang DY, Wu A, et al. Efficacy of magnetic sphincter augmentation versus nissen fundoplication for gastroesophageal reflux disease in short term: a meta-analysis. Can J Gastroenterol Hepatol. 2017;2017:1–7.
80. Skubleny D, Switzer NJ, Dang J, Gill RS, Shi X, et al. LINX® magnetic esophageal sphincter augmentation versus nissen fundoplication for gastroesophageal reflux disease: a systematic review and meta-analysis. Surg Endosc. 2017;31(8):3078–84.
81. Bell R, Lipham J, Louie B, Williams V, et al. Laparoscopic magnetic sphincter augmentation versus double-dose proton pump inhibitors for management of moderate to severe regurgitation in GERD: a randomized controlled trial. Gastrointest Endosc. 2019;89:14–22.e1.
82. Hawasli A, Taraki M, Tarboush M. Laparoscopic management of severe reflux after sleeve gastrectomy using the LINX® system: technique and one year follow up case report. Int J Surg Case Rep. 2017;30:148–51.
83. Rona KA, Reynolds J, Schwameis K, et al. Efficacy of magnetic sphincter augmentation in patients with large hiatal hernias. Surg Endosc. 2017;31(5):2096–102.
84. Buckley FP 3rd, Bell RCW, Freeman K, et al. Favorable results from a prospective evaluation of 200 patients with large hiatal hernias undergoing LINX magnetic sphincter augmentation. Surg Endosc. 2018;32(4):1762–8.
85. Tatum JM, Lipham JC. Extraluminal approaches to gastroesophageal reflux disease. Thorac Surg Clin. 2018;28(4):521–6.
86. Crowell MD. Implanted electrical devices and gastroesophageal reflux disease: an effective approach to treatment. Expert Rev Gastroenterol Hepatol. 2013;7(3):189–91.
87. An investigation of the EndoStim Lower Esophageal Sphincter (LES) stimulation system for the treatment of reflux (LESS GERD). ClnicalTrials.gov Identifier: NCT02749071.
88. Hoppo T, Rodriguez L, Soffer E, Crowell MD, Jobe BA. Long-term results of electrical stimulation of the lower esophageal sphincter for treatment of proximal GERD. Surg Endosc. 2014;28(12):3293–301.
89. Kappelle WF, Bredenoord AJ, Conchillo JM, Ruurda JP, et al. Electrical stimulation therapy of the lower oesophageal sphincter for refractory gastro-oesophageal reflux disease- interim results of an international multicenter trial. Aliment Pharmacol Ther. 2015;42(5):614–25.
90. Rodriguez L, Rodriguez P, Gomez B, et al. Two-year results of intermittent electrical stimulation of the lower esophageal sphincter treatment of gastroesophageal reflux disease. Surgery. 2015;157(3):556–67.
91. Soffer E, Rodriguez L, Rodriguez P, Gomez B, et al. Effect of electrical stimulation of the lower esophageal sphincter in gastroesophageal reflux disease patients refractory to proton pump inhibitors. World J Gastrointest Pharmacol Ther. 2016;7(1):145–55.
92. Rodriguez L, Rodriguez PA, Gomez B, et al. Electrical stimulation therapy of the lower esophageal sphincter is successful in treating GERD: long term 3-year results. Surg Endosc. 2016;30(7):2666–72.
93. Borbely Y, Bouvy N, Schulz HG, et al. Electrical stimulation of the lower esophageal sphincter to address gastroesophageal reflux disease after sleeve gastrectomy. Surg Obes Relat Dis. 2018;14(5):611–5.

20 Evaluation and Treatment of the Patient with Recurrent Symptoms

Victoria Lyo and James Patrick Dolan

Introduction

Anti-reflux surgery was first introduced by Rudolph Nissen in 1955 to treat significant gastroesophageal reflux disease [1]. Almost 40 years later, the laparoscopic approach to fundoplication was introduced into surgical practice [2] and is currently the favored approach for treating reflux. Commonly, either the 360° (Nissen) or a posterior 270° partial fundoplication (Toupet) is the most popular anti-reflux procedure, with the anterior 180° (Dor) fundoplication reserved for selected situations such as after Heller myotomy for achalasia. Based on this effective surgical approach, the majority of patients with abnormal 24-hour pH scores, typical primary symptoms, and a good response to acid suppression therapy will have a favorable response after surgery [3]. However, between 2 and 30% of patient can "fail" after anti-reflux surgery in a manner that depends on how "failure" is defined [4–7]. Patients can develop heartburn, dysphagia, or gas bloating after anti-reflux surgery, or there may be an anatomic failure of the anti-reflux wrap after the operation. Such anatomic postoperative failures are generally classified as a disrupted fundoplication, a slipped fundoplication with stomach slipping above the diaphragm or above the wrap, a malpositioned fundoplication, a herniated fundoplication above the diaphragm, or a fundoplication that is too tight or long (Fig. 20.1) [7].

In this chapter, we will review the anatomic and physiologic evaluation of patients with these new or recurrent symptoms after anti-reflux surgery and provide a guide for their management.

Patients with Dysphagia

The evaluation of new or recurrent symptoms depends on the timing after surgery. Postoperative dysphagia within 3 months of surgery is fairly common and occurs in up to 30–40% of cases: the etiology is often multifactorial [7]. Esophageal and fundoplication edema, transient esophageal dysmotility, and hematomas due to needle injury can all cause temporary gastroesophageal junction outflow obstruction. As a general rule, dysphagia in this setting can be managed conservatively unless there is concomitant dehydration, weight loss, bleeding, or persistent vomiting. Because we anticipate some degree of dysphagia in all our patients, we recommend that all adhere to a liquid diet for 2 weeks postoperatively, followed by a soft diet for 2 weeks, avoiding raw vegetables, hard meats, and breads that may worsen postoperative dysphagia or precipitate food impaction or retching.

Beyond the early postoperative period, dysphagia occurs in 2–5% of cases up to 5 years after surgery [8, 9]. Causes of postoperative dysphagia

V. Lyo · J. P. Dolan (✉)
Department of Surgery, Oregon Health & Science University, Portland, OR, USA
e-mail: vlyo@ucdavis.edu; dolanj@ohsu.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_20

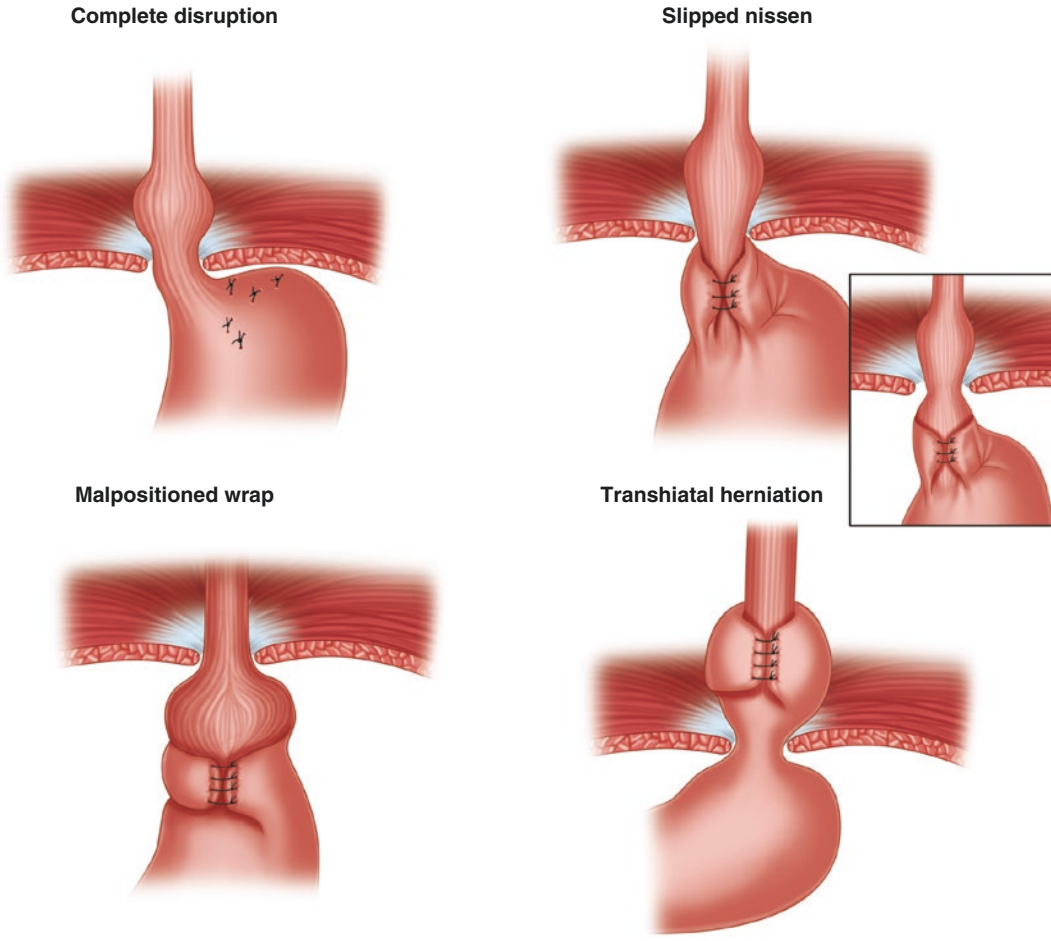


Fig. 20.1 Types of surgical failure of Nissen fundoplication (Image reused with permission © Lippincott-Raven [10])

can be divided into distinct categories. Fundoplication issues include overly tight wrap, twisted wrap, slipped, or malpositioned fundoplication. Another category is that of a normal fundoplication with tight or constricted hiatal closure. Undiagnosed esophageal motility disorders such as achalasia, ineffective esophageal motility, and eosinophilic esophagitis may also cause evolving dysphagia. Finally, recurrent paraesophageal hernias in the setting of a prior repair with full or partial fundoplication may manifest as dysphagia [8–11]. A solid predictor of postoperative dysphagia is preoperative dysphagia [12]. Interestingly, preoperative motility studies can be of poor predictive value [13].

Workup and Treatment

When liquids are not tolerated after 6–12 weeks postoperatively, we recommend evaluation with a barium esophagram that includes ingestion of a 13-mm barium pill (or "tablet" as it is also termed). This study will identify any major anatomic abnormalities as well as stenosis at the gastroesophageal junction if the barium pill fails to pass after more than 30 seconds. If the esophagram shows normal passage of both contrast and the barium pill, then a functional problem most likely exists. In these instances, if symptoms are mild to moderate, then reassurance can be provided. It has been our experience that reassurance alone (in conjunction with a

thorough dietary history and counselling) can resolve dysphagia in approximately 40% of cases without any further interventions. In all cases, however, plans should be made for an esophageal motility study if symptoms do not resolve within 2–4 weeks from consultation. Overall, the current literature suggests that 50% of patients with mild dysphagia without weight loss and few dietary restrictions will resolve their symptoms within a year [14, 15]. In instances when stenosis is demonstrated at the gastroesophageal junction by no (or delayed) passage of the barium pill, endoscopic balloon dilation should be considered as the primary intervention in a timely fashion without further studies to abrogate continuing caloric malnutrition. In the minority of instances, when the barium esophagram demonstrates an obvious, significant anatomic abnormality such as a slipped or herniated fundoplication with nonpassage of the barium pill, we recommend expedient reoperation if dysphagia is debilitating. This may entail proceeding without a formal motility study with an understanding between the patient and surgeon that a partial fundoplication may be the anatomic outcome of reoperation and that an endoscopy will be performed in the operating room prior to surgery.

Upper endoscopy should be performed in almost all patients with persistent postoperative dysphagia, with the exception of cases where an obvious immediate diagnosis is evident on the barium esophagram. Endoscopy allows detection of additional findings not easily appreciated on a contrast study, such as eosinophilic esophagitis and/or esophageal rings. Endoscopy also better characterizes the gastroesophageal junction and fundoplication including the resistance to endoscope passage. On retroflexion, an intact Nissen fundoplication will have a characteristic long valve body adhering to the endoscope circumferentially through all phases of respiration. The gastroesophageal junction will be located below the crura, confirming the wrap is around the distal esophagus [17]. A slipped fundoplication or re-herniation of the wrap above the diaphragm, may be apparent on endoscopy and may substantiate the symptom of dysphagia within the correct clinical setting (Fig. 20.2).

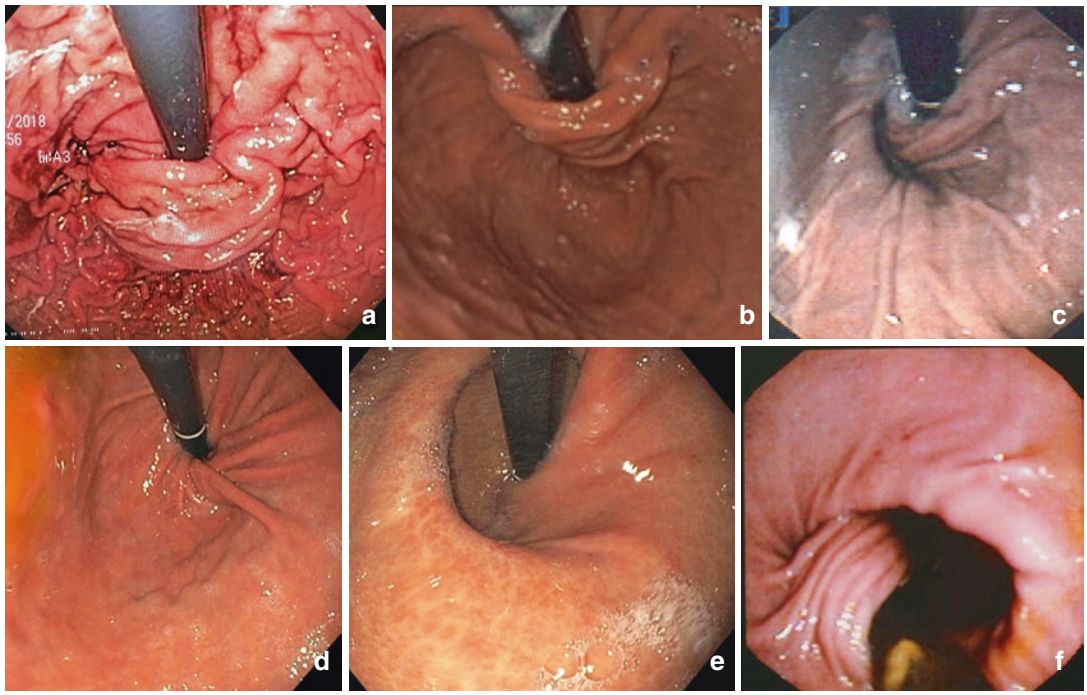


Fig. 20.2 A retroflexed gastroscope identifies most abnormalities of the fundoplication. (**a**, **b**) Retroflexed view of a well-formed Nissen fundoplication. (**c**) Herniated fundoplication. (**d**) Partially disrupted fundoplication. (**e**) Disrupted fundoplication and recurrent hernia. (**f**) Twisted valve in a "two-compartment stomach" (Image C and F reused with permission © Springer Nature [16])

Patients with severe dysphagia and a normal esophagram, or patients with an abnormal esophagram, should be referred for esophageal motility study. These results should aid in the diagnosis of any underlying esophageal motility disorder, such as ineffective esophageal motility, esophageal spasm, achalasia, or increases gastroesophageal junction pressure, which may be contributing to symptoms and can provide information that might assist with definitive treatment. The decision to operate will depend on the patient's nutritional status and severity of dysphagia as previously noted. For those patients with persistent dysphagia, weight loss, and ineffective motility shown on manometry, we would recommend converting a Nissen to a Toupet fundoplication after maximizing nutritional status. In cases when a hypertensive lower esophageal sphincter is diagnosed in conjunction with esophageal aperistalsis, a Heller myotomy with Dor fundoplication may be performed to attempt resolution of symptoms [14–16]. Often, this may necessitate takedown of the prior fundoplication, and this procedure is usually difficult but not impossible. If motility is normal, and a slipped fundoplication without a hiatal problem is visualized, then a revision to a floppy Nissen fundoplication should be considered.

Patients with Recurrent Reflux or Heartburn Symptoms

Recurrent symptoms such as chest pain, heartburn, and regurgitation are also common in the early postoperative period and are often best managed with reassurance and attention to diet. It is worth remembering that patients with evidence of significant esophagitis or gastritis preoperatively may not have full healing of these conditions for some time after surgery. When symptoms are similar to before surgery, a trial of acid suppression is appropriate in these individuals, as they will likely resolve with therapy. When symptoms persist or recur after 3 months post-operatively, further workup is warranted. On initial consideration, it might be tempting to conclude that a partial wrap might be associated with a high rate of reflux symptoms and, consequently, frame our response to patient concerns. In reality, this is not the case. A recent meta-analysis, examining the results of 13 randomized clinical trials found no difference in persistent reflux symptoms between laparoscopic Nissen and Toupet fundoplications [18]. It may also be a surprise to many practitioners who provide both medical and surgical treatment of reflux disease, that between 2 and 40% of patient experience some degree of recurrence of their symptoms at 5 years after their initial operation [7, 11, 19, 20]. It is also worth noting that between 15% and 50% of patients are prescribed proton pump inhibitor (PPI) therapy postoperatively, mainly by their primary care provider, and that there is increased use of these medications as follow-up time increases [20, 21]. Other aggregate causes of recurrent reflux symptoms include poor initial evaluation, technically inadequate fundoplication, disrupted or slipped fundoplication, recurrent hiatal hernia with intrathoracic wrap migration, undiagnosed esophageal dysmotility, or infection. Earlier symptoms may suggest a technically inadequate initial fundoplication or a disrupted fundoplication, but both present with decreased lower esophageal sphincter pressure. With careful questioning, it is not infrequent that a patient may attribute onset of recurrent symptoms to a retching event, gastrointestinal illness, or after a particular episode of vigorous activity or coughing.

Many studies have attempted to identify predictors of poor symptomatic outcome after fundoplication, but consistent factors have not been reliably identified. One group followed patients for 11 years postoperatively and found that those with atypical symptoms, no response to acid-suppressive therapy, and those with a BMI >35 kg/m^2 were more likely to fail anti-reflux surgery, as evidenced by reoperation, poor patient satisfaction, or severe symptoms [22]. However, a large meta-analysis of 63 studies did not find consistent evidence that age, sex, BMI, or preoperative response to acid suppression, esophagitis, or dysmotility was associated with postoperative outcomes [23]. Based on our review of quality studies and our own experience, we have found that preoperative predictors of success after fun-

doplication include the presence of typical GERD symptoms, responsiveness to PPI therapy, and abnormal 24-hour pH study with a positive symptom index. We have also found that patients with atypical symptoms, or symptoms associated with cough, chest pain, or hoarseness often fail to achieve full resolution of these symptoms postoperatively.

Workup and Treatment

Recurrent symptoms of reflux alone can be poor indicators of a specific physiologic or anatomic issue, and objective studies should be performed in all cases where conventional dietary and behavior modifications have not helped. We usually start our workup with a barium esophagram and barium pill to identify anatomic abnormalities of the fundoplication or re-herniation. Barium swallow can reveal multiple abnormalities such as free reflux of contrast or loss of a normal fundoplication filling defect, suggestive of a disrupted fundoplication. A new or recurrent hiatal hernia may be present and associated with slippage of the proximal stomach above the wrap or migration of the entire wrap above the diaphragm. If these findings are seen, we recommend upper endoscopy to better delineate the anatomy and help determine if other esophageal pathology is present. If findings are normal, reassurance with or without a trial PPI therapy can be attempted. If symptoms persist, an upper endoscopy should be performed with plans for a concurrent pH study unless significant esophagitis is visualized and biopsied. With a normal esophagram, most patients will have normal follow-up studies, but up to 10% will have findings on esophagogastroduodenoscopy (EGD) that were not detected on esophagram. A disrupted fundoplication, for example, may be seen on endoscopy as a patulous gastroesophageal junction or loose wrap seen on retroflexion (Fig. 20.2) [16, 17]. When no anatomic deformities are seen on esophagram or endoscopy, a 24-hour pH monitoring study is often normal.

Definitive treatment in cases where symptoms are persistent and severe will probably warrant reoperation to reduce a hiatal hernia if one if present, or to revise the prior hiatal repair or fundoplication. When arriving at this point, a thorough workup should include esophagram, endoscopy (with biopsy as indicated by findings), and pH study. Dysmotility is occasionally reported by the radiologist performing the esophagram and is usually best confirmed with esophageal manometry. If there is significant dysmotility on manometry, even if the patient has no swallowing symptoms, we would still recommend conversion of a Nissen to a partial fundoplication to eliminate any swallowing difficulties after the reoperation. When the esophageal motility is normal, then a redo Nissen fundoplication can be performed. Careful patient counselling as to the expectations of outcomes is essential prior to any revision operation.

Patients with Gas Bloat

Gas bloating after fundoplication refers to a wide range of symptoms that may include abdominal distension, postprandial fullness, nausea, generalized abdominal discomfort, and the inability to belch and/or vomit with the associated sensation of trapped abdominal gas. Habitual swallowing to clear gastric acid reflux with resultant aerophagia may be a learned response in quite a number of patients. This can contribute to postoperative gas bloat, since air trapping cannot be relieved by belching with a competent fundoplication [7, 24]. Patients with postoperative gas bloat symptoms may either have an exacerbation of a preoperative functional problem, a novel postoperative problem, or may have overt delayed gastric emptying resulting from vagal injury. Those in the first group generally suffer from aerophagia or unidentified preoperative delayed gastric emptying. The second group of individuals are generally those with sensitivity to narcotic pain medications or preexisting diabetes with a postoperative elevation in serum glucose levels. Rarely, patients in this group may have suffered from transient vagal nerve traction or thermal injury that will resolve over time or have a sizable intra-thoracic stomach that has been returned to the abdomen. Patients in the latter category gen-

erally have significant undiagnosed gastroparesis or have suffered injury to both vagal nerves. The prevalence of gas bloat syndrome is reported to be as high as 85% in the first 3 months after surgery [25, 26], but these symptoms mostly resolve, resulting in a prevalence of 7.5% at 5 years [8, 11]. Fortunately, in a study of patients requiring revision surgery, only 4.6% of cases were found to have gas-related symptoms or gastroparesis [11, 27].

Patients with preoperative aerophagia, those with narcotic dependence or long-standing diabetes, and patients who undergo a Nissen fundoplication as compared to a Toupet may be at higher risk for postoperative gas bloating. In a small study of 56 patients with reflux and aerophagia, those undergoing a Nissen fundoplication compared to Toupet were more likely to report bloating, postprandial fullness, and flatulence [24]. Furthermore, a meta-analysis of five studies also showed increased gas-related symptoms after Nissen fundoplication (31%) over Toupet (24%) [18].

Workup and Treatment

Antiemetics are the first-line treatment for initial postoperative nausea and bloating during the first few months after operation. A cocktail of simethicone, ondansetron, promethazine, and a promotility agent such as metoclopramide is often used. When symptoms are more severe or persist beyond the initial 3-month postoperative period, additional investigation is warranted [7, 14, 16]. Abrupt withdrawal of PPI therapy may also contribute to postoperative nausea or other ill-defined symptoms. Initial workup may begin with a barium swallow and EGD to identify any evidence of gastritis, *H. pylori* infection, fundoplication disruption, herniation, or even too tight of a wrap. Residual food in the stomach on endoscopy after a 12-hour fast is suggestive of gastroparesis. In this case, and in cases where esophagram is normal, a gastric emptying study with a 4-hour solid-phase evaluation should be performed to evaluate gastric retention. We have found no utility in liquid phase alone or abbreviated gastric emptying studies.

When delayed gastric emptying is detected, pro-motility agents are the first line of treatment. Metoclopramide (Reglan) or erythromycin is our usual agent of choice. However, caution should be maintained for any neurologic or cardiac side effects depending on the specific agent. Optimization of diabetes management and cessation or minimization of narcotic use can also be helpful. If symptoms are not alleviated with these measures, we usually proceed with a pyloric botulinum toxin (Botox®) injection or pyloric balloon dilatation to see if these interventions improve gastric emptying. If these measures are successful, patients can then elect for interval surveillance. When repeat Botox® injection or balloon dilatation is required within 3 months of an initial endoscopic intervention, it is reasonable to discuss the option of a repeat endoscopic intervention or a laparoscopic pyloromyotomy or pyloroplasty. Placement of a gastric stimulation device is usually of little utility in this patient population. Conversion to a subtotal gastrectomy with Roux-en-Y gastrojejunostomy reconstruction is a final option, but outcomes, in this patient population, are often less than ideal.

When all studies are normal, other etiologies such as irritable bowel syndrome and small intestinal bacterial overgrowth (SIBO) should be considered. Up to 15% of patients can also have postprandial diarrhea after fundoplication, and it is usually mild and low volume [11]. Evaluation of these etiologies include a hydrogen breath test for SIBO, a trial of antibiotics for SIBO, a trial of anti-motility drugs, or cholestyramine [11]. For patients with aerophagia, simethicone multiple times daily be beneficial, and patients may benefit from a dietary evaluation or, in the least, should be counseled to eat more slowly with attention to specific food triggers.

Reoperation for Fundoplication Failure and Resultant Symptoms

Some centers perform reoperative anti-reflux surgery through a laparotomy or thoracotomy. When undertaken by an experienced foregut team, the laparoscopic approach should be successful in

over 97% of cases, especially if the initial operation was done laparoscopically. Consequently, it is generally advised that revision surgery should be performed at a high-volume foregut unit in order to optimize outcomes.

In our center, we utilize the standard five-trocar upper abdominal configuration. Adhesiolysis using the ultrasonic shears to lyse the dense gastrohepatic scarring between the left lateral section of the liver and the lesser curvature of the stomach is almost always needed before placing the liver retractor. The successful retraction of the liver above the operative field is the first critical maneuver of the operation. This gives a broad view of the anatomy and allows us to determine our initial approach for revision. The goals of the initial dissection are to completely identify and isolate the diaphragmatic hiatus and to safely identify the esophagus. Often, starting the initial approach from the patient's left side with the intent to identify the column of the left crus is easier. Adhesions from the previously divided short gastric are easily cleared, and this allows for reduction of any recurrent hernia and the greater curvature of the stomach. Following this, a retro-gastric dissection inferior to the decussation of the right and left crura can be performed to prepare for the lesser curvature dissection. Next, we begin our lesser curvature dissection by identifying the most inferior portion of the caudate lobe of the liver. From this point, we use the harmonic scalpel to free up the dense gastrohepatic ligament scar tissue as we move superiorly toward the column of the right crus. This can be a challenging dissection, made more difficult by the usual welding of scar tissue of the prior wrap to the shoulder of the right crus. Dissection in this area – usually between the 9 and 12 o'clock position on the crura – may result in removal of some portions of Glisson's capsule. Troublesome bleeding, as a consequence, may be treated with local application of topical agents such as Surgicel® (Ethicon, Ohio). Invariably, following the inferior margin of the caudate lobe will lead to the column of the right crus. This area is usually involved in the densest adhesions between the wrap and the hiatus, and tedious dissection from in inferior and superior may be needed to complete a 360-degree dissection around the hiatus; a Penrose drain is then placed in the abdomen, and the distal esophagus is encircled with it. Gentle tension on the Penrose drain facilitates reduction of the stomach and distal esophagus into the abdomen so as to facilitate a circumferential mediastinal dissection. In reoperative surgery, a pleural rent (particularly on the left) is not uncommon and can lead to a capnothorax. Good communication between the surgical and anesthesia teams can identify any pulmonary or hemodynamic consequences of this. Usually, pausing the operation and releasing pneumoinsufflation, or passing a red rubber catheter into the rent will help equalize the pressure in the chest and abdomen and allow for the case to progress. Unusually, a thoracostomy tube may have to be placed in instances where pulmonary or hemodynamic instability is profound and not responsive to less-invasive means.

Once the fundoplication and distal esophagus are mobilized from the chest, the fundoplication is taken down with sharp dissection along the track of the prior anterior sutures. Adhesions formed between the fundoplication and upper stomach are divided to recreate normal anatomy. Identification of the anterior and posterior vagus nerves during this dissection is important to minimize the chance of injury. At times, an old hernia sac or gastroesophageal fat pad remnant is seen and resected. Next, with the esophagus and stomach in their normal position off tension, intra-abdominal esophageal length is assessed. If 3 centimeters of intra-abdominal esophagus is not present, a Collis gastroplasty should be performed. Any hiatal defect is then closed over a bougie with interrupted permanent sutures (we prefer 0-Ticron with felt pledgets) with or without mesh reinforcement. Recreation of a fundoplication will be determined by the patient's underlying esophageal motility and symptoms.

While the success rates of first operations are between 90 and 95%, each successive operation is associated with deteriorating results [16]. Generally, second and third operations are successful between 80–90% and 50–66% of the time, respectively. Considering that fourth operations are rarely successful, some experts would recommend creation of a subtotal gastrectomy with Roux-en-Y gastrojejunostomy or esophageal resection.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Nissen R. Eine einfache Operation zur Beeinflussungder Refluxoesophagitis. Schweiz Med Wochenschr. 1956;86:590–2.
2. Dallemagne B, Weerts JM, Jehaes C, Markiewicz S, Lombard R. Laparoscopic Nissen fundoplication: preliminary report. Surg Laparosc Endosc. 1991;1:138–43.
3. Campos GM, Peters JH, DeMeester TR, Oberg S, Crookes PF, Tan S, DeMeester SR, et al. Multivariate analysis of factors predicting outcome after laparoscopic Nissen fundoplication. J Gastrointest Surg. 1999;3(3):292–300.
4. Dallemagne B, Weerts J, Markiewicz S, Dewandre JM, Wahlen C, Monami B, et al. Clinical results of laparoscopic fundoplication at ten years after surgery. Surg Endosc. 2006;20(1):159–65.
5. Cuschieri A, Hunter J, Wolfe B, Swanstrom LL, Hutson W. Multicenter prospective evaluation of laparoscopic antireflux surgery. Preliminary report. Surg Endosc. 1993;7(6):505–10.
6. Fein M, Bueter M, Thalheimer A, Pachmayr V, Heimbucher J, Freys SM, et al. Ten-year outcome of laparoscopic antireflux surgery. J Gastrointest Surg. 2008;12(11):1893–9.
7. Hinder RA, Klingler PJ, Perdikis G, Smith SL. Management of the failed anti-reflux operation. Surg Clin North Am. 1997;77:1083–98.
8. Pessaux P, Arnaud JP, Delattre JF, Meyer C, Baulieux J, Mosnier H. Laparoscopic antireflux surgery: five-year results and beyond in 1340 patients. Arch Surg. 2005;140(10):946–51.
9. Hunter JH, Swanstrom L, Waring JP. Dysphagia after laparoscopic antireflux surgery. Ann Surg. 1996;224(1):51–7.
10. Hinder RA. Gastroesophageal reflux disease. In: Bell Jr RH, Rikkers LF, Mulholland MW, editors. Digestive tract surgery: a text and atlas. Philadelphia: Lippincott-Raven Publishers; 1996. p. 19.
11. Lin DC, Chun CL, Triadafilopoulos G. Evaluation and management of patients with symptoms after anti-reflux surgery. Dis Esophagus. 2015;28(1):1–10.
12. Herron DM, Swanström LL, Ramzi N, Hansen PD. Factors predictive of dysphagia after laparoscopic Nissen fundoplication. Surg Endosc. 1999;13(12):1180–3.
13. Cole SJ, van den Bogaerde JB, van der Walt H. Preoperative esophageal manometry does not predict postoperative dysphagia following anti-reflux surgery. Dis Esophagus. 2005;18(1):51–6.
14. Hunter JG. Approach and management of patients with recurrent gastroesophageal reflux disease. J Gastrointest Surg. 2001;5(5):451–7.
15. Patti MG, Feo CV, De Pinto M, Arcerito M, Tong J, Gantert W, et al. Results of laparoscopic antireflux surgery for dysphagia and gastroesophageal reflux disease. Am J Surg. 1998;176:564–8.
16. Hunter JG, Fennerty MB. Persistent symptoms after anti-reflux surgery and their management. In: Ferguson MK, Bennerty MB, editors. Managing failed anti-reflux therapy. 1st ed. London: Springer-Verlang; 2006. p. 78–89.
17. Jobe BA, Kahrilas PJ, Vernon AH, et al. Endoscopic appraisal of the gastroesophageal valve after antireflux surgery. Am J Gastroenterol. 2004;99(2):233–43.
18. Tian Z, Wang B, Shan C, Zhang W, Jiang D, Qiu M. A meta-analysis of randomized controlled trials to compare long-term outcomes of nissen and toupet fundoplication for gastroesophageal reflux disease. PLoS One. 2015;10(6):e0127627.
19. Morgenthal CB, Shane MD, Stival A, Gletsu N, Milam G, Swafford V, et al. The durability of laparoscopic Nissen fundoplication: 11-year outcomes. J Gastrointest Surg. 2007;11:693–700.
20. Van Meer S, Bogte A, Siersema PD. Long-term follow up in patients with gastroesophageal reflux disease with specific emphasis on reflux symptoms, use of anti-reflux medication and anti-reflux surgery outcome: a retrospective study. Scand J Gastroenterol. 2013;48(11):1242–8.
21. Dominitz JA, Dire CA, Billingsley KG, Todd-Stenberg JA. Complications and antireflux medication use after antireflux surgery. Clin Gastroenterol Hepatol. 2006;4(3):299–305.
22. Morgenthal CB, Lin E, Shane MD, Hunter JG, Smith CD. Who will fail laparoscopic Nissen fundoplication? Preoperative prediction of long-term outcomes. Surg Endosc. 2007;21(11):1978–84.
23. Ip S, Tatsioni A, Conant A, Karagozian R, Fu L, Chew P, Raman G, et al. Predictors of clinical outcomes following fundoplication for gastroesophageal reflux disease remain insufficiently defined: a systematic review. Am J Gastroenterol. 2009;104(3):752–8.
24. Granderath FA, Kamolz T, Granderath UM, Pointner R. Gas-related symptoms after laparoscopic 360 degrees Nissen or 270 degrees Toupet fundoplication in gastrooesophageal reflux disease patients with aerophagia as comorbidity. Dig Liver Dis. 2007;39(4):312–8.
25. Frantzides CT, Carlson MA, Zografakis JG, Moore RE, Zeni T, Madan AK. Postoperative gastrointestinal complaints after laparoscopic Nissen fundoplication. JSLS. 2006;10(1):39–42.
26. Richter JE. Gastroesophageal reflux disease treatment: side effects and complications of fundoplication. Clin Gastroenterol Hepatol. 2013;11(5):465–71.
27. Lamb PJ, Myers JC, Jamieson GG, Thompson SK, Devitt PG, Watson DI. Long-term outcomes of revisional surgery following laparoscopic fundoplication. Br J Surg. 2009;96:391–7.

From Heartburn to Lung Fibrosis and Beyond

21

Benjamin E. Haithcock

Introduction

End-stage lung disease (ESLD) represents a spectrum of pulmonary processes culminating in pulmonary failure. These entities may include idiopathic pulmonary fibrosis (IPF), cystic fibrosis (CF), and connective tissue diseases such as scleroderma. A precipitating factor contributing to the severity of these diseases includes gastroesophageal reflux disease (GERD). The definition of GERD incorporates a wide breadth of pathophysiologic consequences and is not solely limited to increased acid exposure in the esophagus. Even though increased aspiration of gastric acid has been described as one of the etiologies responsible for some aspects of ESLD, other factors leading to the aspiration of gastrointestinal contents play a role in some of the findings associated with ESLD. These pathways include upper esophageal sphincter disorders and esophageal dysmotility of various categories, including connective tissue disorders, impaired lower esophageal sphincter function, pepsin reflux, biliary reflux, abnormal gastric emptying, and duodenal reflux. The correlation with GERD may need to incorporate several of these pathways resulting in aspiration and lung damage. These pathways leading to lung damage may also occur in patients undergoing lung transplant resulting in different degrees of chronic lung allograft dysfunction (CLAD), specifically the phenotype resulting in bronchiolitis obliterans syndrome [1]. The initial etiology of either ESLD or chronic lung allograft dysfunction progression is not as clear. Lo et al. proved that increase total reflux, not just acid reflux, may be associated with poorer early posttransplant outcomes [2].

There have been several case reports that suggest that early management of patients with evidence of GERD may benefit from medical or surgical management of their reflux. Most studies have been clear that early surgical management of gastroesophageal reflux symptoms stabilizes the progression of decreasing FVC in patients with ESLD. In addition, there have been studies that suggest an improvement of FVC following minimally invasive antireflux surgery and an improvement in the pulmonary destruction in some patients with ESLD.

GERD and IPF

A number of studies have demonstrated the role of GERD relationship in patients with IPF. Tobin et al. describe 17 patients with biopsy-proven IPF that demonstrated increased esophageal acid exposure as measured through dual-sensor, ambulatory esophageal pH monitoring. This acid exposure was significantly greater than eight control patients with ILD other than IPF. Four of the 17 patients studied had typical symptoms of

B. E. Haithcock (✉)
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA
e-mail: benjamin_haithcock@med.unc.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_21

reflux. The authors concluded that patients with IPF have a high prevalence of increased esophageal acid exposure. Gastroesophageal reflux in these patients typically occurs at night and extends into the proximal esophagus. They also surmised that acid reflux may be a contributing factor in the pathophysiology of IPF [3]. The same group evaluated 65 patients with IPF that underwent both 24-hour pH monitoring and esophageal manometry. They showed that 87% of IPF patients had abnormal acid exposure. Seventy-six percent of this study group had abnormal distal acid exposure, and 63% had proximal abnormal esophageal acid exposure. Despite the high percentage of acid exposure measured by pH monitoring, only 47% experienced classic GERD symptoms. Esophageal manometry in these patients with IPF showed normal peristaltic activity [4]. This study did not show a clear relationship of abnormal esophageal peristalsis and IPF. Other studies have been less clear about the role of abnormal peristalsis in patients with IPF. Sweet et al. evaluated 109 patients awaiting lung transplant. Fifty-five percent of these patients had hypotensive lower esophageal sphincter, and 47% demonstrated impaired esophageal peristalsis. Only 25% of these patients had a diagnosis of IPF [5].

GERD and Connective Tissue Disorders

Despite these equivocal studies, there remains a concern among clinicians about the contribution of abnormal esophageal peristalsis to ESLD. This is very apparent in patients with connective tissue disorders such as scleroderma. In these patients, the smooth muscle of the esophagus atrophies resulting in weak muscular contraction and replacement of the esophageal muscle wall with fibrosis. This fibrosis occurs in the mid and distal portion of the esophagus while preserving the striated muscle of the upper esophagus [6]. Diagnosis of esophageal dysfunction in these patients is based on esophageal manometry depicting the low-amplitude peristaltic waves in the lower two-third of the esophagus. This eventually may lead to aperistalsis with reduced lower esophageal sphincter pressure [7]. The reflux and often silent aspiration may contribute to the lung disease seen in these patients. Because of the pulmonary effects related to patients with connective tissue disorders, this may become a relative contraindication for lung transplantation in some centers.

GERD in Cystic Fibrosis

In patients with cystic fibrosis (CF), it has been suggested that the progression of bronchiectasis is related to the degree of their reflux. To evaluate the presence of duodenogastric reflux in patients with CF, Hallberg et al. studied 10 patients with CF and compared them to 7 health volunteers; all patients had normal migrating motor complexes. All participants underwent gastroduodenal manometry and intragastric perfusion for evaluation of bilirubin and bile acids. Eight CF patients had higher gastric bilirubin levels and five CF patients had bile acid regurgitation. These findings demonstrated that CF patients had an increased incidence of duodenogastric reflux when compared to healthy patients [8]. To determine if the presence of bile acids in sputum of CF patients correlated with their severity of disease, Pauwels et al. obtained sputum from 41 CF patients. The sputum was tested for bile acids and neutrophil elastase. Spirometry and BMI were also assessed at the time of sputum collection. This demonstrated that more than half of the patients with CF had bile acids present in their sputum, suggesting aspiration of duodenogastric contents. This aspiration was associated with increased airway inflammation, the degree of lung function impairment, as well as the need for antibiotics [9].

GERD After Lung Transplant

Several studies have demonstrated the association of chronic lung allograft dysfunction with gastroesophageal reflux and increased acid exposure to the allograft. This may be due to changes

in the anatomy of chest in patients after lung transplant. The etiology may also be related to undiagnosed GERD in patients with ESLD prior to their transplant. In addition, nonacidic reflux has been suggested as another nonimmunologic mechanism for chronic lung allograft dysfunction, as seen in patients with cystic fibrosis. One study of a subset of patients undergoing transplantation estimated the incidence of pretransplant GERD at 35% and the incidence of posttransplant GERD to be 65% [10].

The course of the esophagus through the thoracic cavity is important in its relationship to post-lung transplant CLAD. As the esophagus courses through the thoracic inlet, it deviates to the left and then approaches midline in the mid chest cavity around the level of the carina of the trachea. The esophagus remains along the thoracic vertebra bodies and then deviates to the left as it passes through the esophageal hiatus of the diaphragm.

During the course of lung transplant, the esophagus, vagus nerve, or esophageal collaterals may be injured anywhere along the path of the intrathoracic esophagus. This may occur at the thoracic inlet as the esophagus is entering the chest. In patients who have had previous pneumothoraces, there may be dense adhesions in the area leading to a challenging dissection. This can result in potential injury to the recurrent laryngeal nerves or proximal vagal nerves resulting in upper esophageal sphincter dysfunction or vocal cord paralysis. In patients with infectious components related to their ESLD, such as in patients with CF, there are typically large lymph nodes and bronchial arterial collaterals, especially around the mid portion of the esophagus as it passes near the carina. Dissection in this area may lead to further injury of the vagus nerve or collaterals. There may be incidental ligation of the nerve or arterial collaterals of the esophagus as hemostasis from lung transplant is occurring. If the patient is undergoing a repeat lung transplant, there may be injury anywhere along the esophagus because of dense adhesions. Injury to the vagus nerve and its branches may result in either esophageal or gastric dysfunction. This can lead to either esophageal or gastric dysmotility and resultant reflux [11]. This has been further characterized by Reid et al., who presented their initial findings of complications in 11 heart lung transplants. The authors identified five recipients who developed chronic aspiration. This was evident by these recipients having a chronic cough and either delayed gastric emptying or esophageal dysmotility. Imaging studies supporting this were either a nuclear study or a barium meal. Three of these patients had esophageal manometry performed demonstrating decreased primary peristalsis or diminished amplitude of the primary peristaltic wave. At the time of evaluation, these five patients had evidence of bronchiectasis. Three of these patients were identified to have obliterative bronchiolitis. Most of the five patients who improved after medical therapy were instituted to inhibit reflux. The authors believed the etiology of this cohort of patients was due to injury of the vagus nerve during the course of the heart–lung transplant [12]. This initial report has been confirmed by other studies suggesting that post-thoracic transplant patients experience esophageal or gastric dysmotility due to a possible injury to the vagus nerves or its branches during the conduct of the transplant [13, 14]. Another etiology of CLAD after lung transplant may be related to bile salts. Bile acid aspiration has been associated with biomarkers of injury following lung transplantation. This suggests a possible etiology for lung allograft injury suggesting a possible pathway due to nonacid reflux [15].

Taken together, a combination of one or several of these issues contribute to the further progression of the lung destruction in patients with ESLD. During the workup and evaluation of these patients, these physiologic issues must be taken into account in the studies performed.

Because of the above concerns, these patients should be considered for anti-reflux surgery. The evaluation should include evaluation of acid exposure in these patients. Esophageal manometry is also important in determining the degree of esophageal dysmotility present in this patient population. Gastric motility studies should be included in these patients to assist in optimum management. Imaging studies of the chest

including CT scans will assist in evaluating anatomic issues contributing to these patients' GERD.

The data is sparse regarding optimum timing of intervention in these patients. In addition, there is limited data regarding the effectiveness of medical and surgical therapy for management of these patients reflux disease.

ARS Before Lung Transplant

There is a growing trend that GERD plays a role in either the etiology and/or progression of idiopathic pulmonary fibrosis. The 5-year survival in these patients ranges from 5 to 15%. There have been several case series that have found an association between early surgical management of GERD and a decrease in the clinical pulmonary manifestations of IPF. A phase 2 randomized controlled trial was performed that compared surgical management of gastroesophageal reflux disease with laparoscopic anti-reflux surgery versus best medical management of GERD in patients with idiopathic pulmonary fibrosis. This was a 1:1 randomization process, randomizing 58 patients. The primary end-point was changes in FVC and reduction of clinical symptoms related to the patients IPF, including acute exacerbation, respiratory related hospitalization, and death. The study did demonstrate feasibility of minimally invasive anti-reflux surgery performed in these patients, but it did not reach its primary endpoints. Despite having a decrease in FVC, respiratory-related hospitalization, and death, this was not statically significant [16].

Still the question remains as to when is the best timing of anti-reflux surgery for patients in the perioperative period surrounding lung transplantation. To avoid the issues surrounding CLAD, Linden et al. evaluated the risk and physiologic effects of laparoscopic fundoplication in patients on the lung transplant list. Of the 149 patients that were on the lung transplant list at the time of their study, 19 were found to have reflux as identified by symptoms, pH studies, and esophageal manometry. What was identified was that the patients that underwent fundoplication had no decrease in lung function, stability of their exercise capacity, and stability of their oxygen requirements. The control patients had a statistically significant deterioration in oxygen requirement [17].

Evaluation of these patients for anti-reflux surgery should occur during the initial evaluation for lung transplantation, if not prior. The evaluation should include standard preoperative assessment, including symptom questionnaire, barium swallow, pH probe, and esophageal manometry. This will provide the clinician with determination of severity of symptoms and lifestyle limitations. The barium swallow will assist in assessing esophageal and gastric-emptying anatomic evaluation of the patient's upper GI tract. A pH probe will assist in determining the severity of reflux, and manometry studies will assist in the evaluation esophageal function. Test results can help determine feasibility of transplant in the future and preoperating planning for anti-reflux procedure. To minimize morbidity and mortality in this patient population, minimally invasive approaches to the anti-reflux procedure should be performed.

ARS After Lung Transplantation

The medical management for patients who develop CLAD after lung transplant is challenging. The use of azithromycin has been suggested as a treatment modality for CLAD because of medication's anti-inflammatory action and promotility qualities. Studies have demonstrated that azithromycin does decrease the bile concentration in BAL aspirates and decreases the number of reflux events in CLAD patients; the study did not find any evidence to support the role of the drug at decreasing the progression of CLAD induced by aspiration [18, 19].

Several studies have demonstrated that the effectiveness of early anti-reflux surgery decreases the frequency of nonimmune CLAD [20].

Currently, the most successful management of GERD in patients following lung transplant is an anti-reflux operation. Davis et al. evaluated 128 post-lung transplant patients using ambulatory

24-hour esophageal pH probe. Surgical fundoplication was performed in 43 of these patients of which 26 had BOS. After fundoplication, 3 patients had improvement in the BOS scores, while 13 patients had reversal of their BOS such that they no longer met criteria. There was also a 24% improvement in lung function after fundoplication. This study clearly demonstrated antireflux surgery in patients after lung transplant improves lung function and can improve criteria related to BOS [21].

Conflict of Interest The author has no conflict of interest to declare.

References

1. Gauthier JM, Hachem RR, Kreisel D. Update on chronic lung allograft dysfunction. Curr Transplant Rep. 2016;3(3):185–91.
2. Lo WK, Burakoff R, Goldberg HJ, Feldman N, Chan WW. Pre-lung transplant measures of reflux on impedence are superior to pH testing alone in predicting early allograft injury. World J Gastroenterol. 2015;21(30):9111–7.
3. Tobin RW, Pope CE 2nd, Pellegrini CA, Emond MJ, Sillery J, Raghu G. Increased prevalence of gastroesophageal reflux in patients with idiopathic pulmonary fibrosis. Am J Respir Crit Care Med. 1998;158(6):1804–8.
4. Raghu G, Freudenberger TD, Yang S, Curtis JR, Spada C, Hayes J, Sillery JK, Pope CE 2nd, Pellegrini CA. High prevalence of abnormal acid gastro-oesophageal reflux in idiopathic pulmonary fibrosis. Eur Respir J. 2006;27(1):136–42.
5. Sweet MP, Herbella FA, Leard L, Hoopes C, Golden J, Hayes S, Patti MG. The prevalence of distal and proximal gastroesophageal reflux in patients awaiting lung transplantation. Ann Surg. 2006;244(4):491–7.
6. Treacy WL, Baggenstoss AH, Slocumb CH, Code CF. Scleroderma of the esophagus: a correlation of histologic and physiologic findings. Ann Intern Med. 1963;59(3):351–6.
7. Ebert E. Esophageal disease in scleroderma. J Clin Gastroenterol. 2006;40(9):769–75.
8. Hallberg K, Fandriks L, Strandvik B. Duodenogastric bile reflux is common in cystic fibrosis. J Pediatr Gastroenterol Nutr. 2004;38(3):312–6.
9. Pauwels A, Decraene A, Blondeau K, Mertens V, Farre R, Proesmans M, Bleyenbergh PV, Sifrim D, Dupont L. Bile acids in sputum and increased airway inflammation in patients with cystic fibrosis. Chest. 2012;141(6):1568–74.
10. Young LR, Hadjiliadis D, Davis RD, Palmer SM. Lung transplantation exacerbates gastroesophageal reflux disease. Chest. 2003;124:1689–93.
11. Suen HC, Hendrix H, Patterson GA. Special article: physiologic consequences of pneumonectomy. Consequences of the esophageal function. Chest Surg Clin N Am. 2002;12:587–95.
12. Reid KR, McKenzie FN, Menkis AH, Novick RJ, Pflugfelder PW, Kostuk WJ, Ahmad D. Importance of chronic aspiration in recipients of heart-lung transplants. Lancet. 1990;336:206–8.
13. Kirk AJB, Colquhoun IW, Corris PA, Hilton CJ, Dark JH. Impaired gastrointestinal motility in pulmonary transplantation. Lancet. 1990;336:752.
14. Au J, Hawkins T, Venables C, Morritt G, Scott CD, Gascoigne AD, Corris PA, Hilton CJ, Dark JH. Upper gastrointestinal dysmotility in heart-lung transplant recipients. Ann Thorac Surg. 1993;55(1):94–7.
15. Neujahr DC, Uppal K, Force SD, Fernandez F, Lawrence C, Pickens A, Bag R, Lockard C, Kirk AD, Tran V, Lee K, Jones DP, Park Y. Bile acid aspiration associated with lung chemical profile linked to other biomarkers of injury after lung transplantation. Am J Transplant. 2014;14(4):841–8.
16. Raghu G, Pellegrini CA, Yow E, Flaherty KR, Meyer K, Noth I, Scholand MB, Cello J, Ho LA, Pipavath S, Lee JS, Lin J, Maloney J, Martinez FJ, Morrow E, Patti MG, Rogers S, Walters PJ, Yates R, Anstrom KJ, Collard HR. Laparoscopic anti-reflux surgery for the treatment of idiopathic pulmonary fibrosis (WRAP-IPF): a multicentre, randomised, controlled phase 2 trial. Lancet Respir Med. 2018;6(9):707–14.
17. Linden PA, Gilbert RJ, Yeap BY, Boyle K, Deykin A, Jaklitsch MT, Sugarbaker DJ, Bueno R. Laparoscopic fundoplication in patients with end-stage lung disease awaiting transplantation. J Thorac Cardiovasc Surg. 2006;131:438–46.
18. Mertens V, Blondeau K, Van Oudenhove L, Vanaudenaerde B, Vos R, Farre R, Pauwels A, Verleden G, Van Raemdonck D, Sifrim D, Dupont LJ. Bile acids aspiration reduces survival in lung transplant recipients with BOS despite azithromycin. Am J Transplant. 2011;11(2):329–35.
19. Vos R, Vanaudenaerde BM, Verleden SE, Ruttens D, Vaneylen A, Van Raemdonck DE, Dupont LJ, Verleden GM. Antiinflammatory and immunomodulatory properities of azithromycin involved in treatement and prevention of chronic lung allograft rejection. Transplantation. 2012;94(2):101–9.
20. Cantu E III, Appel JZ III, Hartwig MG, Woreta H, Green C, Messier R, Palmer SM, Davis RD Jr. Early fundoplication prevents chronic allograft dysfunctionin patients with gastroesophageal reflux disease. Ann Thorac Surg. 2004;78:1142–51.
21. Davis RD Jr, Lau CL, Eubanks S, Messier RH, Hadjiliadis D, Steele MP, Palmer SM. Improved lung allograft function after fundoplication in patients with gastroesophageal reflux disease undergoing lung transplantation. J Thorac Cardiovasc Surg. 2003;125:533–42.

Endoscopic Treatments for Barrett's Esophagus

22

Uma M. Sachdeva, Hans Gerdes, and Daniela Molena

Introduction

Barrett's esophagus is defined as intestinal metaplasia of the epithelial lining of the esophagus and develops as a result of damage due to chronic acid and bile irritation. The squamous cells lining the esophagus transforms into intestinalized epithelium, which is associated with increased cell proliferation and serves as a precursor lesion to esophageal adenocarcinoma. Barrett's esophagus is present in 2–7% of the population and is the only identifiable precursor lesion for esophageal adenocarcinoma. The progression from Barrett's esophagus to esophageal adenocarcinoma is stepwise and based on the degree of dysplasia, ranging from no dysplasia to low-grade dysplasia, high-grade dysplasia/carcinoma in situ, and invasive adenocarcinoma. Early identification of Barrett's metaplasia as a precursor lesion to esophageal adenocarcinoma is important due to the poor survival of patients who progress to develop invasive adenocarcinoma, which has a 5-year survival of less than 20%. The rate of progression from non-dysplastic Barrett's esophagus or Barrett's with low-grade dysplasia to adenocarcinoma is less than 1% per year; however, the rate of progression from low-grade dysplasia to high-grade dysplasia is more unclear. This has been reported to be as high as 10–35%; however, other studies report no observed link between low-grade dysplasia and progression to high-grade dysplasia [1, 2]. For this reason, surveillance protocols and endoscopic interventions for non-dysplastic Barrett's esophagus or low-grade dysplasia have been controversial. In contrast, the incidence of progression from high-grade dysplasia to adenocarcinoma has been reported to range from 6 to 7% per year to as high as 29% per year [3, 4]; therefore high-grade dysplasia requires endoscopic or surgical intervention and close surveillance. For this reason, Barrett's esophagus must be considered in terms of histologic grade, with grade of dysplasia critically important in the decision of whether to pursue interventional endoscopic eradication therapies and in determining follow-up surveillance protocols.

Diagnosis of Barrett's Esophagus

Critical to the determination of the grade of dysplasia in patients with Barrett's esophagus is expertise in obtaining an accurate diagnosis, both visually and pathologically. Studies to identify the most accurate protocol for surveillance endoscopy have shown that initial endoscopic inspection should be performed using

U. M. Sachdeva · H. Gerdes
Memorial Sloan Kettering Cancer Center, New York, NY, USA

D. Molena (✉)
Esophageal Surgery Program, Thoracic Surgery Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA
e-mail: molenad@mskcc.org

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_22

high-definition, white light endoscopy by physicians who are well trained in the identification of Barrett's-associated changes. Standard surveillance includes inspection and biopsy of any visualized lesions, such as nodules, ulcers, or mucosal irregularities, as well as four-quadrant biopsies taken every 1 cm of the length of the Barrett's segment [1–3]. The sensitivity of white light endoscopy for detection and diagnosis of Barrett's esophagus is reported to range from 80 to 90% [5–7]. One study showed that inspection of each 1-cm segment for longer than 1 minute resulted in increased detection of suspicious lesions [8]. Several studies also indicate that Barrett's changes favor certain locations within the esophagus, with the majority of lesions found between 1 o'clock and 5 o'clock with the patient lying in the left lateral decubitus position [9].

There are no established protocols for screening asymptomatic patients for Barrett's esophagus with endoscopy. Risk factors for Barrett's esophagus and esophageal adenocarcinoma include age >50 years, male sex, white race, chronic reflux symptoms, family history of Barrett's esophagus, smoking, and obesity. Given that less than 1% of patients with non-dysplastic Barrett's changes progress to adenocarcinoma annually, yearly surveillance is not recommended for histology less than low-grade dysplasia [10]. In fact, the American Society for Gastrointestinal Endoscopy (ASGE) recommends consideration of no surveillance for this cohort [1]. However, if surveillance endoscopy is undertaken, it is recommended to perform white light endoscopy every 3–5 years with four-quadrant biopsies every 2 cm. Because the determination of grade of dysplasia is often difficult, all samples should be reviewed by one or two expert GI pathologists. In cases where the degree of dysplasia is indeterminate even after expert evaluation, the ASGE recommends increasing antisecretory therapy to eliminate esophageal inflammation and repeating endoscopy with biopsy to re-evaluate for presence and degree of dysplasia. Low-grade dysplasia on surveillance endoscopy warrants repeat EGD in 6 months to confirm the diagnosis, followed by surveillance EGD annually with four-quadrant biopsies taken every 1–2 cm. Low-grade dysplasia may alternatively be treated with endoscopic eradication therapy, though no specific recommendations regarding ablative therapy versus surveillance are given in the current guidelines. Confirmed high-grade dysplasia should be considered for endoscopic ablative or eradication therapies, which have been shown to result in improved outcomes relative to the traditional surveillance regimen, which included endoscopic evaluation every 3 months with four-quadrant biopsies taken every 1 cm. All samples biopsied should be placed into separate containers indicating the location of each resected lesion or biopsied segment in order to facilitate subsequent endoscopic treatment or repeat sampling, if needed.

Barrett's changes appear as salmon or pink patches on the mucosa, in contrast to the whitish-gray appearance of the native squamous mucosa that lines the normal esophagus (Fig. 22.1). These changes often lie adjacent to the native squamocolumnar junction at the Z line, just proximal to the EG junction. While visual inspection may suggest Barrett's changes, the diagnosis is histopathologic. Given that the grade is a critical indicator of the risk for progression to adenocarcinoma, accurate histologic diagnosis is essential and should be performed by GI pathologists who are expert in identifying all stages of Barrett's-associated changes.

In addition to white light endoscopy, the use of narrow-band imaging has been investigated for enhanced detection of mucosal abnormalities that might indicate Barrett's-associated dysplasia (Fig. 22.2). Narrow-band imaging filters white light to wavelengths specific for hemoglobin absorption, thus highlighting mucosal vasculature, and in this way has been shown in increase the detection of dysplasia [11–13].

Complicating an already complex range of diseases, histologic progression from no dysplasia to low-grade dysplasia to high-grade dysplasia to invasive esophageal adenocarcinoma is not

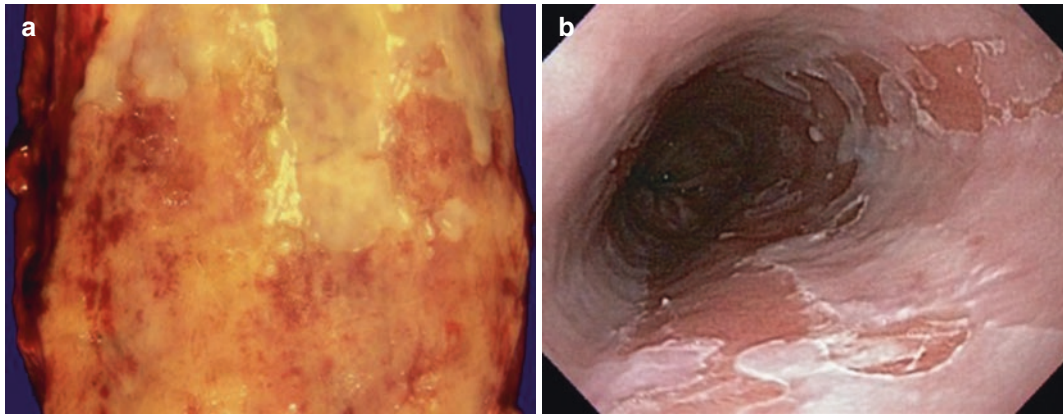


Fig. 22.1 (**a**) Gross appearance of esophageal specimen with Barrett's metaplasia (salmon-colored patches) with adjacent native squamous epithelium (white). (**b**) Endoscopic appearance of Barrett's changes (pink patches) extending proximally from the EG junction

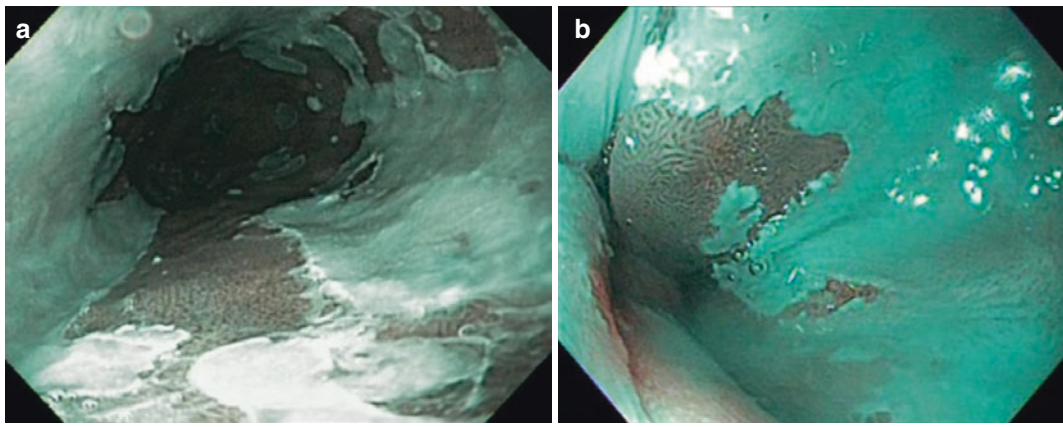


Fig. 22.2 Narrow-band imaging showing Barrett's metaplasia (**a**) and Barrett's esophagus with high-grade dysplasia (**b**)

necessarily stepwise and linear, with one study showing that half of patients who developed high-grade dysplasia or esophageal adenocarcinoma had only non-dysplastic Barrett's metaplasia seen on previous biopsies [14]. This finding underlies the importance of adequate endoscopic inspection, surveillance protocols, and accurate histologic assessment by expert pathologists (Fig. 22.3), as patients who have adenocarcinoma detected through surveillance EGD demonstrate consistently improved survival relative to patients whose cancer was not detected through surveillance protocols [15–17].

Endoscopic Interventions

Endoscopic interventions include both excisional techniques, such as endoscopic mucosal resection and endoscopic submucosal dissection, and ablative techniques, including radiofrequency ablation and cryoablation. The primary indications for ablative therapies are for treatment of flat Barrett's dysplasia or for treatment of areas of residual disease following endoscopic resection of visible dysplastic lesions. The indications for each endoscopic technique will be reviewed, with the standard approach favoring resection of

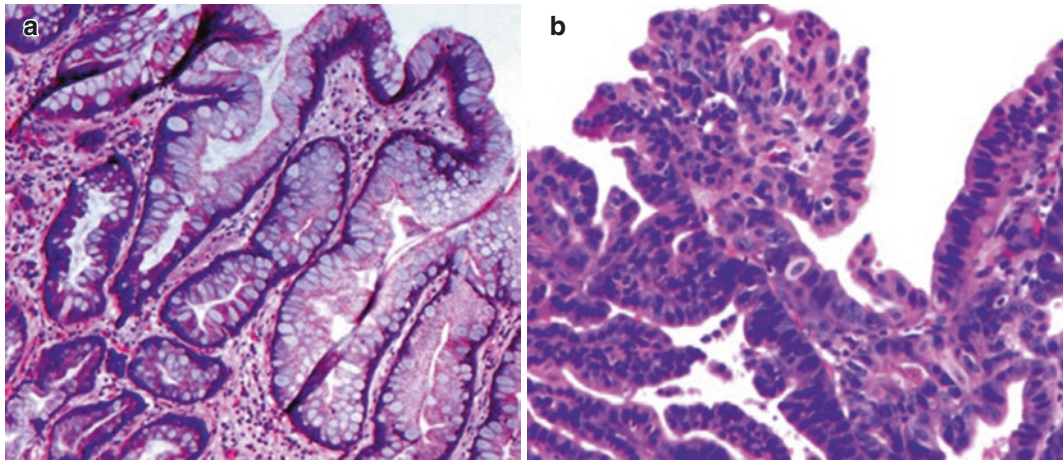


Fig. 22.3 (**a**) Histologic appearance of non-dysplastic Barrett epithelium showing mucinous glandular metaplasia with characteristic goblet cells. (**b**) Histologic appearance of Barrett's esophagus with high-grade dysplasia, including cellular crowding due to abnormal proliferation and increased nucleus/cytoplasm ratio

any visually identified lesions, such as nodularity or ulcerations, and ablation of the remainder of the identified dysplastic Barrett's segment.

Photodynamic Therapy (PDT)

The first endoscopic ablative therapy to gain widespread acceptance was photodynamic therapy. This was investigated in a randomized control trial where patients with high-grade dysplasia were randomized to receive either porfimer sodium PDT with omeprazole or omeprazole alone [18]. At 5 years, 77% of patients treated with PDT achieved eradication of high-grade dysplasia, while only 39% of patients receiving omeprazole alone had regression of disease. Fifteen per cent of patients who received PDT progressed to esophageal adenocarcinoma, while 29% of patients treated with only omeprazole progressed to development of cancer. Retrospective analysis of patients with high-grade dysplasia who underwent PDT or esophagectomy found similar rates of overall and cancer-free survival at 5 years [19]. Despite its early success, PDT has become less popular in the current era due to the cost of porfimer sodium, the prolonged posttreatment photosensitivity, and the rate of esophageal strictures following treatment, which has been reported to be as high as 50%.

Argon Plasma Coagulation (APC)

APC is another early endoscopic technique used for eradication of Barrett's esophagus and involves coagulation of adjacent tissue by ionized argon gas injected at target areas from the tip of an endoluminal probe. Advantages of APC include the relatively low cost of argon gas and the no-contact technique, which might result in greater safety of the procedure. It has been successfully used for treatment of Barrett's esophagus even in the absence of dysplasia and is delivered over the course of multiple sessions. In one series of 50 patients treated with APC and followed for 1 year, 34 patients had more than 90% eradication of Barrett's lesions, while 16 patients had persistent Barrett's changes after a median of four treatments [20]. Fifteen of the 34 patients who had macroscopically cleared their disease, however, had persistent buried glands under new squamous epithelium following treatment. At 1-year follow-up, 6 of these patients had persistent buried glands, while 2 out of 19 patients without prior buried glands developed subsquamous glands within 1 year. Given the risk for progression of these glands to high-grade dysplasia or adenocarcinoma, these patients require ongoing surveillance endoscopies to evaluate for progression of disease beneath the regenerated squamous cell lining, which is harder to detect than surface disease. Adverse effects following APC included posttreatment chest pain and transient dysphagia or odyno-

phagia, but there were no posttreatment strictures seen at the time point of 1 year [20]. A separate study of 32 patients evaluated the long-term results of APC and demonstrated that two-thirds of patients who had complete eradication of Barrett's changes following treatment maintained this result at long-term follow-up [21]. This study, however, did not demonstrate a protective effect of APC against development of adenocarcinoma in patients treated for non-dysplastic Barrett's esophagus. This was attributed to the retrospective design of the study and inclusion of older APC devices and lower dosage of proton pump inhibitors; however, this result has supported the recommendation that patients with non-dysplastic Barrett's esophagus should not be referred for endoscopic ablative therapies in most cases. The incidence of buried glands reported for APC in this study was 19%, which is markedly better than the reported rate for PDT, which has been documented as up to 51% [21]. However, this is still significantly higher than the reported rate for radiofrequency ablation (0.9%), which has become the gold standard treatment for eradication of dysplastic Barrett's lesions.

Radiofrequency Ablation (RFA)

Radiofrequency ablation was developed for treatment of Barrett's esophagus-associated dysplasia and has become standard therapy for treatment of symptomatic non-dysplastic and low-grade dysplastic Barrett's esophagus, as well as high-grade dysplasia or carcinoma in situ. RFA gained popularity after it was tested against proton pump inhibitor therapy alone in a study called the AIM-Dysplasia trial [22]. In this study, patients with dysplastic Barrett's changes were randomized to RFA with omeprazole or omeprazole only. 2.4% of patients treated with RFA with omeprazole progressed to cancer at 1 year, as compared with 19% of patients who progressed in the omeprazole only arm. A stricture rate of 7.6% was observed following RFA treatment.

RFA is performed by initially assessing the extent of Barrett's metaplasia using white light endoscopy, as well as any visually identified lesions such as nodules or ulcerations [23]. Visible lesions are dealt with using EMR or other resection strategies, but in the absence of any identified lesions, the complete Barrett's segment is treated with RFA. The RFA probe inserts into the esophagus adjacent to the endoscope and is comprised of a copper electrode sheet mounted on the surface of a balloon (Barrx 360 Express RFA balloon catheter, Medtronic Inc). It is positioned roughly 1 cm cranial to the proximal-most extent of the identified Barrett's segment. The balloon is inflated, and good mucosal contact is confirmed, after which RF energy is deployed from the electrode across the surface of the balloon over approximately 1 second. The balloon automatically deflates after discharge of energy, and a circumferential burn is visible (Fig. 22.4a). The balloon is then advanced distally, and the process is repeated, avoiding overlap in segments, until

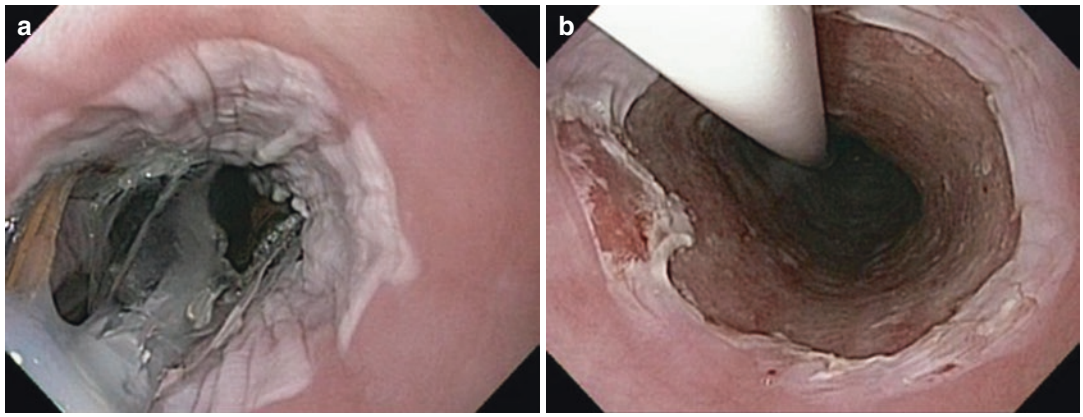


Fig. 22.4 Appearance of esophageal mucosa following radiofrequency ablation using balloon applicator (**a**) and subsequent debridement of necrotic tissue (**b**)

the esophagogastric junction is reached. At this point, the catheter is removed, and the ablated segments are mechanically debrided using a transparent cap mounted on the tip of the endoscope (Fig. 22.4b), after which the full ablation is repeated for a second round. The total recommended energy delivered is 10 J/cm^2. Previous models of this catheter that are still commercially available may lack the automatic inflation of this device and therefore require pretreatment sizing of the esophageal diameter with an initial sizing balloon prior to deploying the RFA treatment balloon. Alternatively, rectangular ablation catheters can be positioned at the end of the endoscope through a hinge attached to a rubber cap that is placed on the tip of the endoscope (Barrx 90 RFA focal catheter, Barrx Ultra Long RFA focal catheter, Barrx 60 RFA focal catheter, Medtronic Inc) or can be placed through the working channel of the endoscope (Barrx Channel RFA endoscopic catheter, Medtronic Inc).

RFA treatment has been associated with postprocedure chest discomfort, as well as a stricture rate of 6–11.8% [3, 10, 22]. Recurrence rates following RFA have been reported to be 8–10% in randomized control trials but as high as 26–33% in retrospective studies [10]. For this reason, active surveillance following RFA treatment is necessary, in addition to posttreatment use of proton pump inhibitors. Recurrent or persistent lesions can be treated with further ablative therapy or excisional techniques.

Cryoablation

In contrast to heat-based ablative techniques such as PDT, APC, or RFA, cryotherapy utilizes a cold-based technique to induce cellular necrosis and sloughing through tissue disruption caused by repeated freeze–thaw cycles. Cryotherapy can be applied to the esophagus through a spray, with either liquid carbon dioxide or liquid nitrogen (CryoSpray, CSA Medical, Baltimore, MD), which is applied through a low-flow continuous delivery system using a noncontact method [24]. Flow of liquid nitrogen across the cryoprobe is 4–6 L over 20 seconds, achieving a temperature of −196 °C. A separate decompression catheter is required to evacuate the gas due to the rapid expansion of liquid nitrogen. In contrast, the carbon dioxide spray catheter delivers 6–8 L of gas per minute, resulting in temperatures ranging from −70 to −78 °C. Either gas is applied in two 20-second application cycles or four 10-second cycles to induce a freeze-thaw cycle in the adjacent tissue. Recently, a delivery balloon that can be deployed through the working channel of the endoscope has been developed to allow focal ablation of an area roughly 2 cm^2 through release of nitrous oxide at −85 °C. The advantage of the cryoballoon is immediate venting of gas back through the balloon into the catheter. Cryotherapy has been shown to eradicate 81% of high-grade dysplasia and 91% of low-grade dysplasia in initial prospective studies [25]. Cryotherapy has been suggested as follow-up therapy for treatment-resistant disease following RFA, as its mechanism of crystallization followed by subsequent necrosis may allow for deeper penetration into tissues. In one study, 16 patients who had persistent dysplasia after three RFA treatments, progression of dysplasia while receiving RFA treatment, or treatment failure as reported by the endoscopist were treated with cryospray therapy using liquid nitrogen [26]. Seventy five percent of these patients achieved complete eradication of dysplasia, while 31% achieved complete eradication of intestinal metaplasia. However, a recent prospective single-center analysis using carbon dioxide cryopsray following endoscopic resection of any visible lesions was less promising, with complete eradication of intestinal metaplasia in only 11% of patients [27]. This failure of therapy in the majority of patients included in this study has been attributed to the use of carbon dioxide rather than liquid nitrogen, though the results were concerning enough to terminate the trial prematurely. Nevertheless, a follow-up retrospective study of 64 patients who underwent cryotherapy with a carbon dioxide cryospray, including 28 patients

who had undergone prior PDT or RFA and 16 patients who had undergone prior EMR, showed complete eradication of Barrett's metaplasia in 67% of patients [28]. Studies are currently underway to evaluate the cryoballoon focal ablation system, which has already passed safety and feasibility studies, with 100% of patients showing complete eradication of the treated Barrett's areas in targeted trials [29, 30].

Complications of cryotherapy include chest pain and discomfort, which have been reported in 17.6% of patients [31]. Pain scores, however, seem to be less than those reported for RFA, though no direct comparative studies of the two modalities exist at present [24]. Stricture rate is reported to range from 3 to 9%, and perforation is a rare but reported event, which may be more of a concern in theory given the distention of the GI tract from gas released with use of the cryosprays. A durable response to cryosprays has been observed at 5 years, with retrospective studies reporting complete eradication of dysplasia in 88% of patients at 5 years and complete eradication of intestinal metaplasia in 75% of treated patients at 5 years [32].

The risk of buried metaplasia or subsquamous Barrett's changes has been reported to be higher for cryotherapies relative to RFA. Ablative therapies are effective by causing necrosis and sloughing of the surface cells of the esophagus and subsequent replacement of these cells with normal native squamous cells lining the esophagus. However, if not all dysplastic cells are eradicated by ablative therapies, new squamous epithelium can be grown on top of residual dysplastic cells and allow sub-squamous high-grade dysplasia or adenocarcinoma to develop. Because these abnormal cells lie beneath normal-appearing squamous epithelium, they can evade visual surveillance as well as superficial biopsies and may not be detected until a later stage. While this can occur with any ablative therapy, the reported rate of sub-squamous metaplasia following RFA is 0.9% [33], while the reported rate following cryotherapy is as high as 9.1% [27, 30, 34–36].

Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD)

Endoscopic mucosal resection can be used to resect visible lesions, nodules, or ulcerations of the esophagus, short-segment Barrett's esophagus with dysplasia, superficial adenocarcinoma (T1a), and esophageal squamous cell carcinoma. The EMR procedure may involve either the cap-assisted mucosectomy or the ligation-and-snare/multiband ligation technique. During cap-assisted mucosectomy, saline is injected into the submucosal space under the target lesion to elevate the mucosa. A snare is then used to surround the area and strangulate the base, and the lesion is then suctioned into a specialized cap on the tip of the endoscope. During multiband ligation, the target area is suctioned into a cap at the tip of the endoscope, and a rubber band is deployed around the base of the target tissue (Fig. 22.5). This tissue is then resected using a snare positioned below the base of the rubber band. EMR is highly effective at removing Barrett's lesions; however, it cannot be used on lesions spanning over 50% of the circumference of the esophagus to avoid debilitating stricture formation. Additionally, the EMR technique can resect small lesions in their entirety, but

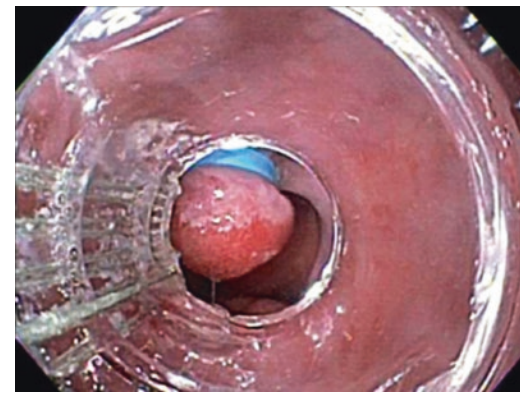


Fig. 22.5 Endoscopic mucosal resection using multiband ligation technique. The band is placed at the base of the target lesion, after which it is excised using a snare. It is important to place the snare below the band to ensure adequate free margin from the submucosa

larger lesions often require piecemeal resection, which can result in tissue distortion that affects histopathologic evaluation and can leave positive margins that require repeat resection or even follow-up esophagectomy for complete removal of malignant tissue. The advantage of EMR over ablative therapies is that histopathologic samples are sent to pathology and tissue can be evaluated for depth of invasion, while ablative therapy destroys the surface tissue to allow for reepithelialization with squamous epithelium but does not provide tissue samples for pathologic diagnosis. Following EMR, patients should remain on proton pump inhibitors to promote healing of ulcerations following the resection, as well as undergo repeat endoscopy 8 weeks after the procedure. EMR has been reported to effectively eradicate superficial neoplastic tissue in 91–98% of cases and eradicate the dysplastic Barrett's segment in 80% of cases [37, 38]. It has therefore become the first-line treatment for superficial esophageal adenocarcinoma (T1a), followed by surveillance endoscopy to evaluate for recurrence or residual disease [39]. Some groups advocate for concurrent RFA ablation of the complete Barrett's segment at the time of EMR of visible lesions [40], though these techniques are more commonly performed in a sequential fashion, with initial resection of visible dysplastic or neoplastic lesions followed by ablation of the residual Barrett's segment. Reported complications following EMR include bleeding in 10% of cases [37, 41, 42], perforation in 3–7% of cases [43–45], and stricture formation in 17–37% of cases [46], though this is directly related to the length and circumference of the resected mucosal region. Strictures following EMR are managed with endoscopic dilatation.

Endoscopic submucosal dissection (ESD) is a related technique that can be used for resection of larger specimens, allowing for en bloc rather than piecemeal resection of larger lesions and more accurate histologic staging due to less tissue distortion. While ESD has gained popularity in Asia, its use is still less common than EMR in Western countries, and relative to EMR, ESD is more technically complex and requires longer procedure times. The technique involves the placement of marks several millimeters outside of the target area for resection, followed by the injection of glycerin or hyaluronic acid solution into the submucosa of that area. The mucosa outside of the marked territory is then resected en bloc through meticulous submucosal dissection. The reported rate for en bloc resection of esophagogastric junction superficial adenocarcinoma is 100%, with an 80% rate of curative resection [1]. Relative to EMR, ESD has been reported to have a lower local recurrence rate, with one study reporting 3.13% recurrence following ESD for esophageal squamous cell carcinoma, as compared with 23.91% recurrence following EMR [47]. Adverse events are similar to those associated with EMR, including bleeding, perforation, and stricture formation [47–49].

Endoscopic Ultrasound

Endoscopic ultrasound is used to determine the depth of invasion of esophageal mucosal lesions and is essential for adequate local staging of esophageal malignancies (Fig. 22.6). Accurate T staging of esophageal neoplasms is essential, as superficial mucosal lesions (T1a) are candidates for EMR or ESD, while lesions invading into the submucosa (T1b) should be referred for esophagectomy due to their higher rate of nodal spread, which is reported to range from 16 to 22%. While EUS has been shown to be highly effective at diagnosing invasion into the muscularis propria

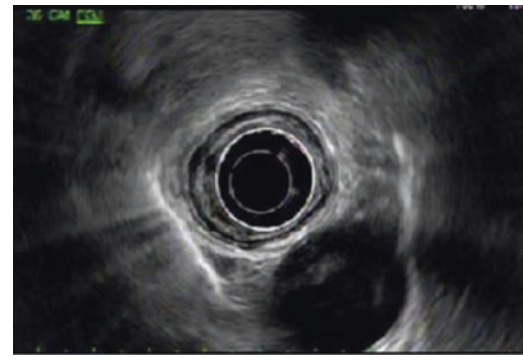


Fig. 22.6 Endoscopic ultrasound image of a T1a adenocarcinoma, with the lesion confined to the mucosal layer

(T2) and beyond, its ability to accurately distinguish between high-grade dysplasia, T1a and T1b disease, is limited. This is due to the similar sonographic appearance of mucosal thickening in the setting of Barrett's-associated inflammation, superficial mucosal lesions, and lesions invading into the submucosa. Investigations into high-frequency probes for improved diagnosis are ongoing; however, even with high-resolution ultrasonography, the sensitivity of EUS in diagnosing T1b lesions is reported to be only 48% [50]. For this reason, EUS currently has limited utility in Barrett's-related disease and very early-stage esophageal neoplasms, but it is highly effective for identifying and characterizing more advanced lesions with local invasion and for identifying associated nodal disease.

Conclusions

Endoscopic interventions for Barrett's esophagus are highly effective techniques for eradication of Barrett's-associated dysplastic regions and superficial adenocarcinoma confined to the esophageal mucosa. Treatments include both ablative therapies and excisional techniques, which are most commonly applied in an independent or sequential fashion, though concurrent application is currently being investigated. Most ablative therapies, such as RFA or cryotherapy, are applied to dysplastic regions in the setting of Barrett's-related changes to prevent progression to high-grade dysplasia or the development of adenocarcinoma. Ablation of non-dysplastic Barrett's changes has not been shown to decrease the incidence of subsequent esophageal cancer; however, it may be considered in the setting of symptomatic disease. EMR and ESD are resection techniques applied to early mucosal neoplasms or to any visible lesions, nodules, or ulcerations seen on surveillance endoscopy and allow for complete resection of abnormal tissue and histopathologic evaluation for depth of invasion and margin of resection. Following either ablative or excisional techniques, it is essential that patients remain on an acid suppressive regimen using proton pump inhibitors and undergo follow-up endoscopies for surveillance to evaluate for residual or recurrent disease. Complications of endoscopic treatments include chest pain, bleeding, perforation, and stricture formation, the most common of which are pain and stricturing. Posttreatment strictures can be managed effectively with endoscopic dilation. The development of endoscopic treatments for Barrett's-associated dysplasia and early-stage neoplasms has allowed for effective treatment of these conditions through minimally invasive techniques and decreased the necessity for esophagectomy and its associated morbidity and mortality for early cancerous and precancerous lesions of the esophagus and esophagogastric junction.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Committee ASoP, Evans JA, Early DS, et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest Endosc. 2012;76:1087–94.
2. Duits LC, Phoa KN, Curvers WL, et al. Barrett's oesophagus patients with low-grade dysplasia can be accurately risk-stratified after histological review by an expert pathology panel. Gut. 2015;64:700–6.
3. Brimhall B, Wani S. Current endoscopic approaches for the treatment of Barrett esophagus. J Clin Gastroenterol. 2017;51:2–11.
4. Rastogi A, Puli S, El-Serag HB, Bansal A, Wani S, Sharma P. Incidence of esophageal adenocarcinoma in patients with Barrett's esophagus and high-grade dysplasia: a meta-analysis. Gastrointest Endosc. 2008;67:394–8.
5. Kim SL, Waring JP, Spechler SJ, et al. Diagnostic inconsistencies in Barrett's esophagus. Department of Veterans Affairs Gastroesophageal Reflux Study Group. Gastroenterology. 1994;107:945–9.
6. Woolf GM, Riddell RH, Irvine EJ, Hunt RH. A study to examine agreement between endoscopy and histology for the diagnosis of columnar lined (Barrett's) esophagus. Gastrointest Endosc. 1989;35:541–4.
7. Eloubeidi MA, Provenzale D. Does this patient have Barrett's esophagus? The utility of predicting Barrett's esophagus at the index endoscopy. Am J Gastroenterol. 1999;94:937–43.
8. Gupta N, Gaddam S, Wani SB, Bansal A, Rastogi A, Sharma P. Longer inspection time is associated with increased detection of high-grade dysplasia and esophageal adenocarcinoma in Barrett's esophagus. Gastrointest Endosc. 2012;76:531–8.

9. Cassani L, Sumner E, Slaughter JC, Yachimski P. Directional distribution of neoplasia in Barrett's esophagus is not influenced by distance from the gastroesophageal junction. Gastrointest Endosc. 2013;77:877–82.
10. Yachimski P, Hur C. Evidence-based endoscopic management of Barrett's esophagus. Gastroenterol Rep (Oxf). 2015;3:54–62.
11. Sharma P, Hawes RH, Bansal A, et al. Standard endoscopy with random biopsies versus narrow band imaging targeted biopsies in Barrett's oesophagus: a prospective, international, randomised controlled trial. Gut. 2013;62:15–21.
12. Wolfsen HC, Crook JE, Krishna M, et al. Prospective, controlled tandem endoscopy study of narrow band imaging for dysplasia detection in Barrett's Esophagus. Gastroenterology. 2008;135:24–31.
13. Mannath J, Subramanian V, Hawkey CJ, Ragunath K. Narrow band imaging for characterization of high grade dysplasia and specialized intestinal metaplasia in Barrett's esophagus: a meta-analysis. Endoscopy. 2010;42:351–9.
14. Sharma P, Falk GW, Weston AP, Reker D, Johnston M, Sampliner RE. Dysplasia and cancer in a large multicenter cohort of patients with Barrett's esophagus. Clin Gastroenterol Hepatol. 2006;4:566–72.
15. Wong T, Tian J, Nagar AB. Barrett's surveillance identifies patients with early esophageal adenocarcinoma. Am J Med. 2010;123:462–7.
16. Fountoulakis A, Zafirellis KD, Dolan K, Dexter SP, Martin IG, Sue-Ling HM. Effect of surveillance of Barrett's oesophagus on the clinical outcome of oesophageal cancer. Br J Surg. 2004;91:997–1003.
17. Corley DA, Levin TR, Habel LA, Weiss NS, Buffler PA. Surveillance and survival in Barrett's adenocarcinomas: a population-based study. Gastroenterology. 2002;122:633–40.
18. Overholt BF, Wang KK, Burdick JS, et al. Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. Gastrointest Endosc. 2007;66:460–8.
19. Prasad GA, Wang KK, Buttar NS, et al. Long-term survival following endoscopic and surgical treatment of high-grade dysplasia in Barrett's esophagus. Gastroenterology. 2007;132:1226–33.
20. Basu KK, Pick B, Bale R, West KP, de Caestecker JS. Efficacy and one year follow up of argon plasma coagulation therapy for ablation of Barrett's oesophagus: factors determining persistence and recurrence of Barrett's epithelium. Gut. 2002;51:776–80.
21. Milashka M, Calomme A, Van Laethem JL, et al. Sixteen-year follow-up of Barrett's esophagus, endoscopically treated with argon plasma coagulation. United European Gastroenterol J. 2014;2:367–73.
22. Shaheen NJ, Overholt BF, Sampliner RE, et al. Durability of radiofrequency ablation in Barrett's esophagus with dysplasia. Gastroenterology. 2011;141:460–8.
23. Munoz-Largacha JA, Litle VR. Endoscopic mucosal ablation and resection of Barrett's esophagus and related diseases. J Visc Surg. 2017;3:128.
24. Overwater A, Weusten B. Cryoablation in the management of Barrett's esophagus. Curr Opin Gastroenterol. 2017;33:261–9.
25. Ghorbani S, Tsai FC, Greenwald BD, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's dysplasia: results of the National Cryospray Registry. Dis Esophagus. 2016;29:241–7.
26. Sengupta N, Ketwaroo GA, Bak DM, et al. Salvage cryotherapy after failed radiofrequency ablation for Barrett's esophagus-related dysplasia is safe and effective. Gastrointest Endosc. 2015;82:443–8.
27. Verbeek RE, Vleggaar FP, Ten Kate FJ, van Baal JW, Siersema PD. Cryospray ablation using pressurized CO_2 for ablation of Barrett's esophagus with early neoplasia: early termination of a prospective series. Endosc Int Open. 2015;3:E107–12.
28. Canto MI, Shin EJ, Khashab MA, et al. Safety and efficacy of carbon dioxide cryotherapy for treatment of neoplastic Barrett's esophagus. Endoscopy. 2015;47:591.
29. Scholvinck DW, Kunzli HT, Kestens C, et al. Treatment of Barrett's esophagus with a novel focal cryoablation device: a safety and feasibility study. Endoscopy. 2015;47:1106–12.
30. Kunzli HT, Scholvinck DW, Meijer SL, Seldenrijk KA, Bergman J, Weusten B. Efficacy of the CryoBalloon Focal Ablation System for the eradication of dysplastic Barrett's esophagus islands. Endoscopy. 2017;49:169–75.
31. Greenwald BD, Dumot JA, Horwhat JD, Lightdale CJ, Abrams JA. Safety, tolerability, and efficacy of endoscopic low-pressure liquid nitrogen spray cryotherapy in the esophagus. Dis Esophagus. 2010;23:13–9.
32. Ramay FH, Cui Q, Greenwald BD. Outcomes after liquid nitrogen spray cryotherapy in Barrett's esophagus-associated high-grade dysplasia and intramucosal adenocarcinoma: 5-year follow-up. Gastrointest Endosc. 2017;86:626–32.
33. Gray NA, Odze RD, Spechler SJ. Buried metaplasia after endoscopic ablation of Barrett's esophagus: a systematic review. Am J Gastroenterol. 2011;106:1899–908; quiz 909.
34. Halsey KD, Chang JW, Waldt A, Greenwald BD. Recurrent disease following endoscopic ablation of Barrett's high-grade dysplasia with spray cryotherapy. Endoscopy. 2011;43:844–8.
35. Xue HB, Tan HH, Liu WZ, et al. A pilot study of endoscopic spray cryotherapy by pressurized carbon dioxide gas for Barrett's esophagus. Endoscopy. 2011;43:379–85.
36. Shaheen NJ, Greenwald BD, Peery AF, et al. Safety and efficacy of endoscopic spray cryotherapy for Barrett's esophagus with high-grade dysplasia. Gastrointest Endosc. 2010;71:680–5.

37. May A, Gossner L, Pech O, et al. Local endoscopic therapy for intraepithelial high-grade neoplasia and early adenocarcinoma in Barrett's oesophagus: acute-phase and intermediate results of a new treatment approach. Eur J Gastroenterol Hepatol. 2002;14:1085–91.
38. Ciocirlan M, Lapalus MG, Hervieu V, et al. Endoscopic mucosal resection for squamous premalignant and early malignant lesions of the esophagus. Endoscopy. 2007;39:24–9.
39. Standards of Practice Committee, Wani S, Qumseya B, et al. Endoscopic eradication therapy for patients with Barrett's esophagus-associated dysplasia and intramucosal cancer. Gastrointest Endosc. 2018;87:907–31.e9.
40. Barret M, Belghazi K, Weusten BL, Bergman JJ, Pouw RE. Single-session endoscopic resection and focal radiofrequency ablation for short-segment Barrett's esophagus with early neoplasia. Gastrointest Endosc. 2016;84:29–36.
41. Ell C, May A, Pech O, et al. Curative endoscopic resection of early esophageal adenocarcinomas (Barrett's cancer). Gastrointest Endosc. 2007;65:3–10.
42. Shami VM, Villaverde A, Stearns L, et al. Clinical impact of conventional endosonography and endoscopic ultrasound-guided fine-needle aspiration in the assessment of patients with Barrett's esophagus and high-grade dysplasia or intramucosal carcinoma who have been referred for endoscopic ablation therapy. Endoscopy. 2006;38:157–61.
43. Pouw RE, van Vilsteren FG, Peters FP, et al. Randomized trial on endoscopic resection-cap versus multiband mucosectomy for piecemeal endoscopic resection of early Barrett's neoplasia. Gastrointest Endosc. 2011;74:35–43.
44. Pech O, Behrens A, May A, et al. Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's oesophagus. Gut. 2008;57:1200–6.
45. Esaki M, Matsumoto T, Hirakawa K, et al. Risk factors for local recurrence of superficial esophageal cancer after treatment by endoscopic mucosal resection. Endoscopy. 2007;39:41–5.
46. Chennat J, Konda VJ, Ross AS, et al. Complete Barrett's eradication endoscopic mucosal resection: an effective treatment modality for high-grade dysplasia and intramucosal carcinoma--an American single-center experience. Am J Gastroenterol. 2009;104:2684–92.
47. Ishihara R, Iishi H, Takeuchi Y, et al. Local recurrence of large squamous-cell carcinoma of the esophagus after endoscopic resection. Gastrointest Endosc. 2008;67:799–804.
48. Ishihara R, Yamamoto S, Hanaoka N, et al. Endoscopic submucosal dissection for superficial Barrett's esophageal cancer in the Japanese state and perspective. Ann Transl Med. 2014;2:24.
49. Ishihara R, Iishi H, Uedo N, et al. Comparison of EMR and endoscopic submucosal dissection for en bloc resection of early esophageal cancers in Japan. Gastrointest Endosc. 2008;68:1066–72.
50. Wray A, Rice P, Love M. Endoscopic ultrasound in Barrett's oesophagitis with dysplasia. Ulster Med J. 2012;81:70–3.

Part III

Bariatric Surgery

Historical Notes on the Surgical Treatment of Morbid Obesity

23

Antonio Carlos Valezi and Fernando A. M. Herbella

Introduction

Obesity is a complex disease with serious social, psychological, and clinical dimensions that affects all ages and socioeconomic groups. The significant increase in the incidence of obese people characterizes an epidemic of global proportions [1]. In the United States, obesity is associated with 5 of the 10 leading causes of mortality, and over 60% of American adults are today overweight [2]. Overweight increases the risk of developing diseases such as hypertension, diabetes, dyslipidemia, coronary heart disease, stroke, osteoarthritis, sleep apnea, complications of pregnancy, menstrual irregular periods, hirsutism, and urinary incontinence. It also increases breast, colon, endometrial, and prostate cancer [3, 4]. The extreme forms of obesity rarely respond to behavioral, dietary, or drug treatments [5]. Surgery is the most effective treatment for severe obesity. Its benefits include weight loss and resolution or improvement of associated diseases with acceptable risks [6, 7].

Surgical treatment of obesity seeks safe, efficient, and well-tolerated procedures for these challenging patients. A variety of surgical procedures have been employed over time [8], but all the techniques are based on two fundamental principles: decreasing intestinal absorption and/or limiting gastric capacity. Operations for weight loss can be divided into restrictive and malabsorptive procedures or a combination of the two. Malabsorptive procedures reduce the absorption of nutrients, while restrictive techniques decrease food intake. Some operations combine both mechanisms. This chapter reviews the history aspects of bariatric surgical procedures.

A. C. Valezi
Department of Surgery, State University of Londrina, Londrina, Brazil

F. A. M. Herbella (✉)
Gastrointestinal Surgery – Esophagus and Stomach Division, Department of Surgery,
Federal University of São Paulo, São Paulo, Brazil
e-mail: herbella.dcir@epm.br

Malabsorptive Procedures

Jejunoileal Bypass

The first surgical procedure for the treatment of obesity is credited to Viktor Henrikson who described in 1952 a resection of 105 cm of the small intestine for the purpose of weight loss [9].

In 1954, Kremen et al. [10], after experiments in dogs, performed jejunoileal bypass in humans. The procedure consisted in an anastomosis of the 50 cm proximal jejunum with the terminal ileum. Almost simultaneously, Varco performed the same procedure but without scientific documentation. Payne et al. [11] published a series of cases in which a 38–51-cm-long segment of proximal jejunum was anastomosed to the transverse colon. This technique resulted in good weight loss but with diarrhea and severe

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_23

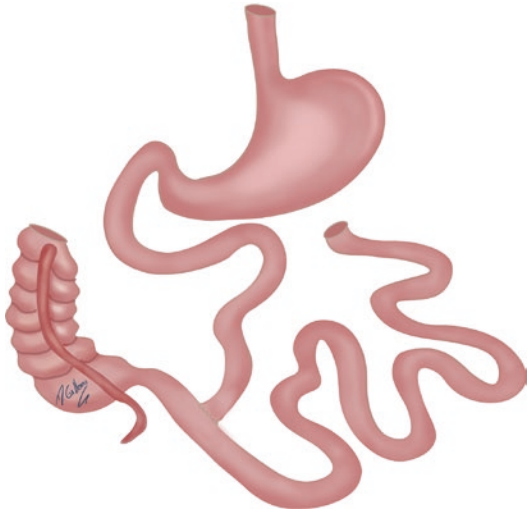


Fig. 23.1 Jejunoileal bypass. (With permission from Debora Gallegos Saliby)

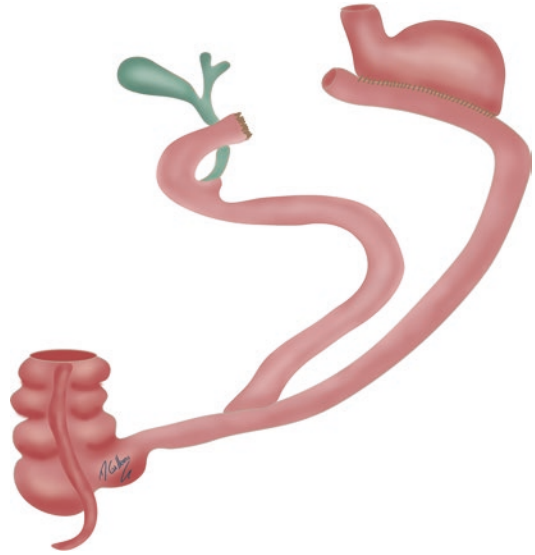


Fig. 23.2 Biliopancreatic diversion. (With permission from Debora Gallegos Saliby)

electrolyte problems. Later, the same author proposed anastomosing the proximal 36 cm of jejunum to the distal 10 cm of ileum in an end-to-side technique (Fig. 23.1) [12]. Variations were proposed in which an end-to-end anastomosis was performed, and the closed-loop segment of the small intestine was connected to the cecum, to the transverse colon, or to the sigmoid colon.

Despite the popularity of these procedures in the 1960s and the good results regarding weight loss and resolution of comorbidities, serious complications occurred. The defunctionalized segment was responsible for bacterial overgrowth that generated arthralgia, distension, abdominal pain, and even liver failure. The occurrence of severe diarrhea was frequent. Many patients had protein depletion and vitamin deficiency. In the 1970s other less morbid procedures were developed, and the jejunoileal bypass was abandoned.

Malabsorptive Procedures

Biliopancreatic Diversion

Scopinaro et al. in 1979 [13] described an alternative to jejunoileal bypass and created the procedure known as biliopancreatic diversion (Fig. 23.2). This procedure consists of a partial distal gastrectomy with closure of the duodenal stump. The jejunum was divided 250 cm proximal to the ileocecal valve. The distal limb (Roux limb) was anastomosed to the stomach. The proximal limb (biliopancreatic limb) was anastomosed to the ileum 50 cm proximal to the ileocecal valve. This technique avoided blind-loop syndrome by maintaining pancreatic and biliary flow through the deviant bowel, and as there was contact between the food and the digestive fluids at 50 cm, the absorption was better than the jejunoileal bypass. This technique presented excellent results in regard to weight loss and resolution of comorbidities but was not free of complications. The most important were diarrhea, anemia, dumping stoma ulceration, protein deficiency, and calcium and vitamin D hypo-absorption.

Duodenal Switch

In order to reduce the problems of biliopancreatic diversion, Douglas S. Hess and Douglas W. Hess [14] created in 1998 a variation of the biliopancreatic diversion – the duodenal switch (Fig. 23.3). The gastric restriction continued to be present through vertical partial gastrectomy along the greater curvature with resection of

70–80% of the stomach (sleeve gastrectomy). The duodenum was sectioned 3 cm distal to the pylorus. The small intestine was measured in its totality. Forty percent of this distance was calculated and measured retrograde from the ileocecal valve, the small intestine was sectioned at this point, and the distal limb was anastomosed to the duodenum, and the proximal limb was anastomosed to the ileum 75–100 cm proximal to the ileocecal valve.

Pylorus preservation leads to slower gastric emptying and a lower incidence of dumping. The segment of duodenum present in intestinal transit decreased the incidence of stoma ulcers. In addition, due to this segment of duodenum in the alimentary transit, calcium and iron absorption improved greatly with lower incidence of anemia and calcium problems. The common alimentary channel of 75–100 cm was longer than the biliopancreatic diversion, therefore allowing better absorption of nutrients.

In 1995 Picard Marceau et al. [15] had already performed a similar procedure. They, however, did not transect the duodenum, only stapled it. The duodenal cross-stapling frequently permeated obviating the benefits of the operation.

Gastric Bypass

Restriction of the gastric capacity for the treatment of obesity was initiated by Edward Mason after observing weight loss in patients undergoing gastrectomy for the treatment of peptic ulcers. Mason and Ito [16], in 1967, sectioned the stomach horizontally, near the gastric fundus, creating a reservoir with about a 100 ml capacity, and gastrojejunostomy of 20 mm in the great curvature (Fig. 23.4). The rest of the stomach was left in the abdominal cavity. The results of weight loss were satisfactory with minimal side effects.

At first, authors were not concerned with the size of pouch or gastrojejunostomy. In 1977, Alder and Terry [17] stated that the larger the pouch, the greater the chance of its dilation, concluding that the ideal size of the pouch would be around

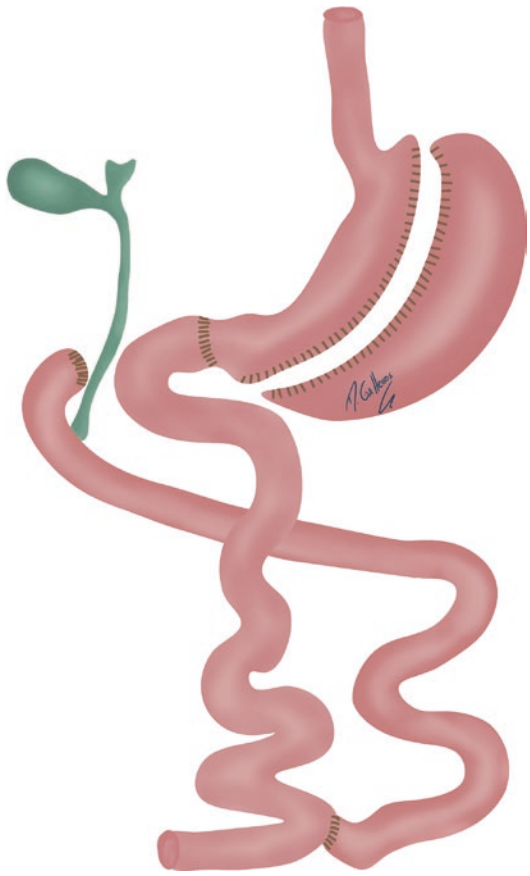


Fig. 23.3 Duodenal switch. (With permission from Debora Gallegos Saliby)

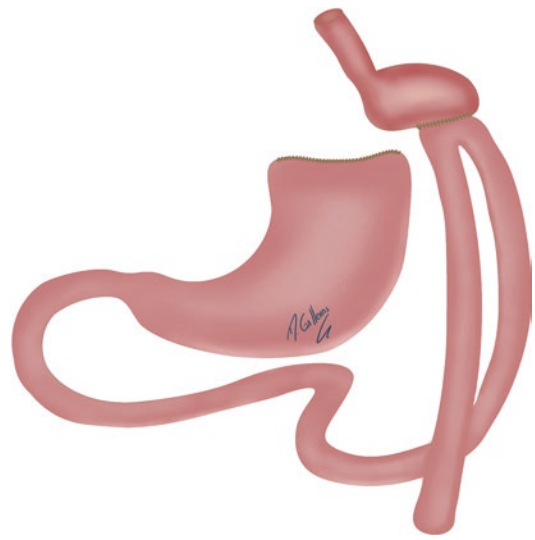


Fig. 23.4 Gastric bypass Mason and Ito. (With permission from Debora Gallegos Saliby)

30 ml. In the same year, Alden [18] with the intention of minimizing leaks proposed not the section the stomach but only the horizontal stapling. However, this technique was soon abandoned due to frequent failure of staple lines and restoration of the gastric cavity completely with weight regain.

Mason et al. [19], in 1975, modified the procedure by proposing a narrower anastomosis, between 8 and 12 mm, postulating that the narrower anastomosis would increase weight loss. In the same study, they proposed to reduce the gastric reservoir to 60 ml.

Griffen et al. [20] in 1981 recommended the Roux-en-Y gastrojejunal anastomosis (Fig. 23.5). This modification reduced the tension in the gastrojejunal anastomosis, eliminated the alkaline reflux in the pouch, and added a poorly absorptive component, reducing the incidence of leaks, reducing the side effects of the procedure, and increasing weight loss.

Torres et al. [21] in 1983 started to use the lesser curvature of the stomach to make the pouch, since an anastomosis in the proximal portion of the stomach and along the great curvature was difficult in obese patients and the pouch dilates less when performed along the lesser curvature. They constructed a pouch based on the lesser curvature of the upper stomach with an approximate capacity of 35 ml, a gastrojejunostomy of 18 mm in diameter, and jejunojejunostomy in Roux-en-Y configuration at 90 cm from the gastric pouch.

Another modification was the use of prostheses in the terminal portion of the gastric pouch to prevent its dilation and to decrease the emptying of the stomach. Laws and Piantadosi [22] in 1981 and Linner [23] in 1986 used silicone rings for this purpose. Fobi and Flemming [24], in 1986, practiced a technique by constructing the gastric pouch along the lesser curvature and the jejunojejunostomy 100 cm from the gastroenterostomy applying a silicone ring above this anastomosis. Capella et al. [25], in 1991, described a similar procedure but with a smaller pouch with a capacity of only 15 ml, also with a silicone ring at the distal end of the pouch. Later, they replaced the silicone ring with a polypropylene mesh. They emphasized the idea to limiting gastric emptying in order to obtain better to weight loss.

In order to increase weight loss, Salmon [26] proposed that the Roux limb should be longer than 150 cm as compared to the traditional 100 cm length. Wittgrove et al. [27], in 1996, performed the first laparoscopic gastric bypass (Fig. 23.6).

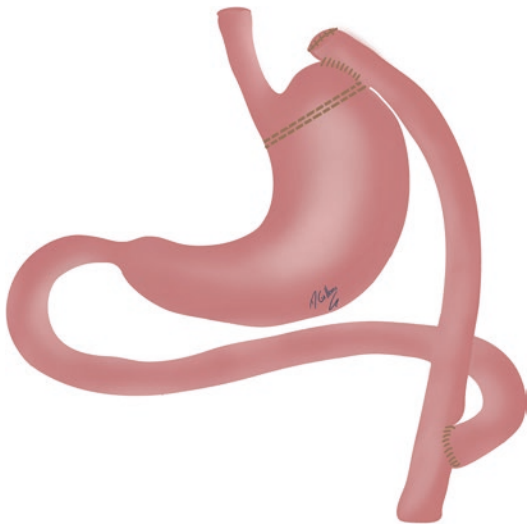


Fig. 23.5 Roux-en-Y gastric bypass. (With permission from Debora Gallegos Saliby)

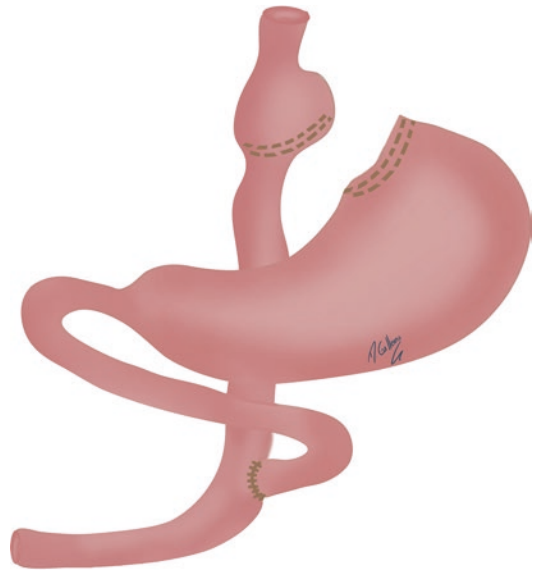


Fig. 23.6 Roux-en-Y gastric bypass. (With permission from Debora Gallegos Saliby)

Although the gastric bypass had an advantage over the biliopancreatic diversion and duodenal switch with less diarrhea and liver problems, weight loss was lower, and bypassing stomach and duodenum had the potential of leading to calcium and iron absorption problems in addition to vitamin B_{12} deficiency.

Pure Restrictive Procedures

Gastroplasty

The first gastroplasty was proposed by Printen and Mason [28] in 1973 (Fig. 23.7). The procedure consisted of horizontal stapling of the gastric fundus, creating a proximal pouch with a stoma next to the great curvature that connected this small pouch with the remaining stomach. This operation was abandoned due to unsatisfactory weight loss, probably related to failure of the stapled line, dilation of the pouch, or enlargement of the communication channel. To avoid leaks of the stapling line, Gomes [29], in 1980, suggested two lines of stapling and reinforced the stoma with Mersilene mesh or polypropylene rings. These modifications were difficult to perform and caused fibrosis, erosions of the mesh into the stomach, and dilation of the pouch. Carey and Martin [30] proposed in 1981 stapling the stomach with two staple lines but with the outlet channel between the small proximal pouch and the rest of the stomach located midway between the lesser and greater curvature, with 1 cm diameter. Despite the efforts mentioned above, the problem of stapling leaks persisted, and gastric dilatation also occurred frequently.

Long and Collins [31] in 1980 proposed the oblique stapling starting on the lesser curvature toward the angle of His, making the pouch next to the lesser curvature. The stapling had about 12 cm of extension, with a stoma diameter of 1–2 cm. The stoma was reinforced with a polypropylene suture to avoid its dilation. This technique decreased the chance of pouch dilation because the wall of the stomach is thicker along the small curvature. Laws [32] introduced, in 1981, the use of silicone ring around the stoma to prevent its enlargement.

Mason [33] in 1982 developed the vertical banded gastroplasty. This procedure consisted of vertical stapling along the lesser curvature toward the angle of His, calibrated over a bougie to ensure a diameter of 10–12 mm. The pouch should not have more than a 50 ml capacity (Fig. 23.8). The outlet of the pouch was reinforced by a polypropylene mesh. Initially only the stapling of the stomach was done, but due to

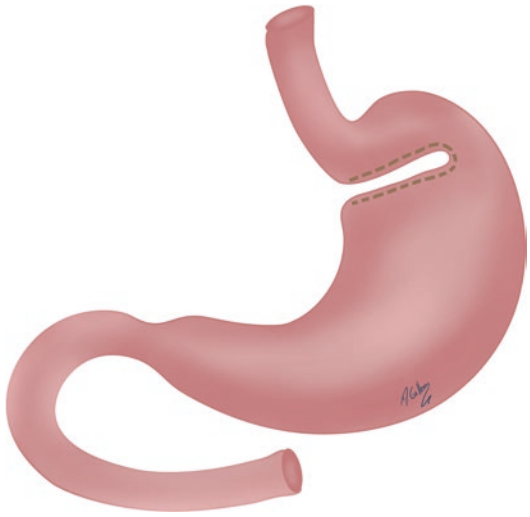


Fig. 23.7 Gastroplasty. (With permission from Debora Gallegos Saliby)

Fig. 23.8 Gastroplasty Mason. (With permission from Debora Gallegos Saliby)

the constant failure of the stapling line, section of the stomach was subsequently performed.

Although the initial results were satisfactory, long-term follow-up showed better results with other surgical techniques. The interest in gastroplasties decreased.

Gastric Banding

The gastric band was designed to be less invasive, avoiding any changes in the anatomy of the digestive tract or stomach, in order to reduce food intake by creating a small gastric reservoir.

Wilkinson and Peloso [34] in 1981 placed a 2-cm-wide Marlex band along the proximal part of the stomach. In 1983, Molina and Oria [35] described the same procedure using a Dacron band. These materials led to fibrosis and gastric erosion in such a way that complications were very frequent, and therefore were soon abandoned, but the idea remained.

Silicone band with an internal balloon was then designed. This balloon could be inflated through a portal placed in the subcutaneous tissue to control the volume of the balloon and thus the diameter of the gastric outlet. Hallberg and Forsell [36] were the first to use the gastric adjustable band in humans in 1985. In 1986, Kuzmak [37] showed better results with the adjustable gastric band compared to the unadjusted band. With the advent of laparoscopy, the gastric banding became a very widespread option for the treatment of obesity (Fig. 23.9).

With long-term follow-up, side effects of this procedure began to be reported, such as band slippage, erosion, esophageal dilation, and weight loss lower than other surgical procedures. Reoperations were described in large numbers of patients to correct the complications or to convert the gastric banding into another surgical procedure.

Sleeve Gastrectomy

This technique consists of a vertical gastrectomy with resection of 80% of the stomach, removing the gastric fundus and large part of the body, leaving the tubular-shaped stomach, and preserving only the antrum. The stomach looks like a sleeve.

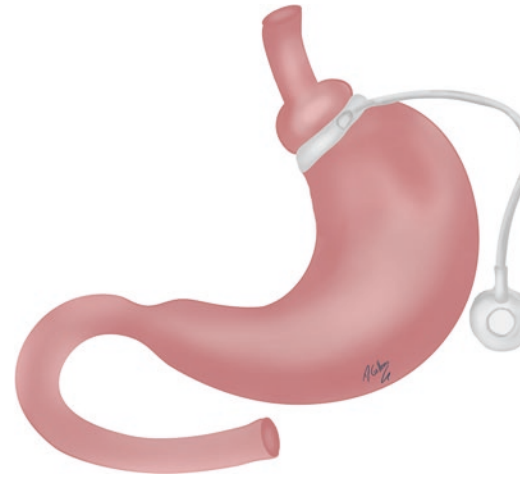


Fig. 23.9 Gastric band. (With permission from Debora Gallegos Saliby)

This procedure was initially proposed by Johnston [38], in order to avoid the mesh placed in vertical banded gastroplasty. The technique consisted of stapling the stomach close to the lesser curvature, calibrated over a 32-French bougie more distal to that proposed in vertical gastroplasty and directed to the angle of His. This technique created a tube next to the lesser curvature. This procedure was called "Magenstrasse and Mill" where there was restriction to the volume of food intake and the gastric antrum received the food and prepared it for emptying controlled by the pylorus that remained intact.

This technique allowed weight regain due to reflux of food into the large gastric chamber through the common canal at the antrum. In order to avoid this side effect, the resection of the stomach was proposed, starting the stapling along the greater curvature 4–6 cm proximal to the pylorus. The vertical gastrectomy also came to be used as staging procedure [39] in super obese, preceding the duodenal switch. Many of these patients had considerable weight loss, and thus the next procedure became often unnecessary so that the use of a sleeve gastrectomy was started as a single procedure for the treatment of obesity. Due to

Fig. 23.10 Sleeve gastrectomy. (With permission from Debora Gallegos Saliby)

the lower incidence of dumping and good weight loss, this technique has been widely used for the treatment of obesity (Fig. 23.10).

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Martin LF, Hunter S, Lauve RM, O'Leary JP. Severe obesity: expensive to society, frustrating to treat, but important to confront. South Med J. 1995;88:895–902.
2. Vainio H, Kaaks R, Bianchini F. Weight control and physical activity in câncer prevention: international evaluation of evidence. Eur J Cancer Prev. 2002;11:94–100.
3. Kushner RF. Medical management of obesity. Semin Gastrointest Dis. 2002;13:123–32.
4. Von Eyben FE, Mouritsen E, Holm J, Montvilas P, Dimcevski G, Suciu G, et al. Intra-abdominal obesity and metabolic risk factors: a study of young adults. Int J Obes Relat Metab Disord. 2003;27:941–9.
5. De Maria EJ. Bariatric surgery for morbid obesity. N Engl J Med. 2007;356(21):2176–83.
6. Patterson EJ, Urbach DR, Swanstrom LL. A comparison of diet and exercise therapy versus laparoscopic Roux-en-Y gastric bypass surgery for morbid obesity: a decision analysis model. J Am Coll Surg. 2003;196:379–84.
7. Fobi M, Lee H, Felahy B, Che K, Ako P, Fobi N. Choosing an operation for weight control, and the transected banded gastric bypass. Obes Surg. 2005;15:114–21.
8. Dietel M, Shikora SA. The development of the surgical treatment of morbid obesity. J Am Coll Nutr. 2002;21:365–71.
9. Henrikson V. [Kan tunnfarmsresektion forsvaras som terapi mot fettsot? Nordisk Medicin. 1952;47:744]. Can small bowel resection be defended for therapy for obesity? Obes Surg. 1994;4:54–5.
10. Kremen A, Linner J, Nelson C. An experimental evaluation of the nutritional importance of proximal and distal small intestine. Ann Surg. 1954;140:439–44.
11. Payne J, DeWind L, Commons R. Metabolic observations in patients with jejunocolic shunts. Am J Surg. 1963;106:273–89.
12. Payne JH, DeWind LT. Surgical treatment of obesity. Am J Surg. 1969;118:141–7.
13. Scopinaro N, Gianetta E, Civalleri D, et al. Biliopancreatic by-pass for obesity: initial experience in man. Br J Surg. 1979;66:619–20.
14. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. Obes Surg. 1998;8:267–82.
15. Lagace M, Marceau P, Marceau S, et al. Biliopancreatic diversion with a new type of gastrectomy: some previous conclusions revisited. Obes Surg. 1995;5:411–8.
16. Mason EE, Ito C. Gastric bypass in obesity. Surg Clin North Am. 1967;47:1345–51.
17. Alder RL, Terry BE. Measurement and standardization of the gastric pouch in gastric bypass. Surg Gynecol Obstet. 1977;144:762–3.
18. Alden JF. Gastric and jejunoileal bypass. A comparison in the treatment of morbid obesity. Arch Surg. 1977;112:799–806.
19. Mason EE, Printen KJ, Hartford CE, Boyd WC. Optimizing results of gastric bypass. Ann Surg. 1975;182:405–14.
20. Griffen WO, Bivins BA, Bell RM. Gastric bypass for morbid obesity. World J Surg. 1981;5:817–21.
21. Torres JC, Oca CF, Garrison RN. Gastric bypass: Roux-en-Y gastrojejunostomy from the lesser curvature. South Med J. 1983;76:1217–24.
22. Laws HL, Piantadosi S. Superior gastric reduction procedure for morbid obesity. Ann Surg. 1981;193:334–40.
23. Linner JH. Surgical treatment of morbid obesity. Mayo Clin Proc. 1986;61:676.
24. Fobi M, Flemming AW. Vertical banded gastroplasty vs gastric bypass in the treatment of obesity. J Natl Med Assoc. 1986;78:1091–8.

25. Capella RF, Capella JF, Mandec H, Nath P. Vertical banded gastroplasty – gastric bypass: preliminary report. Obes Surg. 1991;1:389–95.
26. Salmon PA. Gastroplasty with distal gastric bypass: a new and more successful weight loss operation for the morbidly obese. Can J Surg. 1988;3:111–3.
27. Wittgrove AC, Clark GW, Schubert KR. Laparoscopic gastric bypass, Roux-en-Y technique and results in 75 patients with 3–30 months follow up. Obes Surg. 1996;6:500–4.
28. Printen KJ, Mason EE. Gastric surgery or relief of morbid obesity. Arch Surg. 1973;106:428–31.
29. Gomez CA. Gastroplasty in the surgical treatment of morbid obesity. Am J Clin Nutr. 1980;33:406–15.
30. Carey LC, Martin EW Jr. Treatment of morbid obesity by gastric partitioning. World J Surg. 1981;5:829–31.
31. Long M, Collins JP. The technique and early results of high gastric reduction for obesity. Aust N Z J Surg. 1980;50:146–9.
32. Laws HL. Standardized gastroplasty orifice. Am J Surg. 1981;141:393–4.
33. Mason EE. Vertical banded gastroplasty for obesity. Arch Surg. 1982;117:701–6.
34. Wilkinson LH, Peloso OA. Gastric (reservoir) reduction for morbid obesity. Arch Surg. 1981;116:602–5.
35. Molina M, Oria HE. Gastric segmentation: a new, safe, effective, simple, readily revised and fully reversible surgical procedure for the correction of morbid obesity [abstract 15]. In: 6th Bariatric surgery colloquium. Iowa City, 2–3 June 1983.
36. Hallberg D, Forsell O. Ballongband vid behandling av massiv oberwikt. Svinsk Kiriurgi. 1985;344:106–8.
37. Kuzmak LI. Silicone gastric banding: a simple and effective operation for morbid obesity. Contemp Surg. 1986;28:13–8.
38. Johnston D, Dachtler J, Sue-Ling HM, et al. The magenstrasse and Mill operation for morbid obesity. Obes Surg. 2003;13:10–6.
39. Regan JP, Inabet WB, Gagner M, et al. Early experience with twostage laparoscopic Roux-en-Y gastric bypass as an alternative in the super-obese patient. Obes Surg. 2003;13:861–4.

Importance of a Multidisciplinary Approach for Bariatric Surgery

24

Richard Thompson and Timothy M. Farrell

Introduction

Bariatric surgery is a proven effective treatment for morbid obesity and its associated comorbidities, such as diabetes and hypertension. A multidisciplinary approach is essential to ensure maximum benefits that will last for the rest of the patient's life and for prevention or treatment of complications. Besides the surgeon, the care team consists of the following providers: a primary care provider, a registered dietician, a clinical psychologist, and an exercise physiologist. Patients usually prepare for surgical treatment months before operation, assisted by a bariatric coordinator who helps guide them through the process. Data indicate that patients lose more excess weight and are less likely to regain weight when an intensive multidisciplinary approach is used [1]. This includes preoperative nutritional education and guidance with dieting and a regular exercise program [2–6]. Psychological assessment of mood, social and family support, substance use, cognitive function, psychosocial status, motivation, and willingness to undertake behavioral changes are crucial. An endocrinologist or internist with expertise in obesity treatment helps to optimize the patient for surgery by controlling comorbidities with medications and other therapies. In the postoperative period, continual follow-up with all members of the team significantly contributes to the enduring success of bariatric surgery. Multidisciplinary weight management is recommended by medical societies. The National Weight Control Registry has data showing narrow approaches to weight reduction are rarely effective but that a broad, multifaceted approach is more sustainable [7]. Furthermore, multidisciplinary weight management results in long-term maintenance of weight loss.

Role of the Surgeon

The bariatric surgeon performs an operation designed to aid with weight loss. Over several decades, different operations have been used to variably provide restrictive, malabsorptive, or behavioral strategies to affect weight loss. Currently, the predominant operations are Roux-en-Y gastric bypass and sleeve gastrectomy. These operations have similar short-term outcomes with regard to excess weight loss [8]. Therefore, the choice of operation is determined through a shared decision-making process between the patient, surgeon, and other providers of the multidisciplinary team. Roux-en-Y gastric bypass and sleeve gastrectomy provide similar results with regard to resolution of comorbidities such as diabetes within the first 5 years of surgery. However, further study is needed to deter-

R. Thompson · T. M. Farrell (✉)
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA
e-mail: tfarrell@med.unc.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_24

mine if one operation is more effective in the long term [9]. Some data suggest that 10-year outcomes may be better with gastric bypass, but this operation has the potential for complications such as marginal ulcers and internal hernias [10].

The surgeon manages the patient in the immediate postoperative period. This includes monitored dietary advancement, pain control, and management of fluids. The surgeon is responsible for identification and treatment of postoperative complications, the most common of which include gastrointestinal leak, bleeding, and stricture. Roux-en-Y gastric bypass patients are at risk for developing marginal ulcers at the gastrojejunal anastomosis as well as internal hernias. Leaks are often not identified for days and as a result are often managed with percutaneous drainage. Strictures can be successfully treated with endoscopic dilation. Marginal ulcers are managed medically with acid suppression. Internal hernias may be life-threatening as a potential cause of bowel ischemia and require prompt operative intervention.

Although bariatric surgery allows for dramatic weight loss, there is overwhelming evidence supporting the need for intensive management of patients by a multidisciplinary team before and after operation. With the care and support of a full team, patients can expect better and more durable benefits to their health.

Role of the Specialist in Medical Management of Obesity

Primary care providers are on the front line in the fight against obesity and attendant comorbid conditions such as diabetes and hypertension. It is crucial for physicians to not only screen for obesity and diabetes but also to aggressively manage these conditions early in the course of disease. Appropriate patients should be referred to a Bariatric Center of Excellence, where intake begins with an internist or endocrinologist with expertise in management of obesity.

Optimization of prescribed medication may enhance the benefits of diet and exercise. Medications that are weight neutral or those that enhance weight loss such as metformin, DPP-4 inhibitors, α-glucosidase inhibitors, GLP-1 analogs, SGLT-2 inhibitors, and pramlintide should be prescribed over medications with a known side effect of weight gain. Furthermore, the use of FDA-approved anti-obesity medications such as lorcaserin, naltrexone with bupropion, topiramate with phentermine, and liraglutide is encouraged in certain patients with strong appetites. Patients on insulin may be switched to long-acting insulins like insulin detemir, insulin degludec, and insulin glargine U-300 in order to curb weight gain. Orlistat, a gastric and pancreatic lipase inhibitor, blocks dietary fat absorption by approximately 30%. Both randomized trials and meta-analyses have demonstrated that orlistat treatment can produce weight loss and reduce the incidence of type-2 diabetes in people with impaired glucose tolerance [11]. Several mechanisms have been proposed to account for the anti-diabetic effect of orlistat, such as improved insulin sensitivity, incomplete dietary fat digestion, partial stimulation of glucagon-like polypeptide 1 (GLP-1) release, and decreases in visceral adiposity. Phentermine-extended release with topiramate, lorcaserin, and naltrexone with bupropion are additional medications that can elicit weight loss through action on the central nervous system to reduce appetite. Clinical trials have shown these medications are effective at reducing HbA1c as well as lowering the progression to type-2 diabetes. Liraglutide, a GLP-1 receptor agonist that is approved for use in type-2 diabetes, has also been approved for weight loss [1].

The physicians who counsel patients on proper diet and exercise and who manage excess weight and its comorbidities are often the first to introduce the idea of surgical treatment to enhance excess weight loss. They have the opportunity to identify and refer appropriate surgical candidates. Ideal patients are those with BMI greater than 40 kg/m^2 or BMI greater than 35 kg/m^2 with associated comorbidities such as diabetes, hypertension, or sleep apnea, who are able to tolerate a general anesthetic and operation.

Prior to operative planning, selective referrals to additional specialists should be made at the discretion of the physician. Clinical suspicion for

diseases such as obstructive sleep apnea, reflux, or heart disease warrants preoperative evaluation with the appropriate specialists. Further diagnostic testing helps determine whether a patient is appropriate for surgery or if there is room for further medical optimization in order to minimize the risks associated with surgery. In the case of gastroesophageal reflux, some evidence [12] suggests that a sleeve gastrectomy exacerbates the disease, and thus diagnostic testing may influence which operation is offered to patients.

Role of the Dietician

Although there is a genetic component of obesity, the substantial increased prevalence of the disease in recent years belies the major contributing factors of excess caloric intake combined with a sedentary lifestyle. The morbidly obese population typically subsists on high-fat, high-sugar foods with poor nutritional value. The causes of nutritional deficiencies in this population are multifactorial and include high intake of calorically dense foods with low nutritional quality, limited bioavailability of some nutrients such as Vitamin D, chronic inflammation status that affects iron metabolism, and small intestinal bacterial overgrowth which can lead to deficiencies in thiamin, vitamin B-12, and fat-soluble vitamins. The most common preoperative deficiencies found in studies include vitamin B-12, iron, folic acid, vitamin, and thiamine [13–15].

Patients meet with a registered dietician upon presentation to the bariatric clinic. Evaluation includes review of dietary history and review of adherence to dietary recommendations during previous attempts of weight management. Potential barriers to following a nutrition plan are identified. Each participant should receive a hypocaloric meal plan rounded to the nearest 1200, 1500, or 1800 kilocalorie level for ease of application based on their gender, height, and previous energy intake.

Ideally, patients should begin following recommendations toward a postsurgical diet and make lifestyle modifications 6 months before operation. The overarching recommendation is a diet primarily low in fat and sugar and high in protein and vegetables without starch. Structured meal plans provide approximately 40–45% of daily energy intake from carbohydrates with 14 grams of fiber per 1000 calories, less than 35% from fat with less than 10% from saturated fat, and 1–1.5 g/kg of adjusted body weight from protein [15]. Protein intake is not calculated as a percentage of the total calories in order to avoid unintended reduction in absolute protein intake in a hypocaloric diet, which could accelerate lean muscle loss during weight reduction. Minimizing the loss of lean muscle mass is vital for long-term maintenance of overall weight loss. Patients are encouraged to maintain a food log, which is reviewed weekly by the dietician during the intensive phase of intervention to ensure adherence to the diet.

With most bariatric procedures, there is a restrictive component to intake to which the patient must adjust early in the postoperative period. Most surgeons also limit early diet to 2–3 ounces per hour of liquids to prevent staple line stress during healing. Still, the patient may experience nausea, vomiting, bloating, or epigastric pain. Following discharge, it is not uncommon for patients to develop such symptoms due to noncompliance with recommended dietary guidelines. Early re-involvement of the dietician after surgery, for ongoing education regarding food selections, timing, and volume of meals, is associated with significantly lower readmission rates [16].

Patient surveys indicate that therapeutic continuity is the most important element of follow-up care [17]. This is most often established with the bariatric dietician. Studies have demonstrated an association between the number of follow-up visits and weight loss post-gastric bypass surgery [16, 17]. Proper diet is helpful in reducing the incidence of slow weight loss, weight regain, weight plateauing, dehydration, discomfort, abdominal pain, indigestion, heartburn, and dumping syndrome after surgery, and patients rely on the dietician for guidance. Garg et al. [16] demonstrated that postoperative nutritional consultation resulted in significantly fewer readmissions due to dietary-related problems

and more favorable 3-month change in serum thiamine, high-density lipoprotein, and triglycerides when seen by both surgeon and dietician versus surgeon alone. Attrition rates among bariatric patients range from 3 to 63% depending on the type of surgical procedure as well as the nature and frequency of prescribed follow-up care, and failure to return for follow-up visits is associated with more postoperative complications, lower percentage weight loss, a higher degree of nutritional deficiencies, poorer dietary compliance, and higher rates of surgery-related morbidity. It is estimated that 42% of patients will regain a large proportion of the weight initially lost and reenter the category of morbid obesity. The dietician helps to ensure the success of bariatric surgery by providing patients with practical nutrition knowledge as well as encouragement for physical activity and behavioral changes. Studies show that patients who are lost to follow-up have less success in weight reduction and maintenance and are at greater risk of developing nutritional deficiencies [18].

Vitamin supplementation becomes important due to decreased caloric intake and malabsorption following surgery. Multivitamin formulas should contain at least 45 mg iron, 400 mcg folic acid, and 8–11 mg of zinc. Supplementation with cobalamin (vitamin B12) in a 1000-mcg dose is recommended for all bariatric surgery patients. Daily supplementation of elemental calcium citrate with vitamin D3 is recommended. Patients are encouraged to take full supplements for at least 3 months after surgery, and the care team can then reevaluate at close intervals to best tailor supplementation.

Role of the Exercise Physiologist

Lack of physical activity in the preoperative period is a strong predictor of blunted weight loss following bariatric surgery [19]. In fact, cardiorespiratory fitness measured by oxygen delivery less than 15.8 ml/kg/min is associated with a longer operating time, intubation duration, and estimated blood loss during surgery, as well as more frequent complications including unstable angina, myocardial infarction, and deep vein thrombosis [11]. Exercise, before and after bariatric surgery, is an essential component of the multidisciplinary approach to weight loss. Ideally, an exercise physiologist meets with the patient early in the process and develops a personalized exercise plan based on the individual's age, gender, health status, and exercise capacity. In clinical practice, exercise capacity may be tested by a simple method such as the 6-minute walk test. The common recommendation of 150 minutes per week of aerobic exercise or 10,000 steps per day improves fitness but is not enough for weight reduction or even for maintenance of weight loss. Effective exercise intervention for weight management should include a balanced mix of aerobic exercise to promote cardiovascular health, resistance exercise to maintain muscle mass, and flexibility (stretch) exercise to enhance functional capabilities and reduce risk of injury. Exercise plans may progress gradually over 3–6 months, from 20 minutes per day for 4 days each week to 60 minutes per day for 5–6 days each week. After completing the initial intensive phase, participants are usually encouraged to continue to exercise for 1 hour daily, 5–6 days per week, and to maintain greater than 300 minutes per week, with focus on resistance training to preserve muscle mass. This is important because diabetes worsens sarcopenia. The use of different exercise methods like circuit and interval training reduces boredom and increases duration of exercise. Exercise is particularly important after the intensive phase of weight management; it helps maintain the weight loss achieved during the intensive period.

Current recommendations to increase aerobic fitness in adults advise 150 minutes of moderate or 75 minutes of vigorous physical activity per week [1]. However, fewer than 10% of bariatric surgery candidates meet the activity recommendation prior to surgery and are most commonly categorized as having poor cardiorespiratory fitness. This low level of physical activity may explain why some individuals have an increased risk of composite surgical complications. Presurgical physical activity levels are positively associated with postsurgical physical activity and

increasing physical activity levels prior to surgery may facilitate a beneficial increase in post-surgical exercise behavior. Preoperative exercise counseling combined with pedometry has been shown to increase 6-month postoperative physical activity levels to a greater extent than standard medical care alone [20]. Few data exist regarding the relationship between preoperative patient education and weight management programs on patient weight loss and postoperative outcomes after bariatric surgery. While some researchers have reported the positive impacts of these programs on postoperative weight loss, others, more often, have found undetectable differences. A recent retrospective analysis compared 56 patients who attended a preoperative weight management program to 441 surgical patients who did not attend such a program. The program consisted of lifestyle changes including monitored diet and exercise, as well as education and behavioral strategies. Subgroup analysis revealed a modestly higher excess weight loss at 12 months among Roux-en-Y gastric bypass who attended the weight management programs versus controls (66% compared to 56%) [21].

The Look AHEAD trial from 2014 provides the largest and longest randomized evaluation to date of an intensive lifestyle intervention for weight reduction [22]. The study was initially conceived to evaluate the effect on cardiovascular disease over time. Although the results show no difference between the compared groups for this primary endpoint, the study provides information about the feasibility of inducing and maintaining clinically significant weight loss, defined as a ≥5% reduction in initial body weight. Weight loss of this degree confers health benefits including prevention and resolution of type-2 diabetes, reduction in blood pressure and lipids, amelioration of nonalcoholic fatty liver disease, and improvements in urinary incontinence and sexual dysfunction. The intensive intervention arm emphasized lower caloric intake by restricting fat calories to less than 30% of total and also reducing low-quality carbohydrates such as sugar, sugar-flavored beverages, and high-calorie snacks. Increased exercise levels of 175 minutes per day at least 5 days per week were encouraged. This group had fewer hospitalizations, fewer medications, and lower health-care costs over a 10-year period, making the program cost-effective.

Two recent small randomized controlled trials indicate that physical activity interventions initiated postoperatively can also increase patients' activity levels and contribute to improved surgical outcomes, including weight loss, body composition, and fitness [21]. There is also evidence to suggest that increasing physical activity preoperatively may reduce surgical complications and there is substantial support showing that consistent activity is the most important predictor of long-term weight loss maintenance [23].

Clinicians report that doubt of counseling efficacy and lack of patient interest are barriers to providing exercise counseling in clinical care. These barriers may, in part, be responsible for recent survey results which revealed that only 22% of patients of bariatric surgical centers accredited by the American College of Surgeons Bariatric Surgery Center Network report having received postoperative exercise consultation, despite accreditation requirements to establish procedures for exercise counseling [21]. However, evidence that motivated patients can increase their activity level and obtain the attendant health benefits, if given very clear guidelines and assistance in reaching goals, justifies regular exercise programs in the clinical care of bariatric surgery patients. Clinicians can do their part to increase the exercise level of patients during all phases of their care, including providing referrals for exercise testing, physical therapy, and an exercise specialist as indicated.

Role of the Mental Health Professional

Preoperative psychological assessment of the bariatric patient is an essential component of ensuring optimal outcomes. Morbid obesity is commonly associated with depression and low self-esteem. The social stigma and poor body image associated with obesity contribute to psychopathology. Oftentimes binge eating is the result of poor

impulse control, depression, emotionality, or self-consolation. Psychiatric diseases such as depression and bipolar disorder are associated with less excess weight loss and weight regain in the postoperative population. The preoperative psychological evaluation aids in identification of patients who are capable of adherence to diet and exercise regimens in the long term. It also helps to identify risk factors such as depression, which can be treated with medication and psychotherapy in order to improve weight-loss outcomes. Overeating and binge eating become such an ingrained part of these patients' lives, often serving as a coping mechanism. The psychological component of pathologic eating behavior must be addressed in these patients because once they undergo bariatric surgery, they lose this coping mechanism. This can lead to depression which negatively impacts postoperative weight loss [24].

The primary objective for the psychosocial evaluation is to provide screening and identification of risk factors or potential postoperative challenges that may contribute to a poor postoperative outcomes [25–30]. Patients with such factors benefit from additional management or intervention before and/or after surgery. In some cases, these issues may contraindicate surgery altogether. Another important function that the preoperative psychosocial evaluation process serves is to establish a positive and trusting working relationship between the behavioral health clinician and the patient. When the clinician presents as a support who will help the patient proceed to surgery and ensure the best possible outcomes, the patient's willingness to be open and candid during the evaluation increases. Establishment of trust and rapport during the initial evaluation also serves to enhance the patient's willingness to seek behavioral support after surgery if problems are encountered. Even a patient with excellent postsurgical weight loss may encounter psychosocial difficulties and challenges after surgery, ranging from disruptions in interpersonal relationships and body image dissatisfaction to concerns as serious as substance abuse and even suicidal behavior. The preoperative psychological assessment helps not only with the outcome measure of weight loss but also measures of metabolic status and medical comorbidities, quality of life, and psychosocial and behavioral functioning.

The initial clinic visit consists of a clinical interview, which includes routine general mental health intake assessment of psychopathology and mental status. Patients with severe obesity, and particularly the ones seeking surgical weight loss treatment, are more likely to report current or lifetime mood and anxiety disorders. Post-traumatic stress disorder, social phobia, and panic disorder are common. This visit also clarifies weight history, including weight trajectory over time and past weight-loss attempts. This history helps to identify important environmental and physiologic contributors that have affected the patient's weight. It also allows the evaluator to obtain information about the specific types of weight-loss interventions that have been tried, duration of adherence to the various approaches, and what factors have been helpful in promoting adherence or barriers to sustained behavior change. Developmental and family history, cognition, personality traits and temperament, substance abuse, expectations following surgery, social support, and motivation are all important factors to assess during the interview as they may impact the success of surgery.

Recent literature has consistently demonstrated that personality traits and temperament have an influence on postoperative outcomes. In particular, low conscientiousness, poor impulse control, and elevated neuroticism are related to risk for obesity as well as suboptimal outcomes following bariatric surgery. The trait of persistence, or an ability to continue to pursue one's goals despite immediate setbacks and frustration, is a significant predictor of weight loss after surgery [24].

Following the preoperative psychological assessment, a report is completed which includes recommendations based on the findings of the evaluation. These may include interventions designed to minimize barriers to optimal psychosocial and medical outcomes after surgery. For example, after noting that the patient has depres-

sion, the evaluator will recommend specific methods to ensure that the patient's mood symptoms do not interfere with postsurgical self-care and behavioral adherence or pose a risk for self-harm. The aim of the presurgical evaluation should be to assess the impact that such psychological symptoms or diagnoses would have on postsurgical adherence and self-care. The focus of the assessment is on the extent to which daily functioning is affected, how stable the patient has been and for how long, whether appropriate psychological treatment is in place, and how well any symptoms are being managed at the time of presentation.

Some evidence suggest that postoperative psychological support services also impact outcomes. Existing postsurgical psychological services are characterized by a large variation across bariatric programs, ranging from individual psychotherapy and group therapy to support groups. Recent systematic review with meta-analysis of nine studies looking at the effects of postsurgical psychological services indicate a relatively modest effect on weight loss up to 3 years following bariatric surgery [31]. However, a randomized controlled trial involving 145 patients published in 2015 concluded that psychological support pre- and post-bariatric surgery had no impact on weight loss as measured by BMI and change in BMI after a year [32]. The authors argue that psychological support should be targeted to patients who start to demonstrate weight regain following surgery. Further study with methodological rigor is needed in order to elucidate the role of postoperative psychological services.

Analysis of postsurgical psychosocial factors indicates that the pathologic behaviors of binge eating and grazing, as well as presence of depressive disorders, negatively impact weight-loss outcomes. Conversely, adherence to dietary and physical activity guidelines positively predict weight loss. Postoperative identification of disordered eating and depressive disorder provides an opportunity for targeted behavioral and medical interventions, which may help to attain better long-term weight loss outcomes.

Weight Regain

Among patients who experience weight regain, the return of hunger or food cravings may lead to maladaptive eating behaviors in response to internal and external cues. Acceptance-based behavioral treatments specifically target the psychological challenges patients face by providing them with skills to handle undesirable psychological experiences in the service of core long-term values. Acceptance and commitment therapy directly address the causes of postoperative weight regain by helping patients to make mindful decisions based on their weight-control goals despite the internal states that make doing so challenging. For example, patients learn tools to gain psychological distance from thoughts and emotions, allowing them to act independently of these internal experiences. These kinds of behavioral treatments are especially effective for individuals with greater disinhibition and responsivity to food.

Weight regain is a substantial challenge for patients and providers following bariatric surgery. Understanding risk factors helps prevent or reduce the adverse influence on weight-loss outcomes. Preoperative age, sex, race, body mass index, and diabetes status are reported determinants associated with nonresponsiveness to surgery [11]. Elderly patients exhibit sarcopenia and insulin resistance to a greater degree than younger patients, both of which promote fat storage. Women may have a blunted response in comparison to men due to sex hormones; high testosterone in women increases diabetes risk, and women have relative leptin resistance which may increase caloric intake. Women also have elevated ghrelin levels, resulting in higher total fat mass. Latino and black patients tend to lose less weight; whether this is the result of genetic predisposition, culture, or socioeconomic status remains unclear.

Insulin-resistant diabetes plays a major role in fat distribution and thus excess weight. Excess fatty tissue and diabetes are intricately related and create a vicious cycle. Increased white adipose tissue in the abdominal visceral region increases the expression of macrophages and

inflammatory cytokines including TNF-α and interleukin-6 that, in turn, leads to elevated systemic inflammation. This chronic inflammatory state contributes to insulin resistance. Moreover, increased inflammation in adipose tissue downregulates adiponectin, which exacerbates systemic insulin responsiveness in tissues including the skeletal muscle and liver. This is problematic as insulin resistance promotes β-cell dysfunction, endothelial dysfunction, hyperglycemia, and increased risk of cardiovascular disease.

The development of social media platforms has led to the formation of patient-led discussion groups, which provide information related to bariatric surgery and support to members. The role of social media in health care is in evolution, and it is important for providers to be familiar with its impact on patients because its powerful influence. The quality and veracity of information presented to potential surgical candidates as well as those who have undergone weight loss surgery are questionable and can confuse or mislead members if the information is contradictory to that which is provided in clinical settings. It stands to reason that the management of social media groups and the information and support they provide should fall to the health-care providers for this population. It remains unclear what influence social media has on surgical outcomes, but it will be important for clinicians to be aware of its presence, to get involved, and monitor its long-term effects.

Conclusions

A multidisciplinary approach to the bariatric patient clearly leads to better and more sustainable weight-loss results. Bariatric operations are not "quick fixes" to obesity; rather, they comprise one integral element which acts synergistically with those of diet, exercise, medical management, and cognitive–behavioral therapy to provide the best outcomes. Future studies of this population are required in order to more fully understand how these elements determine outcomes. For instance, it remains to be seen how the timing and content of exercise regimens impact the amount of excess weight loss and the sustainability of those results. Frequency and method of psychological counseling may positively affect results, but this requires further examination. Closer follow-up with a bariatric dietician and primary care physician may also play a role, although this remains to be fully characterized. More intensive lifestyle interventions and involvement in support groups have the potential for positive influence, but these need to be more clearly defined and standardized in order to measure their effects. Information obtained directly from patients suggests the importance of support systems before and after surgery; many report that peer, dietetic, and psychological support positively influence weight loss outcomes in the long term [33]. As more high-quality studies are produced and long-term data become available, the multidisciplinary team is best positioned to deliver what is needed for patients to have the best possible outcomes.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Hamdy O, Ashrafzadeh S, Mottalib A. Weight management in patients with type 2 diabetes: a multidisciplinary real-world approach. Curr Diab Rep. 2018;18(9):66.
2. Egberts K, Brown WA, O'Brien PE. SFR-111 Optimising lifestyle factors to achieve weight loss in surgical patients. Surg Obes Relat Dis. 2011;7:368.
3. McCullough PA, Gallagher MJ, Dejong AT, et al. Cardiorespiratory fitness and short-term complications after bariatric surgery. Chest. 2006;130(2):517–25.
4. Shah M, Snell PG, Rao S, et al. High-volume exercise program in obese bariatric surgery patients: a randomized, controlled trial. Obesity (Silver Spring). 2011;19(9):1826–34.
5. Koball AM, Jester DJ, Domoff SE, Kallies KJ, Grothe KB, Kothari SN. Examination of bariatric surgery Facebook support groups: a content analysis. Surg Obes Relat Dis. 2017;13(8):1369–75.
6. Graham YN, Hayes C, Mahawar KK, Small PK, Attala A, Seymour K, Woodcock S, Ling J. Ascertaining the place of social media and technology for bariatric patient support: what do allied health practitioners think? Obes Surg. 2017;27(7):1691–6.
7. Thomas JG, Bond DS, Phelan S, Hill JO, Wing RR. Weight-loss maintenance for 10 years in the

National Weight Control Registry. Am J Prev Med. 2014;46(1):17–23.
8. Peterli R, Wölnerhanssen BK, Vetter D, Nett P, Gass M, Borbély Y, Peters T, Schiesser M, Schultes B, Beglinger C, Drewe J. Laparoscopic sleeve gastrectomy versus Roux-Y-gastric bypass for morbid obesity—3-year outcomes of the prospective randomized Swiss Multicenter Bypass Or Sleeve Study (SM-BOSS). Ann Surg. 2017;265(3):466.
9. Murphy R, Clarke MG, Evennett NJ, Robinson SJ, Humphreys ML, Hammodat H, Jones B, Kim DD, Cutfield R, Johnson MH, Plank LD. Laparoscopic sleeve gastrectomy versus banded Roux-en-Y gastric bypass for diabetes and obesity: a prospective randomised double-blind trial. Obes Surg. 2018;28(2):293–302.
10. Shoar S, Saber AA. Long-term and midterm outcomes of laparoscopic sleeve gastrectomy versus Roux-en-Y gastric bypass: a systematic review and meta-analysis of comparative studies. Surg Obes Relat Dis. 2017;13(2):170–80.
11. Gilbertson NM, Paisley AS, Kranz S, et al. Bariatric surgery resistance: using preoperative lifestyle medicine and/or pharmacology for metabolic responsiveness. Obes Surg. 2017;27:3281.
12. Stenard F, Iannelli A. Laparoscopic sleeve gastrectomy and gastroesophageal reflux. World J Gastroenterol: WJG. 2015;21(36):10348.
13. Muschitz C, Kocijan R, Haschka J, Zendeli A, Pirker T, Geiger C, Müller A, Tschinder B, Kocijan A, Marterer C, Nia A. The impact of vitamin D, calcium, protein supplementation, and physical exercise on bone metabolism after bariatric surgery: the BABS study. J Bone Miner Res. 2016;31(3):672–82.
14. Sherf Dagan S, Goldenshluger A, Globus I, Schweiger C, Kessler Y, Kowen Sandbank G, Ben-Porat T, Sinai T. Nutritional recommendations for adult bariatric surgery patients: clinical practice. Adv Nutr. 2017;8(2):382–94.
15. Leahy CR, Luning A. Review of nutritional guidelines for patients undergoing bariatric surgery. AORN J. 2015;102(2):153–60.
16. Garg T, Birge K, Rosas U, Azagury D, Rivas H, Morton JM. A postoperative nutritional consult improves bariatric surgery outcomes. Surg Obes Relat Dis. 2016;12(5):1052–6.
17. Aarts MA, Sivapalan N, Nikzad SE, Serodio K, Sockalingam S, Conn LG. Optimizing bariatric surgery multidisciplinary follow-up: a focus on patient-centered care. Obes Surg. 2017;27(3):730–6.
18. Endevelt R, Ben-Assuli O, Klain E, Zelber-Sagi S. The role of dietician follow-up in the success of bariatric surgery. Surg Obes Relat Dis. 2013;9(6):963–8.
19. Hatoum IJ, Stein HK, Merrifield BF, Kaplan LM. Capacity for physical activity predicts weight loss after Roux-en-Y gastric bypass. Obesity. 2009;17(1):92–9.
20. Pratt KJ, Jalilvand A, Needleman B, Urse K, Ferriby M, Noria S. Postoperative outcomes based on patient participation in a presurgery education and weight management program. Surg Obes Relat Dis. 2018;14:1714–23.
21. King WC, Bond DS. The importance of pre and post-operative physical activity counseling in bariatric surgery. Exerc Sport Sci Rev. 2013;41(1):26.
22. Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity. 2014;22(1):5–13.
23. Donnelly JE, Blair SN, Jakicic JM, Manore MM, Rankin JW, Smith BK, American College of Sports Medicine. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. Med Sci Sports Exerc. 2009;41(2):459–71.
24. Schag K, Mack I, Giel KE, Ölschläger S, Skoda EM, von Feilitzsch M, Zipfel S, Teufel M. The impact of impulsivity on weight loss four years after bariatric surgery. Nutrients. 2016;8(11):721.
25. Sheets CS, Peat CM, Berg KC, White EK, Bocchieri-Ricciardi L, Chen EY, Mitchell JE. Post-operative psychosocial predictors of outcome in bariatric surgery. Obes Surg. 2015;25(2):330–45.
26. Bradley LE, Forman EM, Kerrigan SG, Butryn ML, Herbert JD, Sarwer DB. A pilot study of an acceptance-based behavioral intervention for weight regain after bariatric surgery. Obes Surg. 2016;26(10):2433–41.
27. Jalilvand A, Dewire J, Detty A, Needleman B, Noria S. Baseline psychiatric diagnoses are associated with early readmissions and long hospital length of stay after bariatric surgery. Surg Endosc. 2018;25:1–6.
28. Sogg S, Lauretti J, West-Smith L. Recommendations for the presurgical psychosocial evaluation of bariatric surgery patients. Surg Obes Relat Dis. 2016;12(4):731–49.
29. Calderone A, Fabio Calabro P, Lippi C, Jaccheri R, Vitti J, Santini F. Psychopathological behaviour and cognition in morbid obesity. Recent Pat Endocr Metab Immune Drug Discov. 2016;10(2):112–8.
30. Paone E, Pierro L, Damico A, Aceto P, Campanile FC, Silecchia G, Lai C. Alexithymia and weight loss in obese patients underwent laparoscopic sleeve gastrectomy. Eat Weight Disord-St Anorexia Bulimia Obes. 2017;28:1–6.
31. Beck NN, Johannsen M, Støving RK, Mehlsen M, Zachariae R. Do postoperative psychotherapeutic interventions and support groups influence weight loss following bariatric surgery? A systematic review and meta-analysis of randomized and nonrandomized trials. Obes Surg. 2012;22(11):1790–7.
32. Ogden J, Hollywood A, Pring C. The impact of psychological support on weight loss post weight loss surgery: a randomised control trial. Obes Surg. 2015;25(3):500–5.
33. Sharman M, Hensher M, Wilkinson S, Williams D, Palmer A, Venn A, Ezzy D. What are the support experiences and needs of patients who have received bariatric surgery? Health Expect. 2017;20(1):35–46.

Bariatric Surgery: Clinical Presentation and Evaluation

25

Marco Di Corpo, Francisco Schlottmann, and Marco G. Patti

Introduction

Obesity is defined by the World Health Organization (WHO) as an excessive fat accumulation that may impair health [1]. It is frequently classified using the body mass index (BMI), defined as weight in kilograms divided by the height in meters, squared, which provides a value in units of kg/m^2. According to the NIH, *overweight* encompasses BMIs between 25.0 and 29.9, while *obesity I* is defined as BMI between 30.0 and 34.9 and *obesity II* as 35–39.9. Patients with a BMI ≥40 are referred to as having extreme or morbid *obesity III* [2] and ≥50 kg/m^2 as the *super obese* [1].

The global prevalence of obesity has risen dramatically in recent decades [3]. This rising has been described as "globesity" by the interdisciplinary European guidelines on metabolic and bariatric surgery [4] and is currently affecting both developed and developing countries. Worldwide, the number of people who are overweight or obese climbed from 857 million in 1980 to 2.1 billion in 2013 [5]. A recent study from the WHO showed that for overweight, rates increased from 55.9% of the population in 2010 to 58.7% in 2016 and for obesity, from 20.8% to 23.3% [6].

Obesity, in addition to causing various physical disabilities and psychological problems, has severe deleterious health effects, such as diabetes, high blood pressure, dyslipidemia, and obstructive sleep apnea (OSA), among other disorders [7, 8]. Because of these multiple health risks accompanying excess weight and the absence of an effective nonsurgical weight loss treatments, bariatric surgery has become increasingly common, especially in patients with morbid obesity [9]. This also was proven by the Swedish Obese Subjects (SOS) study, were they confirmed that bariatric surgery is associated with reduced long-term morbidity and mortality, considerably contributing to the evidence base for the increased use of surgery for morbidly obese patients [10, 11].

For many years, bariatric surgery has been synonymous only with weight loss, but these procedures have demonstrated to be effective on the resolution of the comorbid conditions, therefore assuming the role of "metabolic surgery" [12]. In this chapter, we will discuss the metabolic disorders

M. Di Corpo
Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

F. Schlottmann
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

M. G. Patti (✉)
Department of Surgery, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA

Department of Medicine, Center for Esophageal Diseases and Swallowing, University of North Carolina, Chapel Hill, NC, USA
e-mail: marco_patti@med.unc.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_25

associated with obesity and the proper preoperative workup, a cornerstone for the success of bariatric surgery.

Clinical Presentation, Sequelae of Obesity

Obesity is associated with increased mortality. Each 5 kg/m^2 increase in BMI above 25 kg/m^2 increases overall mortality by approximately 30%. At 30–35 kg/m^2, median survival is reduced by 2–4 years and at 40–45 kg/m^2 by 8–10 years [13]. The main causes of death include ischemic heart disease [14], stroke [15], and diabetes-related complications [13]. The vicious cycle resulting in increased mortality in obesity involves insulin resistance, as well as all the components of metabolic syndrome (i.e., hyperglycemia, dyslipidemia, and hypertension).

Metabolic Syndrome

Although several different clinical definitions for metabolic syndrome have been proposed, the International Diabetes Federation; the National Heart, Lung, and Blood Institute; and the American Heart Association have recently proposed [16] that the metabolic syndrome is diagnosed when any three of the following five risk factors are present:

- Fasting plasma glucose ≥100 mg/dL or undergoing drug treatment for elevated glucose.
- HDL-C <40 mg/dL in males or <50 mg/dL in females or undergoing drug treatment for reduced HDL-C.
- Triglycerides ≥150 mg/dL or undergoing drug treatment for elevated triglycerides.
- Waist circumference >102 cm in males or >88 cm in females for people of most ancestries living in the United States. Ethnicity and country-specific thresholds can be used for diagnosis in other groups, particularly Asians and individuals of non-European ancestry who have predominantly resided outside the United States.
- Blood pressure ≥130 mm Hg systolic or ≥85 mm Hg diastolic or undergoing drug treatment for hypertension or antihypertensive drug treatment in a patient with a history of hypertension.

The risk of metabolic syndrome probably begins before birth [17]. The Prediction of Metabolic Syndrome in Adolescence Study showed that the coexistence of low birth weight, small head circumference, and parental history of overweight or obesity places children at the highest risk for metabolic syndrome in adolescence [18]. According to the National Cholesterol Education Program (NCEP) criteria, the prevalence of metabolic syndrome in bariatric surgical patients is 80% [19], and there is evidence that surgical patients with metabolic syndrome are likely to develop hyperglycemia which increases the risk for postoperative complications including surgical site infection [20–22].

Based on the data presented above, patient optimization before surgery is vital to ensure favorable outcomes after surgery. The importance of perioperative management of obese patients cannot be overemphasized.

Type 2 Diabetes Mellitus (T2DM)

Although T2DM is a heterogeneous disease with causes that are yet not fully explained, obesity is considered the primary risk factor [23]. It has been estimated that the risk of developing T2DM is increased 93-fold in women and 42-fold in men who are severely obese when compared to healthy-weight individuals [24, 25]. Currently, only a small proportion of patients with T2DM are not overweight [26].

In the United States, only 52% of patients with T2DM maintain hemoglobin A1c (HbA1c) <7% [27]. Implementing more effective strategies to prevent and treat diabetes has become a top priority in twenty-first-century medicine. Preoperative glycemic control should be optimized using a diabetes comprehensive care plan, including healthy dietary patterns, medical nutrition therapy, physical activity, and as-needed pharmaco-

therapy. Reasonable targets for preoperative glycemic control, which may be associated with improved bariatric surgery outcomes, include a HbA1c value of 6.5–7.0% or less, a fasting blood glucose level of <110 mg/dL, and a 2-hour postprandial blood glucose concentration of <140 mg/dL [28].

There is substantial evidence demonstrating that metabolic surgery achieves superior glycemic control and reduction of cardiovascular risk factors in obese patients with type 2 diabetes compared with various lifestyle/medical interventions [29, 30]. Schauer et al. [31] conducted the STAMPEDE (Surgical Therapy and Medications Potentially Eradicate Diabetes Efficiently) trial , a randomized controlled trial involving 150 patients comparing medical therapy (MT) versus Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) for the treatment of T2DM. The primary outcome was HbA1 <6% with or without the use of medications. At 5 years follow-up, results were available in 139 patients. The primary end point was met by 5% of patients who received MT, compared with 29% of patients who underwent RYGB and 23% of those who underwent SG (P value, RYGB versus MT = 0.01; SG versus MT = 0.03; and RYGB versus SG = 0.53). They concluded that bariatric surgery was clearly superior to MT in terms of glycemic control.

Recently, the American Diabetes Association proposed that "metabolic surgery" (involving procedures initially developed to treat obesity) should be considered as a standard diabetes treatment option for appropriate candidates with inadequately controlled type 2 diabetes and a BMI >30 kg/m^2 or >27.5 kg/m^2 for Asian individuals [32].

Comparison Between RYGB and SG

Some other studies compared T2DM remission rates between SG and RYGB. Pournaras et al. [33] analyzed a cohort of 1006 patients, of whom 209 (20.7%) had T2DM, with a mean follow-up of 23 months. Remission was defined as a return to HbA1c <6%, fasting glucose <5.6 mmol/L at least 1 year after bariatric surgery without the use of hypoglycemic medications. These authors found that remission rates were 26% after SG and 40.6% after RYGB. On the other hand, a recent systematic review, including seven randomized controlled trials with 732 patients, showed that measures of glycemic control (HbA1c and fasting blood glucose levels) improved with both procedures, with similar improvement after laparoscopic RYGB and laparoscopic SG at 12 months postoperatively [34]. In the STAMPEDE trial [31], although no statistically significant difference between the two surgical groups was found for the primary end point, other end points such as the number of antidiabetic medications showed superiority of the RYGB over the SG.

These results have been recently substantiated by two randomized and multicenter trials performed in Finland and in Switzerland, with large number of patients and 5-year follow-up. Both studies confirmed similar results between the RYGB and the SG in terms of metabolic control, which was improved by both procedures [35, 36].

Overall, both RYGB and SG seem to be equally effective in improving or resolving T2DM; however, long-term data are still lacking.

Hypertension

Hypertension is one of the most common comorbidities associated with obesity and a major risk factor for stroke and coronary artery disease. It is estimated that hypertension is present in up to 40–70% of obese patients. Despite the well-known correlation between obesity and hypertension, the underlying mechanisms are not fully understood. Insulin resistance and hyperinsulinemia are frequent in obese patients, and both play a role in elevating the blood pressure. There is evidence showing that hyperinsulinemia stimulates the sympathetic nervous system (SNS) [37]. This is further supported by studies showing a decrease in blood pressure and SNS activity when insulin levels are lowered by low-energy diets. Renin–angiotensin–aldosterone system is

also activated and stimulated in obese patients [38]. This stimulation is a result of an increase in angiotensin production by adipocytes, SNS overstimulation by hyperinsulinemia, and high levels of aldosterone production by free fatty acids [39]. Another potential mechanism implicated in the pathophysiology of obesity-related hypertension is a decrease in natriuretic peptides [40].

Schiavon et al. [41] hypothesized that hypertension improvement after bariatric surgery could be attributable to hemodynamic changes and decreased intra-abdominal pressure associated with weight loss. The reduction of the hyperinsulinemia decreases the renal sodium reabsorption and sympathetic tone. In addition, the reduction in perivascular adipocyte inflammation may help in reducing blood pressure by decreasing arterial stiffness. Interestingly, Ahmed et al. [42] found reduction in systolic (9 mmHg) and diastolic (7 mmHg) blood pressure as early as week 1 after RYGB. This early drop in blood pressure before any significant weight loss suggests a possible weight-independent hormonal mechanism behind this effect of bariatric surgery.

Dyslipidemia

Dyslipidemia can be present in more than 50% of bariatric patients [36]. Dyslipidemia creates a pro-inflammatory state with an increased production of reactive oxygen species, tumor necrosis factor alpha, interleukin-6, and C-reactive protein. This process contributes to atherosclerosis by direct endothelial damage or indirectly by promoting other diseases such as T2DM or hypertension [43].

Bariatric surgery has shown to lower total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, and increase high-density lipoprotein (HDL) cholesterol, allowing a significant number of patients to discontinue statins and other lipid-lowering medications.

Nguyen et al. [44] showed that 1 year after RYGB, mean total cholesterol levels decreased by 16%, triglyceride levels decreased by 63%, LDL cholesterol levels decreased by 31%, and HDL cholesterol levels increased by 39%. In addition, within 1 year, 82% of patients requiring lipid-lowering medications preoperatively were able to discontinue their medications.

These results have been recently confirmed by the two European trials previously discussed [35, 36]. The SLEEVEPASS study showed that after 5 years, medications for dyslipidemia were discontinued in 47% of patients (n = 14/30) after SG and in 60% of patients (n = 24/40) after RYGB (P = 0.15). Of the 38 patients in the whole study group who discontinued dyslipidemia medication, 22 had true dyslipidemia remission (LDL-C level <115.8 mg/dL [3.0 mmol/L] and no dyslipidemia medications); the remission rate was 20% (6/30) in the SG group and 40% (n = 16/40) in the RYGB group [35]. Similarly, the SM-BOSS study (36) showed that a complete remission was seen in 29 (42.6%) of 68 in the SG group versus 33 (62.3%) of 53 in the RYGB group, 5 years after surgery (absolute difference, −0.19%; 95% CI, −0.38% to −0.003%) [36].

Despite both SG and RYGB having metabolic effects in obese patients, the lipid-lowering effect seems to be more pronounced after RYGB. In fact, recent studies have shown that dyslipidemia resolved significantly more often after RYGB compared with SG [45]. This can be attributed to the endocrine changes that occur after RYGB such as an increase in adrenocorticotrophic hormone, GLP, and peptide YY and a decrease in insulin, insulin-like growth factor-1, leptin, and ghrelin [43].

Obstructive Sleep Apnea (OSA)

Obesity is a well-known risk factor for this disorder that has implications beyond disrupted sleep [46]. OSA is characterized by repetitive partial or complete airway collapse causing hypoxemia and/or hypercarbia. It is defined by overnight polysomnography as cessation of airflow of greater than 10 seconds with continued ventilatory effort, five or more times per hour of sleep, with a decrease in arterial oxygen saturation [47]. Signs and symptoms of OSA may include a family report of disruptive snoring, daytime sleepiness, obesity, large neck circumference,

systemic and pulmonary hypertension, cardiac arrhythmias, myocardial ischemia, ventricular hypertrophy, and failure [48, 49]. In addition to BMI, age, male sex, and smoking are well-known risk factors for OSA [50–53].

The prevalence of OSA can be as high as 78% in morbidly obese patients who present for bariatric surgery [54]. Up to 80% of individuals with less severe forms of OSA are undiagnosed [51], while severe OSA is undiagnosed in approximately 10–20% of patients with BMI >35 [55]. Undiagnosed OSA may lead to perioperative complications including difficult mask ventilation and/or intubation, postoperative reintubation, cardiac dysrhythmias, and increased hospital length of stay [20]. The Sleep Heart Health Study found a strong correlation between weight change and progression/regression of OSA (stronger relationship for men than women) [56]. Bariatric surgery is a reasonable option for weight reduction for patients with clinically severe obesity [57, 58].

Obesity is a complex interaction between multiple genetic, socioeconomic, and cultural factors that also are associated with existing or resulting comorbidities and their treatment. The prevalence of obesity continues to be high, as are associated comorbidities and healthcare costs. Early intervention and effective treatment of obesity are needed to reduce costs and improve outcomes for these patients. Metabolic surgery has proven to offer health benefits that extend beyond weight loss, and most patients suffering from these disorders will obtain significant improvements after surgery.

Preoperative Evaluation

Preoperative care of the bariatric patient remains a challenging proposition because of the metabolic, pharmacologic, and system-wide disorders that are the foundational basis for the complications that can ensue. Hence, patients should undergo a routine preoperative assessment with a comprehensive multidisciplinary group. The core team providing such workup should optimally consist of obesity-experienced specialists.

Best preoperative care will yield a comprehensive understanding of a patient's medical status as it pertains to predicted outcomes and psychological ability to comply with required postoperative recommendations for health maintenance and to achieve success following weight loss surgery.

Patient Selection

Perhaps the most important step of the preoperative process is patient selection. Many patients approach bariatric surgeons to help them with their weight without an appreciation of the need for preoperative physical and psychological evaluation, knowledge of surgical options, potential perioperative complications, the need for lifelong follow-up after bariatric surgery, and with unrealistic weight loss expectations. During an initial evaluation, a surgeon should consider if a patient has any hard contraindications for surgery based on history or physical exam. If a patient is acceptable at that point, that only means they are acceptable to continue the workup for bariatric surgery. A multidisciplinary preoperative assessment by a team of endocrinologists, dieticians, psychologists, and the surgeon, to evaluate and educate the patient, helps in appropriate patient selection and ensure that the patient is physically and psychologically fit to undergo weight loss surgery (WLS).

Patient Education

The lack of patient education leads to patient's frustration with the process of preparation for bariatric surgery and the preoperative requirements proposed by the multidisciplinary team. In addition, patients may have unrealistic expectations regarding the potential perioperative complications and weight loss after surgery. Many patients seeking bariatric surgery hold unrealistic expectations, without a complete understanding of the procedures and the subsequent long-term implications [59–61].

Patient's understanding of long-term consequences of bariatric surgery, such as postoperative lifestyle modifications, need for long-term follow-up, and consistent implementation of recommended postoperative regimens, facilitates a more informed decision-making, leading to better outcomes.

Medical Evaluation

A comprehensive medical evaluation entails a meticulous history, a thorough physical examination, and a review of the cardiovascular, pulmonary, and gastrointestinal systems, as well as a metabolic and nutritional status assessment.

Cardiac Evaluation

One of the essential elements of promoting safety in any surgical patient, but especially morbidly obese patients, is adequate evaluation of their cardiac status and cardiac risk preoperatively. Obesity is a well-established risk factor for cardiovascular comorbidities including coronary heart disease (CHD), arrhythmias, left ventricular hypertrophy, and heart failure [62].

Calle et al. [63] ran a prospective study of over a million people followed for 14 years, where they showed that obesity was strongly associated with an increased risk of cardiovascular mortality. This study directly correlated CHD mortality risk with increasing BMI, reporting a twofold to threefold greater risk in individuals who had a BMI of 35 kg/m^2 or higher compared with leaner persons (BMI 18.5–24.9 kg/m^2).

Bariatric patients need a focused cardiac history, which should include history of coronary artery disease (CAD), coronary symptoms, and coronary risk factors (hypertension, diabetes, hyperlipidemia, smoking, stress, sedentary lifestyle, etc.). Cardiac evaluation includes a 12-lead electrocardiogram, followed by assessment of cardiac function with stress testing. The traditional stress testing methods (e.g., treadmill exercise, scintigraphic imaging) may not be feasible in morbidly obese patients given the weight limitations of the testing equipment and the difficulty to accurately interpret the images owing to the patient's body habitus [64, 65]. Pharmacological stress echocardiography, with or without ultrasound contrast agents, is an effective alternative for this patient population that can provide an accurate assessment of cardiac function [66, 67].

Airway and Pulmonary Evaluation

Given that obesity is a risk factor for airway disease secondary to mechanical restriction, routine preoperative pulmonary function tests help assess the pulmonary reserve and identify those at risk for postoperative pulmonary complications [68]. OSA is common among morbidly obese patients, especially males, as discussed above. Recently, a meta-analysis including more than 1000 patients showed that the impact of gaining weight on pulmonary function was greater in men than in women, as each kilogram gained results in a 26 mL FVC (forced vital capacity) and 23 mL FEV_1 (forced expiratory volume in the first second) decrease in men versus 14- and 9-mL decrease, respectively, in women [69]. Knowing that these patients are at a higher risk for morbidity and mortality, it is important to screen all patients for OSA before embarking on bariatric surgery. The most appropriate test to evaluate OSA is nocturnal polysomnography (PSG). Albeit most patients diagnosed with OSA benefit from continuous positive airway pressure (CPAP) or bilevel positive pressure preoperatively [70, 71], it is recommended a period of preoperative adjustment prior to surgery, as many patients have trouble tolerating the face mask.

Venous Thromboembolism (VTE) Evaluation

VTE, including pulmonary embolism (PE) and deep vein thrombosis (DVT), remains a significant cause of mortality and morbidity after bariatric surgery (72). Common factors thought to predispose patients to higher risk of VTE are previous history of VTE, male gender, operative time more than 3 hours, higher BMI, and advanced age [72]. The most common methods

of prophylaxis range from mechanical compression devices with early ambulation alone to the addition of chemoprophylaxis and the use of inferior vena cava filters [73].

A comprehensive assessment and stratification of the risk of adverse events can inform clinical decision-making and help in identifying ideal candidates for bariatric surgery and those that may require closer postsurgical monitoring.

Psychological Support

Bariatric patients have a higher prevalence of psychological disorders than the general population [74], and these psychological factors have been associated with worst surgical outcomes and recurrence of behavioral problems [75]. Hence, the American Association of Clinical Endocrinologists (AACE) and the American Society for Metabolic and Bariatric Surgery (ASMBS) recommend that assessment of bariatric surgery candidates should include presurgical psychological evaluations [28, 76]. The preoperative psychological evaluation also helps establish a trusting working relationship between the behavioral clinician and the patient [77]. The psychological evaluation includes a thorough clinical interview for assessment of

- Weight history
- History of eating behaviors/disorders (including binge eating, anorexia nervosa, night eating syndrome, and compensatory behaviors)
- Current or lifetime history of mood and anxiety disorders
- Cognitive functioning
- Current and past mental health treatment
- Patient knowledge and motivation for weight loss

Nutritional Care and Preoperative Weight Loss

The management of postoperative nutrition begins preoperatively with a thorough assessment of the nutritional status and a strong educational program [78]. Thus, the dietitian's role is a vital component of the bariatric surgery process and should be in charge of the nutritional assessment, preoperative weight loss efforts, and diet education regarding postoperative eating behaviors [79]. In addition, the benefits of weight loss surgery must be balanced against the risk of developing nutritional deficiencies to provide appropriate identification, treatment, and prevention.

Moreover, the ability for a patient to show that he/she can achieve some degree of weight loss before the operation, is generally considered a predictor of a patient's postoperative compliance [80]. Therefore preoperative weight loss should not be considered in isolation when clearance for bariatric surgery is being considered [81]. Conversely, Alami et al. conducted a randomized trial comparing a group of patients with a preoperative 10% weight loss requirement and a group that had no weight loss requirements. The percentage of excess weight loss at 6 months for the weight loss group and non-weight loss group was 53.9% and 50.9% (P = NS) [82].

However, preoperative weight loss should be strongly encouraged as it can facilitate the operation by reducing the abdominal fat and the liver volume (reduction in steatosis), which improves the access to the upper abdomen during laparoscopic surgery and shortens the operative time [83, 84].

Preoperative Gastrointestinal Imaging

Upper GI Contrast Study

When planning to perform surgery on the upper gastrointestinal (GI) tract, it is reasonable to evaluate preexisting anatomical variations. An upper GI contrast swallow offers valuable information regarding the esophageal and gastric anatomy, esophageal clearance, and presence and size of a hiatal hernia. However, the diagnostic yield of these studies is low, and results rarely influence the planned surgical approach. Consequently, there is an emerging consensus that upper GI contrast swallow studies are not a necessary component of the preoperative evaluation for bariatric surgery [85].

Ultrasound

Ultrasonography of the abdomen is usually done to detect presence of gallstones. Given the particularly high incidence of cholelithiasis in obese patients [86], abdominal sonography seems to be advisable as part of the routine preoperative workup. Interestingly, as a result of their habitus, there is a low sensitivity of abdominal ultrasound in morbidly obese individuals [87].

In addition, rapid weight loss induced by bariatric surgery further increases the risk of gallstones formation [87], particularly important for patients undergoing Roux-en-Y gastric bypass because this procedure precludes the endoscopic exploration of the biliary tract in case of choledocholithiasis.

Esophagogastroduodenoscopy (EGD)

Some centers perform EGD routinely in all patients; others perform EGD selectively. These are some of the guidelines currently followed:

- American Society of Metabolic and Bariatric Surgery (ASMBS) recommends to perform EGD in every symptomatic patient and to consider it in asymptomatic ones. (Grade D – low level of evidence.) [28]
- American Society for Gastrointestinal Endoscopy (ASGE) in conjunction with the Society of Gastrointestinal and Endoscopic Surgeons (SAGES) and the American Society for Metabolic and Bariatric Surgery (ASMBS), updating the prior guideline entitled "The Role of Endoscopy in the Bariatric Surgery Patient" [88], recommend that the bariatric surgeon should decide to perform a preoperative EGD after a thorough examination of the patient, taking in consideration the type of bariatric procedure that will be performed. (Low quality of evidence.) [89]
- European Association for Endoscopic Surgery (EAES) recommends EGD in all bariatric patients regardless of symptoms (Grade C – low quality evidence), particularly for patients undergoing RYGB (Grade B – medium-quality evidence) [90].

Current available data regarding the actual impact of preoperative EGD remains scarce. However, we believe that patients should systematically undergo an EGD for several reasons [91, 92].

- Obesity represents a risk factor for several GI diseases that can be detected by EGD.
- The symptomatic evaluation has limited value for the diagnosis of GERD, as symptoms such as heartburn have low sensitivity and specificity.
- Given the high risk of postoperative GERD associated with a SG, the presence of esophagitis or Barrett's esophagus should be considered a contraindication for this procedure.
- The EGD should rule out malignancy of the stomach before gastric bypass, as the remnant stomach will no longer be accessible to endoscopic surveillance.

Conclusions

Obesity is associated with severe health comorbidities and metabolic disorders such as diabetes, hypertension, and dyslipidemia among others. Metabolic surgery has proven to offer health benefits that extend beyond weight loss, and most patients suffering from these disorders will obtain significant improvements after surgery. Before undergoing any bariatric procedure, every obese patient should undergo an adequate preoperative workup by a multidisciplinary bariatric experienced group, including medical evaluation, psychological support, nutritional care, and adequate GI imaging. A comprehensive discussion of patient expectations of postsurgical weight loss, including the potential for weight regain, is strongly recommended.

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Standards Committee, American Society for Bariatric Surgery. Guidelines for reporting results in bariatric surgery. Obes Surg. 1997;7(6):521–2.

2. National Institutes of Health (NIH). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults – the evidence report. Obes Res. 1998;6(2):51S–179S.
3. Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet (London, England). 2011;378(9793):804–14.
4. Fried M, Yumuk V, Oppert JM, Scopinaro N, Torres A, Weiner R, et al. Interdisciplinary European Guidelines on metabolic and bariatric surgery. Gastroenterol Hepatol. 2017;71(6):487–500.
5. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766–81.
6. WHO, Europe RO for. The European health report 2018. More than numbers – evidence for all. Highlights. 2018;164. Available from: http://www.euro.who.int/__data/assets/pdf_file/0003/380478/HEALTH_REPORT_HIGHLIGHTS_2018_EN.PDF?ua=1.
7. Flegal KM, Kit BK, Orpana H, Graubard BI. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. JAMA. 2013;309(1):71–82.
8. Willett WC, Hu FB, Thun M. Overweight, obesity, and all-cause mortality. JAMA. 2013;309(16):1681.
9. Sjöström L. Surgical intervention as a strategy for treatment of obesity. Endocrine. 2000;13(2):213–30.
10. Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial – a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273(3):219–34.
11. Hjorth S, Näslund I, Andersson-Assarsson JC, Svensson P-A, Jacobson P, Peltonen M, et al. Reoperations after bariatric surgery in 26 years of follow-up of the Swedish Obese Subjects Study. JAMA Surg. 2019;154(4):319–26.
12. Schlottmann F, Galvarini MM, Dreifuss NH, Laxague F, Buxhoeveden R, Gorodner V. Metabolic effects of bariatric surgery. J Laparoendosc Adv Surg Tech A. 2018;28(8):944–8.
13. Prospective Studies Collaboration, Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, et al. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet (London, England). 2009;373(9669):1083–96.
14. Canoy D, Boekholdt SM, Wareham N, Luben R, Welch A, Bingham S, et al. Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk cohort: a population-based prospective study. Circulation. 2007;116(25):2933–43.
15. Song Y-M, Sung J, Davey Smith G, Ebrahim S. Body mass index and ischemic and hemorrhagic stroke: a prospective study in Korean men. Stroke. 2004;35(4):831–6.
16. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640–5.
17. Benjamin EJ, Blaha MJ, Chiuve SE, Cushman M, Das S, Rajat D, et al. Heart disease and stroke statistics—2017 update. Circulation. 2017;135:146–603.
18. Efstathiou SP, Skeva II, Zorbala E, Georgiou E, Mountokalakis TD. Metabolic syndrome in adolescence: can it be predicted from natal and parental profile? The prediction of metabolic syndrome in adolescence (PREMA) study. Circulation. 2012;125(7):902–10.
19. Purnell JQ, Selzer F, Smith MD, Berk PD, Courcoulas AP, Inabnet WB, et al. Metabolic syndrome prevalence and associations in a bariatric surgery cohort from the Longitudinal Assessment of Bariatric Surgery-2 study. Metab Syndr Relat Disord. 2014;12(2):86–94.
20. Lang LH, Parekh K, Tsui BYK, Maze M. Perioperative management of the obese surgical patient. Br Med Bull. 2017;124(1):135–55.
21. Zavlin D, Jubbal KT, Balinger CL, Dinh TA, Friedman JD, Echo A. Impact of metabolic syndrome on the morbidity and mortality of patients undergoing panniculectomy. Aesthetic Plast Surg. 2017;41(6):1400–7.
22. Kao LS, Meeks D, Moyer VA, Lally KP. Perioperative glycaemic control regimens for preventing surgical site infections in adults. Cochrane Database Syst Rev. 2009;(3):CD006806.
23. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetologia. 2009;52(1):17–30.
24. Colditz GA, Willett WC, Rotnitzky A, Manson JE. Weight gain as a risk factor for clinical diabetes mellitus in women. Ann Intern Med. 1995;122(7):481–6.
25. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care. 1994;17(9):961–9.
26. Gregg EW, Cheng YJ, Narayan KMV, Thompson TJ, Williamson DF. The relative contributions of different levels of overweight and obesity to the increased prevalence of diabetes in the United States: 1976–2004. Prev Med (Baltim). 2007;45(5):348–52.

27. Ali MK, Bullard KM, Gregg EW. Achievement of goals in U.S. Diabetes Care, 1999–2010. N Engl J Med. 2013;369(3):287–8.
28. Mechanick JI, Youdim A, Jones DB, Timothy Garvey W, Hurley DL, Molly McMahon M, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient – 2013 update: cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and American Society. Surg Obes Relat Dis. 2013;9(2):159–91.
29. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KGMM, Zimmet PZ, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Obes Surg. 2017;27(1):2–21.
30. Sjöström L, Lindroos A-K, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(1):2683–93.
31. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, et al. Bariatric surgery versus intensive medical therapy for diabetes — 5-year outcomes. N Engl J Med. 2017;376(7):641–51.
32. American Diabetes Association. Obesity management for the treatment of type 2 diabetes. Diabetes Care. 2017;40(January):S57–63.
33. Pournaras DJ, Aasheim ET, Søvik TT, Andrews R, Mahon D, Welbourn R, et al. Effect of the definition of type II diabetes remission in the evaluation of bariatric surgery for metabolic disorders. Br J Surg. 2012;99(1):100–3.
34. Osland E, Yunus RM, Khan S, Memon B, Memon MA. Diabetes improvement and resolution following laparoscopic vertical sleeve gastrectomy (LVSG) versus laparoscopic Roux-en-Y gastric bypass (LRYGB) procedures: a systematic review of randomized controlled trials. Surg Endosc. 2017;31(4):1952–63.
35. Salminen P, Helmiö M, Ovaska J, Juuti A, Leivonen M, Peromaa-Haavisto P, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. JAMA. 2018;319(3):241–54.
36. Peterli R, Wölnerhanssen BK, Peters T, Vetter D, Kröll D, Borbély Y, et al. Effect of laparoscopic sleeve gastrectomy vs laparoscopic Roux-en-Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS randomized clinical trial. JAMA. 2018;319(3):255–65.
37. Landsberg L, Aronne LJ, Beilin LJ, Burke V, Igel LI, Lloyd-Jones D, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment. J Clin Hypertens. 2013;15(1):14–33.
38. Engeli S, Böhnke J, Gorzelniak K, Janke J, Schling P, Bader M, et al. Weight loss and the renin-angiotensin-aldosterone system. Hypertens (Dallas, Tex 1979). 2005;45(3):356–62.
39. Schiavon CA, Drager LF, Bortolotto LA, Amodeo C, Ikeoka D, Berwanger O, et al. The role of metabolic surgery on blood pressure control. Curr Atheroscler Rep. 2016;18(8):50.
40. Sarzani R, Salvi F, Dessì-Fulgheri P, Rappelli A. Renin-angiotensin system, natriuretic peptides, obesity, metabolic syndrome, and hypertension: an integrated view in humans. J Hypertens. 2008;26(5):831–43.
41. Schiavon CA, Ikeoka DT, de Sousa MG, Silva CRA, Bersch-Ferreira AC, de Oliveira JD, et al. Effects of gastric bypass surgery in patients with hypertension: rationale and design for a randomised controlled trial (GATEWAY study). BMJ Open. 2014;4(9):e005702.
42. Ahmed AR, Rickards G, Coniglio D, Xia Y, Johnson J, Boss T, et al. Laparoscopic Roux-en-Y gastric bypass and its early effect on blood pressure. Obes Surg. 2009;19(7):845–9.
43. Bays HE, Toth PP, Kris-Etherton PM, Abate N, Aronne LJ, Brown WV, et al. Obesity, adiposity, and dyslipidemia: a consensus statement from the National Lipid Association. J Clin Lipidol. 2013;7(4):304–83.
44. Nguyen NT, Varela E, Sabio A, Tran C-L, Stamos M, Wilson SE. Resolution of hyperlipidemia after laparoscopic Roux-en-Y gastric bypass. J Am Coll Surg. 2006;203(1):24–9.
45. Peterli R, Wölnerhanssen BK, Vetter D, Nett P, Gass M, Borbély Y, et al. Laparoscopic sleeve gastrectomy versus Roux-Y-gastric bypass for morbid obesity – 3-year outcomes of the prospective randomized Swiss Multicenter Bypass Or Sleeve Study (SM-BOSS). Ann Surg. 2017;265(3):466–73.
46. Leppänen T, Kulkas A, Mervaala E, Töyräs J. Increase in body mass index decreases duration of apneas and hypopneas in obstructive sleep apnea. Respir Care. 2019;64(1):77–84.
47. Park JG, Ramar K, Olson EJ. Updates on definition, consequences, and management of obstructive sleep apnea concise review for clinicians. Mayo Clin Proc. 2011;86(6):549–55.
48. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med. 2009;5(3):263–76.
49. Korcarz CE, Peppard PE, Young TB, Chapman CB, Hla KM, Barnet JH, et al. Effects of obstructive sleep apnea and obesity on cardiac remodeling: the wisconsin sleep cohort study. Sleep. 2016;39(6):1187–95.
50. Ware JC, McBrayer RH, Scott JA. Influence of sex and age on duration and frequency of sleep apnea events. Sleep. 2000;23(2):165–70.
51. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328(17):1230–5.
52. Wetter DW, Young TB, Bidwell TR, Badr MS, Palta M. Smoking as a risk factor for sleep-disordered breathing. Arch Intern Med. 1994;154(19):2219–24.
53. Cowie MR. Sleep apnea: state of the art. Trends Cardiovasc Med. 2017;27(4):280–9.
54. Lopez PP, Stefan B, Schulman CI, Byers PM. Prevalence of sleep apnea in morbidly obese

patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. Am Surg. 2008;74(9):834–8.
55. Gottlieb DJ, Somers VK, Punjabi NM, Winkelman JW. Restless legs syndrome and cardiovascular disease: a research roadmap. Sleep Med. 2017;31:10–7.
56. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. Arch Intern Med. 2005;165(20):2408–13.
57. Gastrointestinal surgery for severe obesity: National Institutes of Health Consensus Development Conference Statement. Am J Clin Nutr. 1992;55(2):615S–9S.
58. Rasheid S, Banasiak M, Gallagher SF, Lipska A, Kaba S, Ventimiglia D, et al. Gastric bypass is an effective treatment for obstructive sleep apnea in patients with clinically significant obesity. Obes Surg. 2003;13(1):58–61.
59. Bauchowitz A, Azarbad L, Day K, Gonder-Frederick L. Evaluation of expectations and knowledge in bariatric surgery patients. Surg Obes Relat Dis. 2007;3(5):554–8.
60. Giusti V, De Lucia A, Di Vetta V, Calmes JM, Héraïef E, Gaillard RC, et al. Impact of preoperative teaching on surgical option of patients qualifying for bariatric surgery. Obes Surg. 2004;14(9):1241–6.
61. Wee CC, Hamel MB, Apovian CM, Blackburn GL, Bolcic-Jankovic D, Colten ME, et al. Expectations for weight loss and willingness to accept risk among patients seeking weight loss surgery. JAMA Surg. 2013;148(3):264–71.
62. Zalesin KC, Franklin BA, Miller WM, Peterson ED, McCullough PA. Impact of obesity on cardiovascular disease. Med Clin North Am. 2011;95(5):919–37.
63. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med. 1999;341(15):1097–105.
64. Hammond KL. Practical issues in the surgical care of the obese patient. Ochsner J. 2013;13(2):224–7.
65. Uppot RN, Sahani DV, Hahn PF, Kalra MK, Saini SS, Mueller PR. Effect of obesity on image quality: fifteen-year longitudinal study for evaluation of dictated radiology reports. Radiology. 2006;240(2):435–9.
66. Shah BN, Senior R. Stress echocardiography in patients with morbid obesity. Echo Res Pract. 2016;3(2):R13–8.
67. Supariwala A, Makani H, Kahan J, Pierce M, Bajwa F, Dukkipati SS, et al. Feasibility and prognostic value of stress echocardiography in obese, morbidly obese, and super obese patients referred for bariatric surgery. Echocardiography. 2014;31(7):879–85.
68. Van Huisstede A, Biter LU, Luitwieler R, Castro Cabezas M, Mannaerts G, Birnie E, et al. Pulmonary function testing and complications of laparoscopic bariatric surgery. Obes Surg. 2013;23(10):1596–603.
69. Alsumali A, Al-Hawag A, Bairdain S, Eguale T. The impact of bariatric surgery on pulmonary function: a meta-analysis. Surg Obes Relat Dis. 2018;14(2):225–36.
70. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597–619.
71. Ramirez A, Lalor PF, Szomstein S, Rosenthal RJ. Continuous positive airway pressure in immediate postoperative period after laparoscopic Roux-en-Y gastric bypass: is it safe? Surg Obes Relat Dis. 2009;5(5):544–6.
72. Finks JF, English WJ, Carlin AM, Krause KR, Share DA, Banerjee M, et al. Predicting risk for venous thromboembolism with bariatric surgery: results from the Michigan bariatric surgery collaborative. Ann Surg. 2012;255(6):1100–4.
73. American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. ASMBS updated position statement on prophylactic measures to reduce the risk of venous thromboembolism in bariatric surgery patients. Surg Obes Relat Dis. 2013;9(4):493–7.
74. Mitchell JE, Selzer F, Kalarchian MA, Devlin MJ, Strain GW, Elder KA, et al. Psychopathology before surgery in the longitudinal assessment of bariatric surgery-3 (LABS-3) psychosocial study. Surg Obes Relat Dis. 2012;8(5):533–41.
75. Livhits M, Mercado C, Yermilov I, Parikh JA, Dutson E, Mehran A, et al. Preoperative predictors of weight loss following bariatric surgery: systematic review. Obes Surg. 2012;22(1):70–89.
76. Marek RJ, Heinberg LJ, Lavery M, Merrell Rish J, Ashton K. A review of psychological assessment instruments for use in bariatric surgery evaluations. Psychol Assess. 2016;28(9):1142–57.
77. Sogg S, Lauretti J, West-Smith L. Recommendations for the presurgical psychosocial evaluation of bariatric surgery patients. Surg Obes Relat Dis. 2016;12(4):731–49.
78. Allied Health Sciences Section Ad Hoc Nutrition Committee, Aills L, Blankenship J, Buffington C, Furtado M, Parrott J. ASMBS allied health nutritional guidelines for the surgical weight loss patient. Surg Obes Relat Dis. 2008;4(5 Suppl):S73–108.
79. SAGES Guidelines Committee. SAGES guideline for clinical application of laparoscopic bariatric surgery. Surg Obes Relat Dis. 2009;5(3):387–405.
80. Stefura T, Droś J, Kacprzyk A, Wierdak M, Proczko-Stepaniak M, Szymański M, et al. Influence of preoperative weight loss on outcomes of bariatric surgery for patients under the enhanced recovery after surgery protocol. Obes Surg. 2019;29:1134–41.
81. Krimpuri RD, Yokley JM, Seeholzer EL, Horwath EL, Thomas CL, Bardaro SJ. Qualifying for bariatric surgery: is preoperative weight loss a reliable predic-

tor of postoperative weight loss? Surg Obes Relat Dis. 2018;14(1):60–4.
82. Alami RS, Morton JM, Schuster R, Lie J, Sanchez BR, Peters A, et al. Is there a benefit to preoperative weight loss in gastric bypass patients? A prospective randomized trial. Surg Obes Relat Dis. 2007;3(2):141–5.
83. Holderbaum M, Casagrande DS, Sussenbach S, Buss C. Effects of very low calorie diets on liver size and weight loss in the preoperative period of bariatric surgery: a systematic review. Surg Obes Relat Dis. 2018;14(2):237–44.
84. Alvarado R, Alami RS, Hsu G, Safadi BY, Sanchez BR, Morton JM, et al. The impact of preoperative weight loss in patients undergoing laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2005;15(9):1282–6.
85. Eldar S, Heneghan HM, Brethauer S, Schauer PR. A focus on surgical preoperative evaluation of the bariatric patient – The Cleveland Clinic protocol and review of the literature. Surgeon. 2011;9(5):273–7.
86. Khatua B, El-Kurdi B, Singh VP. Obesity and pancreatitis. Curr Opin Gastroenterol. 2017;33(5):374–82.
87. Quesada BM, Kohan G, Roff HE, Canullán CM, Chiappetta Porras LT. Management of gallstones and gallbladder disease in patients undergoing gastric bypass. World J Gastroenterol. 2010;16(17):2075–9.
88. Anderson MA, Gan SI, Fanelli RD, Baron TH, Banerjee S, Cash BD, et al. Role of endoscopy in the bariatric surgery patient – ASGE Standards of Practice Committee. Gastrointest Endosc. 2008;68(1):1–10.
89. Evans JA, Muthusamy VR, Acosta RD, Bruining DH, Chandrasekhara V, Chathadi KV, et al. The role of endoscopy in the bariatric surgery patient. Gastrointest Endosc. 2015;81(5):1063–72.
90. Sauerland S, Angrisani L, Belachew M, Chevallier JM, Favretti F, Finer N, et al. Obesity surgery: evidence-based guidelines of the European Association for Endoscopic Surgery (E.A.E.S.). Surg Endosc Other Interv Tech. 2005;19(2):200–21.
91. Schlottmann F, Nayyar A, Herbella FAM, Patti MG. Preoperative evaluation in bariatric surgery. J Laparoendosc Adv Surg Tech A. 2018;28(8):lap.2018.0391.
92. Muñoz R, Ibáñez L, Salinas J, Escalona A, Pérez G, Pimentel F, et al. Importance of routine preoperative upper GI endoscopy: why all patients should be evaluated? Obes Surg. 2009;19(4):427–31.

Laparoscopic Roux-en-Y Gastric Bypass

26

Francisco Laxague, Francisco Schlottmann, and Rudolf Buxhoeveden

Surgical Technique

Position of the Patient

After induction of general endotracheal anesthesia, the patient is positioned supine in low lithotomy position with the lower extremities extended on stirrups with pneumatic compression stockings and knees flexed 20–30°. Both arms are left abducted and secured on a board with adequate padding. The surgeon stands on the patient's right side and the first and second assistants on the patient's left side and between the legs, respectively.

Key Note Deep vein thrombosis (DVT) and venous thromboembolism are a major cause of postoperative morbidity in patients undergoing bariatric surgery. Besides the inherent risk for DVT of obese patients, the increased abdominal pressure secondary to the pneumoperitoneum and the steep Trendelenburg position decrease venous return and further increase the risk for DVT. Therefore, pneumatic compression stockings and subcutaneous heparin are strongly recommended.

F. Laxague · R. Buxhoeveden
Department of Surgery, Hospital Alemán of Buenos Aires, Buenos Aires, Argentina

F. Schlottmann (✉)
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires, Buenos Aires, Argentina

Department of Surgery, University of North Carolina, Chapel Hill, NC, USA

Pneumoperitoneum and Trocar Placement

A Veress needle is placed in a left subcostal location through Palmer's point (3 cm below the left costal margin in the midclavicular line). Pneumoperitoneum is established using carbon dioxide to a maximum pressure of 12 mmHg. We use six ports for the procedure. A 12 mm optical port is inserted 10–12 cm below the xiphoid process and 2–3 cm to the left of midline. The remaining five ports are then placed as shown in Fig. 26.1.

Keynote Trocars without blade are used to reduce the rate of herniation. It is important to avoid placing the ports too low, as it makes the operation more challenging. The liver can be

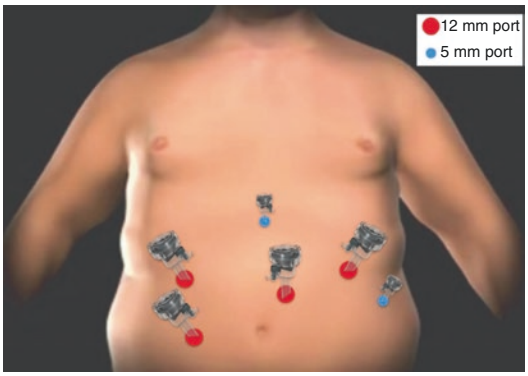


Fig. 26.1 Port placement for laparoscopic Roux-en-Y gastric bypass

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_26

retracted with a locking Allis grasper clamp or Endo Clinch placed through the subxiphoid 5 mm port and secured to the right crus just anterior to the gastroesophageal junction (GEJ).

Gastric Pouch Creation

We start by removing the GEJ fat pad with the harmonic scalpel. The angle of His is then exposed and dissected up to the base of the left crus. The gastrohepatic ligament is incised between the second and third branch of the left gastric artery, and the lesser sac is entered. The gastric section is performed horizontally using 40–50 mm of a 60 mm blue load linear stapler (Fig. 26.2). A 36-Fr gastric lavage tube is advanced by the anesthesiologist to this horizontal staple line. The gastric section is then completed with additional firings of 60 mm blue loads in a vertical direction toward the previously dissected angle of His (Fig. 26.3). The length of the pouch should be approximately 6–8 cm. The gastric remnant staple line is inspected and reinforced with an absorbable running suture (e.g., polyglactin 2.0) to prevent bleeding.

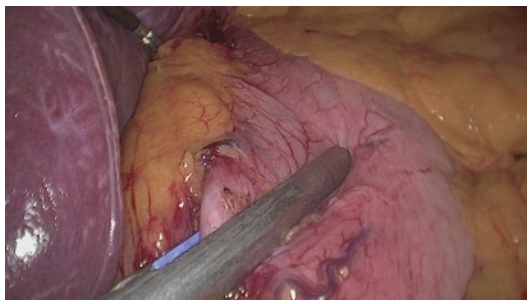


Fig. 26.2 Horizontal gastric section

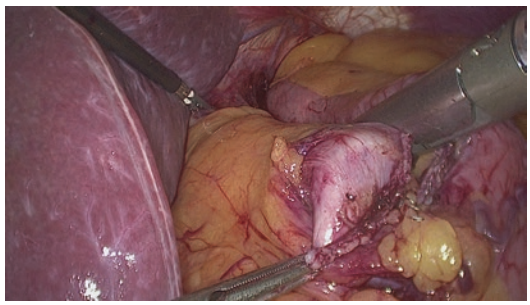


Fig. 26.3 Gastric pouch creation

Keynote During the creation of the gastric tunnel needed for placing the linear stapler, care should be taken to avoid injury of the splenic vessels, the pancreas, or the posterior wall of the stomach. After creation of the gastric pouch, it is critical to verify the complete transection of the stomach to avoid communication between the pouch and the gastric remnant and inspect the staple lines to ensure hemostasis.

Creation of Biliopancreatic and Alimentary Limbs

The greater omentum and the transverse colon are retracted cephalad in order to expose the ligament of Treitz and the inferior mesenteric vein. The jejunum is divided 60 cm (BMI < 50 kg/m^2) or 100 cm (BMI > 50 kg/m^2) distal to the ligament of Treitz using a white load linear stapler. We mark the biliopancreatic limb with a metallic clip to avoid an error when choosing the limb that needs to be sutured to the pouch. The alimentary limb is then raised with the stapler line orientated toward the left upper quadrant in an antecolic antegastric manner.

Keynote If the greater omentum is thick and bulky, it should be divided vertically using the harmonic scalpel to facilitate bringing the Roux limb up to the gastric pouch. Obtaining a tension-free alimentary limb is key to prevent complications of the anastomosis. In extreme cases in which the division of the omentum is insufficient to release tension, the Roux limb should be placed in the retrocolic–retrogastric position.

Gastrojejunostomy

A gastrostomy at the distal end of the gastric pouch just under the staple line is done with the harmonic scalpel. An enterotomy is then performed with the harmonic scalpel on the anti-

mesenteric border of the alimentary limb 4–5 cm away from the stapled end. A side-to-side gastrojejunostomy is created with a blue load linear stapler. We recommend inserting no more than 3 cm of the stapler to create a small anastomosis (Fig. 26.4). The 36-Fr tube is passed through the anastomosis, and the anterior wall is then closed with two layers of running suture using absorbable material (e.g., polyglactin 2.0) (Fig. 26.5).

Keynote The 36-Fr tube enables us to calibrate the anastomosis and avoid suturing the posterior wall inadvertently. A methylene blue test or a pneumohydraulic test is recommended to rule out leaks from the anastomosis.

Jejunojejunostomy

A 120 cm (BMI < 50 kg/m^2) or 150 cm (BMI > 50 kg/m^2) Roux limb is measured to determine the site of the anastomosis. The site chosen for the anastomosis is brought into apposition to the proximal jejunum with the stapled end of the biliopancreatic limb oriented toward the patient's right side and cephalad to the distal Roux limb. Enterotomies are performed using the harmonic scalpel at the anti-mesenteric border of both limbs. A white 60 mm linear stapler is inserted to its full length into both enterotomies to create a side-to-side jejunojejunostomy (Fig. 26.6). The enterotomy is then closed in one layer by running an absorbable suture (e.g., polyglactin 3.0).

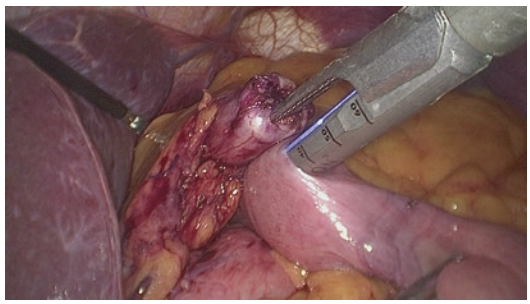


Fig. 26.4 Side-to-side gastrojejunostomy

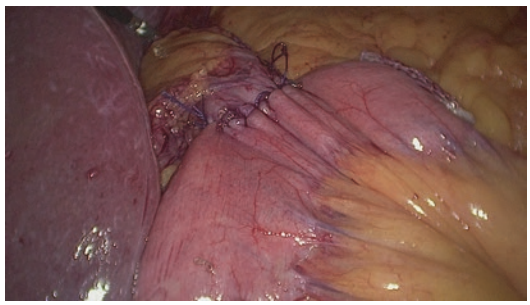


Fig. 26.5 Final configuration of gastrojejunostomy

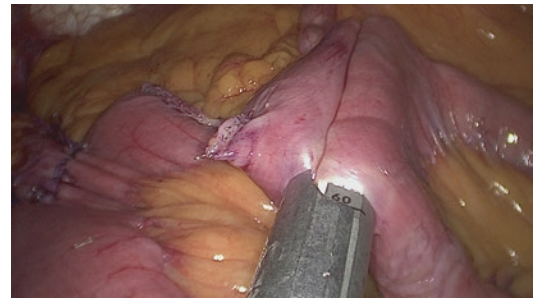


Fig. 26.6 Side-to-side jejunojejunostomy

Keynote The mesentery of both limbs should be properly aligned without twists when performing this anastomosis. If any area of separated serosa is noticed in the anastomosis, it should be approximated with Lembert sutures. An "anti-torsion" stitch between the two limbs of the bowel is useful to prevent future kinking of the anastomosis.

Closure of Mesenteric and Petersen Defect

The mesenteric defect is closed in a running, locking fashion toward the root of the mesentery with nonabsorbable suture material (e.g., polyester 2.0). The Petersen space, limited posteriorly by the transverse colon and anteriorly by the alimentary limb, should be also closed with nonabsorbable suture material.

Keynote Internal hernias are a frequent cause of reoperation after a laparoscopic RYGB. The closure of the mesenteric and Petersen defects is key to prevent this complication.

Technical Controversies in Roux-en-Y Gastric Bypass

Gastric Pouch Size

The association between pouch size and postoperative outcomes remains under debate. Roberts et al. [1] found that a small gastric pouch was associated with better excess weight loss after 1 year, suggesting that efforts to standardize a small pouch size were important for the success of the procedure. However, other studies did not find such correlation. For instance, Topart and colleagues [2] evaluated the gastric pouch size with a barium swallow on 132 patients and found that those patients with a large pouch had similar weight loss compared to those with a normally sized pouch. Similarly, Madan et al. [3] described that larger pouches still resulted in a high rate of success after laparoscopic Roux-en-Y gastric bypass (LRYGB).

A study using the Scandinavian Obesity Surgery Registry included 14,168 patients who underwent LRYGB with linear stapled gastrojejunostomies. The mean length of stapler used for the pouch was 145 mm. Although the relative risk of marginal ulcers increased by 14% for each centimeter of stapler used for the pouch, the size of the pouch did not predict better weight loss at 1 year [4]. Overall, a small pouch would reduce the risk of marginal ulcers but would not be a good predictor of weight loss.

Gastrojejunostomy Technique

There are different gastrojejunal anastomosis techniques: hand-sewn (HSA), circular-stapled (CSA), and linear-stapled (LSA). Whether one technique is superior to the other remains under debate. Lee et al. [5] analyzed 426 patients who underwent LRYGB, 174 with HSA, 110 with CSA, and 142 with LSA, and compared stricture rates and weight loss between the different groups. The study found no significant difference in the rate of strictures between the three techniques, although the LSA group had the lowest requirement for postoperative dilatation. Weight loss was similar between the three anastomotic techniques [5]. Jarry and colleagues [6] analyzed 51 patients with LSA and 53 with HSA and found that there was no significant difference between the two groups with respect to mortality, conversion, early reoperation, surgical complications, leakage, stricture, and bariatric results. However, HSA was associated with shorter operative time and lower costs [6]. Finally, a meta-analysis comprising eight studies with 1321 patients compared LSA versus CSA and found that LSA was associated with a reduced risk of anastomotic stricture and wound infection, as well as a shorter operative time [7].

The Roux limb route could also affect the stricture rate after LRYGB. Ribeiro-Parenti et al. [8] compared the stricture rates between the antecolic and the retrocolic gastrojejunostomy. They included 1500 patients who underwent LRYGB; 572 had an antecolic and 928 a retrocolic gastrojejunostomy, respectively. A significant lower gastrojejunal stricture rate was observed in the retrocolic group, as compared to the antecolic group (1.5% vs. 6.5%, $p < 0.0001$), with no increase in the incidence of internal hernia when the mesenteric defect was closed [8].

Alimentary and Biliopancreatic Limb Length

Many studies showed the association between the limbs length and the improvement of metabolic disorders and weight loss. Pinheiro et al. randomized 105 patients with a BMI $\geq$50 kg/m^2 in two groups: group 1 with a 50 cm biliary limb and a 150 cm Roux limb and group 2 with a 100 cm biliary limb and a 250 cm Roux limb. They found that patients with longer biliary and Roux limbs achieved greater type 2 diabetes control, greater lipid disorder improvement, and a faster excess weight loss [9]. Palha et al. [10] showed that a longer biliopancreatic limb length achieved a distinctive incretin cell pattern at the gastrojejunal anastomosis that could result in better endocrine profiles with reduced insulin resistance.

A retrospective study including 768 patients who underwent LRYGB compared the complication rates and weight loss between

patients with a short alimentary limb (100 cm) or a long one (150 cm). Overall complication rates and weight loss were comparable in both groups [11]. A randomized clinical trial evaluated the effect of different limb lengths on weight loss after gastric bypass and concluded that in patients with a BMI ≤50 kg/m^2, there was no advantage with longer limb lengths. In patients with BMI >50 kg/m^2, however, longer alimentary limb lengths were associated with a higher percentage of patients achieving >50% excess weight loss [12].

Mesenteric Defect Closure

Internal hernias are more common following LRYGB than open gastric bypass [13], and the majority occur after a significant (>50%) excess weight loss [14]. This complication should be suspected in all patients with intense abdominal pain after a LRYGB.

Brolin et al. [15] analyzed 872 consecutive LRYGB patients; the first 654 patients had an incomplete mesenteric closure, while the remaining 218 had a complete closure. Complete closure of the mesenteric defect resulted in a significant reduction in internal mesenteric hernias (0.5 vs. 2.6%). A randomized control trial included 105 patients undergoing laparoscopic antecolic RYGB and randomized the sample in two groups: closed mesenteric defect (n = 50) or open mesenteric defect (n = 55). Interestingly, closure or non-closure of the jejunal mesenteric defect following LRYGB resulted in equivalent internal hernia and complication rates [16].

Hiatal Hernia Repair in Gastric Bypass

Hiatal hernia is a common entity in obese people, with an incidence that ranges from 20 to 53% [17]. Hiatal hernia repair (HHR) has been mostly studied in patients undergoing sleeve gastrectomy because of the strong association between this procedure and postoperative gastroesophageal reflux disease [18]. However, patients with large hiatal hernias undergoing LRYGB could also benefit from HHR [19].

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Roberts K, Duffy A, Kaufman J, et al. Size matters: gastric pouch size correlates with weight loss after laparoscopic Roux-en-Y gastricbypass. Surg Endosc. 2007;21(8):1397–402.
2. Topart P, Becouarn G, Ritz P. Pouch size after gastric bypass does not correlate with weight loss outcome. Obes Surg. 2011;21:1350–4.
3. Madan AK, Tichansky DS, Phillips JC. Does pouch size matter? Obes Surg. 2007;17:317–20.
4. Edholm D, Ottosson J, Sundbom M. Importance of pouch size in laparoscopic Roux-en-Y gastric bypass: a cohort study of 14,168 patients. Surg Endosc. 2016;30:2011–5.
5. Lee S, Davies AR, Bahal S, et al. Comparison of gastrojejunal anastomosis techniques in laparoscopic Roux-en-Y gastric bypass: gastrojejunal stricture rate and effect on subsequent weight loss. Obes Surg. 2014;24:1425–9.
6. Jarry J, Wagner T, de Pommerol M, et al. Laparoscopic Roux-en-Y gastric bypass: comparison between hand-sewn and mechanical gastrojejunostomy. Updates Surg. 2012;64:25–30.
7. Giordano S, Salminen P, Biancari F, et al. Linear stapler technique may be safer than circular in gastrojejunal anastomosis for laparoscopic Roux-en-Y gastric bypass: a meta-analysis of comparative studies. Obes Surg. 2011;21:1958–64.
8. Ribeiro-Parenti L, Arapis K, Chosidow D, et al. Gastrojejunostomy stricture rate: comparison between antecolic and retrocolic laparoscopic Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2015;11:1076–84.
9. Pinheiro JS, Schiavon CA, Pereira PB, et al. Long-long limb Roux-en-Y gastric bypass is more efficacious in treatment of type 2 diabetes and lipid disorders in super-obese patients. Surg Obes Relat Dis. 2008;4:521–5.
10. Palha AM, Pereira SS, Costa MM, et al. Differential GIP/GLP-1 intestinal cell distribution in diabetics' yields distinctive rearrangements depending on Roux-en-Y biliopancreatic limb length. J Cell Biochem. 2018;119:7506–14.
11. Dogan K, Homan J, Aarts EO, et al. A short or a long Roux limb in gastric bypass surgery: does it matter? Surg Endosc. 2017;31:1882–90.
12. Choban PS, Flancbaum L. The effect of Roux limb lengths on outcome after Roux-en-Y gastric bypass: a prospective, randomized clinical trial. Obes Surg. 2002;12:540–5.
13. Higa KD, Ho T, Boone KB. Internal hernias after laparoscopic Roux-en-Y gastric bypass: incidence, treatment and prevention. Obes Surg. 2003;13:350–4.

14. Ahmed AR, Rickards G, Husain S, et al. Trends in internal hernia incidence after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2007;17:1563–6.
15. Brolin RE, Kella VN. Impact of complete mesenteric closure on small bowel obstruction and internal mesenteric hernia after laparoscopic Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2013;9:850–4.
16. Rosas U, Ahmed S, Leva N, et al. Mesenteric defect closure in laparoscopic Roux-en-Y gastric bypass: a randomized controlled trial. Surg Endosc. 2014;29:2486–90.
17. Reche F, Mancini A, Borel AL, et al. Totally robotic combined Roux-en-Y gastric bypass and hiatal hernia repair with biological mesh: technical points. Obes Surg. 2017;27:3349–50.
18. Patti MG, Schlottmann F. Gastroesophageal reflux after sleeve gastrectomy. JAMA Surg. 2018;153:1147–8.
19. Boules M, Corcelles R, Guerron AD, et al. The incidence of hiatal hernia and technical feasibility of repair during bariatric surgery. Surgery. 2015;158:911–8.

Sleeve Gastrectomy

27

Nabeel R. Obeid and Justin B. Dimick

Introduction

Morbid obesity remains a population health crisis in the United States and other countries around the world [1]. Options for treatment include lifestyle modification with dietary counseling and physical activity, endoscopic therapies, and bariatric/metabolic surgery. Bariatric surgery is well established as the most durable and effective treatment for the chronic disease that is obesity [2]. Surgical options include Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), among other less commonly performed procedures such as adjustable gastric banding or biliopancreatic diversion with duodenal switch [3].

Laparoscopic sleeve gastrectomy is currently the most commonly performed bariatric procedure. What is now performed as a primary, stand-alone surgery was once part of a staged operative approach for the treatment of obesity, particularly for patients with super obesity [4]. The sleeve gastrectomy was the first stage of a two-stage operation that began with a longitudinal gastrectomy followed by a biliopancreatic diversion with duodenal switch. It soon became apparent that outcomes following the initial longitudinal gastrectomy, including weight loss and comorbidity resolution, were quite effective, and eventually the procedure became a recognized primary operation for the treatment of obesity [5].

Preoperative Planning

Patients considering bariatric surgery generally undergo thorough preoperative evaluations and testing. This begins with a complete medical history and physical examination, as well as comprehensive nutrition evaluation and counseling. Patients also routinely undergo psychological assessment and are referred for therapy as indicated. Laboratory testing and further medical workup depend on individual patient factors, including presence of obesity-related comorbid conditions.

Foregut evaluation before bariatric surgery is not uniform. Endoscopic evaluation with an esophagogastroduodenoscopy (EGD) and radiographic evaluation with upper gastrointestinal series (UGIS) have both been utilized for assessment of pathology, most notably for hiatal hernias, esophagitis, masses, or mucosal alterations. Some surgeons perform these tests on a selective basis, while others will point to the high rate of pathology found in bariatric surgical patients, thus favoring routine fore-

N. R. Obeid
Department of Surgery, University of Michigan Health System, Ann Arbor, MI, USA

J. B. Dimick (✉)
Health Services Research, Division of Minimally Invasive Surgery, Center for Healthcare Outcomes & Policy, Department of Surgery, University of Michigan Health System, Ann Arbor, MI, USA
e-mail: jdimick@umich.edu

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_27

gut evaluation. D'Silva et al. demonstrated abnormal pathology, such as hiatal hernia, esophagitis, Barrett's esophagus (BE), presence of *H. pylori*, erosions, or polyps, in 79% of pre-bariatric surgery patients [6]. Many of such patients are asymptomatic, with a poor correlation between presence of symptoms and pathologic findings, some of which may alter management strategies [7]. Ultimately, the decision for routine versus selective evaluation of the foregut prior to bariatric surgery remains at the discretion of the surgeon and unless the patient has a high risk of harboring suspected pathology (e.g., symptoms consistent with a hiatal hernia).

There remains significant controversy in the area of pre-surgical evaluation of gastroesophageal reflux disease (GERD) in the bariatric surgery candidate. An EGD is generally recommended for patients with active reflux symptoms to evaluate for mucosal pathology (esophagitis or BE) or lesions. The threshold to perform a thorough workup for reflux disease and the extent of such workup remain variable. For those with severe or intractable reflux, there is literature to support a complete evaluation including manometry and ambulatory pH monitoring, both to confirm the presence or absence of GERD and to guide the choice of surgical procedure [8, 9]. This may aid in avoiding long-standing increased acid exposure to the esophagus, particularly after sleeve gastrectomy [10]. While many will advocate for choosing Roux-en-Y gastric bypass in this setting, this workup may demonstrate integrity of the lower esophageal sphincter and lack of true GERD, potentially altering the decision-making process.

Immediately preceding the date of surgery, patients are generally instructed to follow a very low-calorie diet (VLCD), effectively decreasing visceral adiposity and liver size with resultant decrease in perioperative morbidity [11, 12]. The VLCD usually spans a range of 1–4 consecutive weeks, often depending on the patient's preoperative body mass index (BMI) and presence of fatty liver disease.

Technical Elements

Perioperative pathways are becoming more common in bariatric practices, including anesthesia protocols for minimization of opioid analgesia and postoperative nausea and vomiting. In addition, pharmacologic and mechanical prophylaxis for venous thromboembolism (VTE) is routinely administered.

Standard laparoscopy setup for upper abdominal procedures is employed. Patient positioning may be supine or with split-leg configuration. Monitors are placed at the head of the table for direct view. The stomach should be decompressed, either with an orogastric tube, an endoscope, or a bougie with suction capability. Access to the peritoneal cavity for insufflation can be achieved in numerous ways, including with Veress needle entry at Palmer's point in the left upper quadrant, optical trocar entry, or open Hason technique, although the latter can be difficult due to habitus with thick abdominal wall.

The operation commences with mobilization of the greater curvature of the stomach, starting at a point across from the incisura angularis (Fig. 27.1). The mobilization is usually directed proximally first, making sure to expose the short gastric vessels and splenic hilum at the proximal fundus (Fig. 27.2). The dissection usually requires ligation/division of the proximal-most short gastric vessel in order to fully expose the

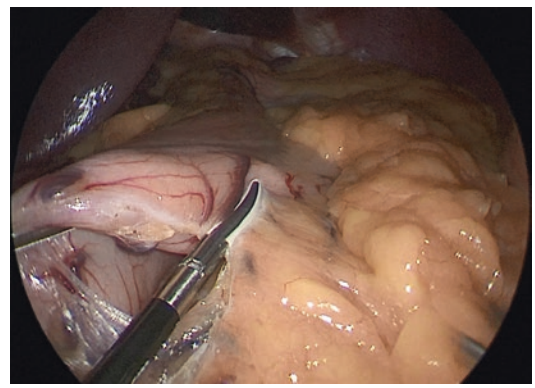


Fig. 27.1 Mobilization of the greater curvature of the stomach (photo courtesy of Nabeel R. Obeid, MD)

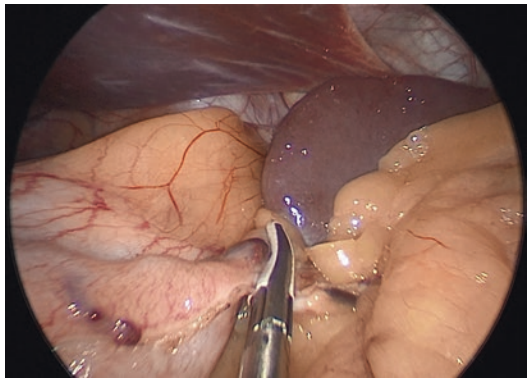


Fig. 27.2 Mobilization of the gastric fundus at the splenic hilum with division of the short gastric vessels (Photo courtesy of Nabeel R. Obeid, MD)

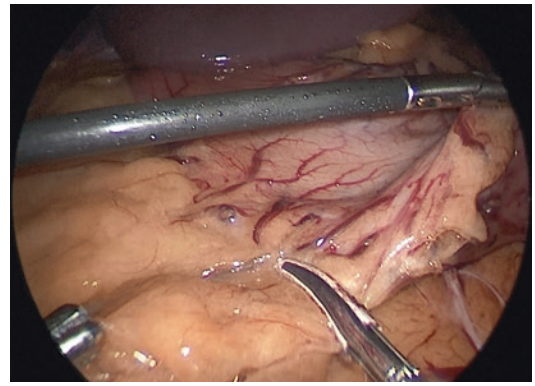


Fig. 27.4 Distal gastric mobilization along the greater curvature (Photo courtesy of Nabeel R. Obeid, MD)

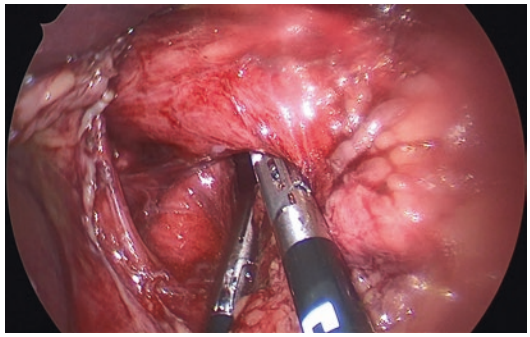


Fig. 27.3 Hiatal dissection with reduction of the hiatal hernia (Photo courtesy of Nabeel R. Obeid, MD)

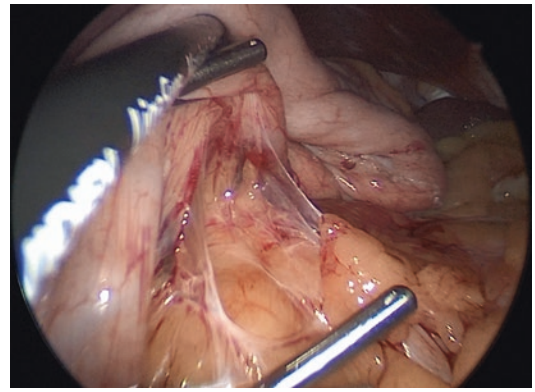


Fig. 27.5 Retrogastric adhesions (Photo courtesy of Nabeel R. Obeid, MD)

left crus of the diaphragm. The angle of His should be fully mobilized off the diaphragm and the gastroesophageal fat pad identified. Assessment for the presence of a hiatal hernia generally occurs at this time and, if identified, may require circumferential hiatal dissection (Fig. 27.3). Intraoperative evaluation of a hiatal hernia remains quite variable in terms of anatomic features used to diagnose and threshold for performing a full dissection.

With the proximal stomach fully mobilized, the dissection continues distally toward the pylorus (Fig. 27.4). The greater curvature is mobilized to a point 4–6 cm proximal to the pylorus, and this serves as the starting point for the longitudinal staple line. The surgeon should assess for retro-gastric adhesions (Fig. 27.5), which should be lysed sharply to avoid kinking, twisting, or difficulty with stapling. While technique may vary, it is generally advisable to position the sizing device along the lesser curvature across the distal stomach toward the duodenum (Fig. 27.6). This will help avoiding excessive narrowing at the incisura angularis. The sizing device may be a bougie or endoscope that is at least 34 Fr in diameter, although some studies have demonstrated a decreased incidence of leak with bougie size of 40 Fr compared to smaller sizes, without a difference in weight loss outcomes [13, 14]. Stapling is performed with a linear cutting–stapling device, progressing from a distal to proximal direction along

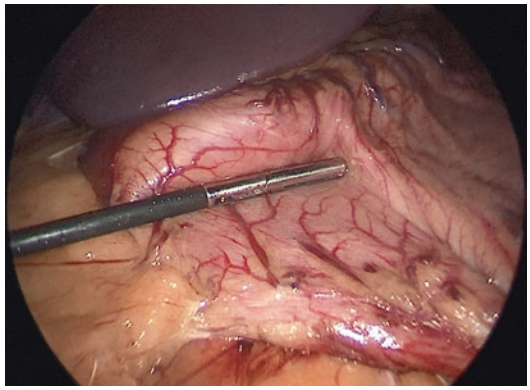


Fig. 27.6 Placement of the bougie calibration tube along the lesser curvature of the stomach (Photo courtesy of Nabeel R. Obeid, MD)

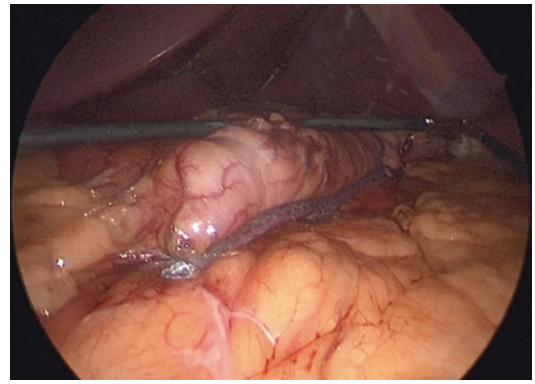


Fig. 27.8 Completed sleeve gastrectomy (Photo courtesy of Nabeel R. Obeid, MD)

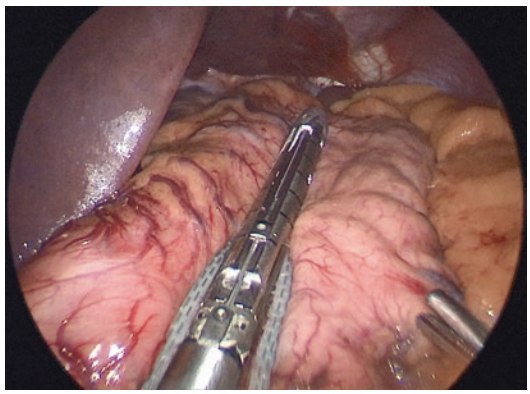


Fig. 27.7 Longitudinal transection of the stomach using a linear cutting stapler along the calibration tube (Photo courtesy of Nabeel R. Obeid, MD)

the sizing device (Fig. 27.7). This may be performed with or without staple line reinforcement (SLR). While controversial, there is evidence to suggest that SLR reduces the rate of hemorrhagic events without altering the leak rate [15]. Once this is completed (Fig. 27.8), the specimen is removed, and an intraoperative leak test may be performed, either with air insufflation or dye.

Postoperative Care

Key concepts for recovery after gastrointestinal surgery are employed, including early ambulation, use of incentive spirometry, and monitoring voids. Early initiation of diet with advancement as tolerated has been shown to be safe and effective in prompt recovery after gastrointestinal surgery [16]. Specifically, post-bariatric surgery, this takes the form of initiation of bariatric clear liquids with advancement to bariatric full liquids by postoperative day 1 and has been shown to decrease length of stay without increasing morbidity [17]. Antiemetic use is important in the bariatric surgical population, as postoperative nausea and vomiting (PONV) are seen not infrequently. Aggressive regimens to combat PONV have been shown to be effective in reducing symptoms and decreasing length of stay [18, 19]. Such regimens may include perioperative administration of ondansetron, dexamethasone, and/or prophylactic placement of transdermal scopolamine patch.

Opioid reduction helps with decreasing PONV, and therefore a multimodal approach to postoperative analgesia is most effective. Local anesthetics employed at the time of surgery, sometimes in the form of transversus abdominis plane blocks, combined with nonsteroidal anti-inflammatory medications, acetaminophen, and opioids, appear to be an effective strategy. The American Society for Metabolic and Bariatric Surgery (ASMBS) has developed perioperative pathways as a resource for evidence-based perioperative management of the bariatric patient, and have published a pathway for sleeve gastrectomy [20].

Routine use of postoperative radiological upper gastrointestinal series (UGIS) to assess for leak has fallen out of favor, especially following sleeve gastrectomy. The vast majority of these tests are negative, and patients who subsequently develop leaks in the first 2–3 weeks following surgery may have had a normal UGI [21]. Vital sign derangements and clinical factors, such as fever, tachycardia, leukocytosis, or elevated pain scores, may serve as screening tools to guide selective use of UGIS to investigate for leak. In addition, UGI may be ordered to evaluate for obstruction or twisting of the sleeve in patients with persistent emesis or dysphagia.

Outcomes

Weight loss is a primary outcome measure following bariatric surgery. There have been several long-term studies (>5 years follow-up data) and meta-analyses specifically focused on the effectiveness of sleeve gastrectomy for weight loss. Percent excess weight loss (EWL) and total weight loss (TWL) are common parameters reported in the literature, and long-term studies show weight loss following sleeve gastrectomy in the range of 53–76% EWL and 24–26% TWL [22–26]. Preoperative BMI has been shown to be a predictor of weight loss success following bariatric surgery, with lower preoperative BMI associated with greater percentage of weight loss [27]. Other factors, such as age and presence of hypertension or diabetes, also seem to accurately predict postoperative weight loss [28]. Weight regain or inadequate weight loss remain challenges, estimated to occur in approximately 28% of sleeve gastrectomy cases long term with a range of 14–37%, but rates are highly inconsistent in the bariatric surgical literature due to nonuniform definitions and methods of reporting [29, 30].

Improvement or remission of obesity-related comorbidities remains an important aspect of metabolic/bariatric surgery. Rates of diabetes remission have been reported to be around 70% overall, regardless of preoperative BMI, and varies among procedure type (89% with biliopancreatic diversion, 77% after RYGB, and 60% following SG) [31]. Five-year data from a randomized trial revealed bariatric surgery with intensive medical therapy was more efficacious in treating hyperglycemia than medical therapy alone [32]. There are now several scoring systems available that surgeons may use to help predict the probability of diabetes remission following bariatric surgery [33, 34]. Nondiabetic comorbid conditions also seem to improve in the post-bariatric surgery patient. Obstructive sleep apnea (OSA) is quite common in patients with morbid obesity, and sleeve gastrectomy has been objectively shown to significantly improve OSA using the modified Epworth Sleepiness Scale questionnaire (92% improvement) and apnea–hypopnea index (81% improvement) [35]. Nonalcoholic fatty liver disease (NAFLD) is increasing in prevalence, and bariatric surgery, including sleeve gastrectomy specifically, has been shown to induce histological improvement in liver fibrosis, therefore gaining significant traction as an indication for bariatric surgery [36–39]. Nontraditional conditions such as pulmonary hypertension and interstitial lung disease no longer appear to be contraindications and actually have been demonstrated to improve following bariatric surgery, which may positively affect candidacy for lung transplantation [40, 41].

Overall rates of morbidity are low, with a 2–3% rate of 30-day major adverse events following sleeve gastrectomy [42]. Early complications were found to occur at a lower rate among those undergoing SG as compared to RYGB [43]. Thirty-day readmission was noted to be lower among SG patients as well (3.8 vs. 6.1% for RYGB), with the most common reasons being nausea, vomiting, and dehydration [44]. A recent meta-analysis reviewed randomized controlled trials for rates of late postoperative complications and found a lower rate of major and minor complications for SG versus RYGB, as well as a greater reduction in need for additional interventions, although none of these reached statistical significance [45]. Sleeve gastrectomy may be performed safely as a reoperative procedure for failed adjustable gastric banding and has a better risk profile when performed as a single-stage conversion as compared to band to RYGB [46].

Using the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database, reported rates of 30-day mortality was 0.1% for SG and 0.2% for RYGB, as well as lower unplanned intensive care unit admissions or reoperation for those undergoing sleeve gastrectomy [47]. Moreover, in a large, population-based study, obese patients who had not undergone bariatric surgery had a higher risk of all-cause mortality compared to patients who had bariatric surgery, with an adjusted hazard ratio of 2.02 over a median follow-up of 4.5 years [48].

Management of Complications

While bariatric surgery has a very favorable risk profile, there are particular perioperative events that may cause significant patient morbidity or, in rare circumstances, mortality. Bleeding can occur following sleeve gastrectomy, most commonly from the longitudinal staple line, although other sources of bleeding can include the cut edge of the mesentery, splenic hilar vessels, diaphragmatic vessels, or parenchymal injuries to the spleen or pancreas. Rates of postoperative bleeding are estimated to be around 0.5–2%, a minority of which may require reoperation [49]. Technique appears to play a partial role in prevention of staple line leaks, with multiple studies demonstrating a reduction in postoperative hemorrhage with the use of staple line reinforcement [50, 51].

Gastric leak following sleeve gastrectomy remains one of the most feared complications. Due to the configuration of the longitudinal gastrectomy, the intraluminal pressure of the sleeve increases relative to a normal stomach, and the most proximal extent of the staple line appears to be most vulnerable to leak. Oftentimes, a distal stricture or twisting related to improper technique, ischemia, or other factors may be found in association with sleeve leaks. Overall leak rate has been reported to be in the range of 0.3–3%, and operative technique may play a role, as some studies found oversewing of the staple line resulted in fewer leaks, while others showed staple line reinforcement to improve outcomes [52, 53]. The primary goal of treatment remains control of intra-abdominal sepsis, which may be achieved with percutaneous drainage or early surgical exploration, as well as parenteral antibiotics and enteral nutrition. In certain circumstances, depending on the acuity, character, and location of the leak, advanced endoscopic interventions such as internal drainage, stenting, clipping, or sewing may be options. For chronic, nonhealing leaks, conversion to a Roux-en-Y configuration may be considered. During workup of a sleeve leak, if a distal obstruction is encountered, it is paramount to address and treat this in order to facilitate healing of the leak. Options include endoscopic dilation or stenting depending on the nature of the obstruction or conversion to Roux-en-Y gastric bypass.

Those undergoing bariatric surgery are at increased risk for venous thromboembolic (VTE) events due to risk factors such as diabetes mellitus, hypertension, and venous stasis, in addition to obesity, although they occur infrequently with a reported incidence of 0.2–3.5% range [54, 55]. Risk also varies with procedure type, with sleeve gastrectomy carrying a higher risk than gastric bypass [56]. Pulmonary embolism (PE) is the leading cause of mortality following bariatric surgery and therefore remains a significant focus on quality improvement and patient safety initiatives [57]. In addition, the vast majority of VTE events occur post-discharge from inpatient hospitalization, usually within 30 days of surgery [58]. A unique but now well-recognized VTE event is porto-mesenteric vein thrombosis (PVT). There is a paucity of literature on this adverse event, but the overall incidence is estimated to be less than 0.5% among all bariatric procedures, with the highest rate following sleeve gastrectomy [59]. The mainstay of therapy is systemic, therapeutic anticoagulation.

Evidence-based protocols are becoming widespread among bariatric surgery programs to help mitigate the risk of VTE. Aggressive prophylaxis is an integral part of these pathways and generally includes lower extremity compression with sequential compression devices (SCDs), early ambulation, and pharmacologic prophylaxis.

Unfractionated (UH) and low-molecular-weight heparins (LMWH) are commonly used, though LMWH is generally preferred due to low-level evidence that suggests a greater reduction in VTE rates without increased risk of bleeding compared with UH [60]. There are now several validated risk calculators readily available as smartphone apps that help to predict the individualized risk of VTE and also assist in making recommendations for post-discharge chemoprophylaxis for those at highest risk.

Gastroesophageal reflux disease following sleeve gastrectomy remains an area of intense investigation. Many surgeons propose significant preoperative reflux as a relative contraindication to sleeve gastrectomy due to concern regarding exacerbation of GERD following the procedure. Others maintain that reflux symptoms may improve with weight loss following sleeve gastrectomy and therefore should not be considered a contraindication. The incidence and significance of post-sleeve GERD (including esophagitis and Barrett's esophagus), as well as the approach to evaluation and management, remain controversial at present time. Reflux symptoms following sleeve gastrectomy have been studied sparingly, but a retrospective review from a single center using the validated GERD Health-Related Quality of Life (GERD-HRQL) survey demonstrated new-onset heartburn to be present among 47% of their cohort, as well as increased rates of dysphagia and regurgitation [61]. This study also concluded that, in their analysis, none of the preoperative variables were able to predict de novo or worsening of reflux in the postoperative period. Other studies have demonstrated the opposite effect, with improvements in reflux symptoms following sleeve gastrectomy [62].

Physiologic changes following sleeve gastrectomy have been demonstrated based on objective analysis with pH studies and high-resolution manometry, reporting an increase in esophageal acid exposure and decrease in lower esophageal sphincter (LES) pressure [63]. Another study correlated the LES distensibility with post-sleeve gastrectomy GERD symptoms and found that, while the LES was weakened post-procedure, there was no predictable correlation to the change in reflux symptoms, arguing that post-sleeve GERD has a multifactorial etiology [64]. To determine rates of esophagitis and Barrett's esophagus following sleeve gastrectomy, one group performed routine endoscopic surveillance at 1 month and 1 year, followed by annually on a selective basis [65]. Those experiencing reflux symptoms were placed on proton pump inhibitor therapy during their follow-up surveillance (100% follow-up at 1 year, declining over time to 29% at 5+ years). They reported a 15.5% rate of esophagitis and 1.2% rate of Barrett's esophagus based on histological examination.

Prevention of post-sleeve reflux by surgical technique has been described, with specific data suggesting routine circumferential hiatal dissection during sleeve gastrectomy may in fact be a risk factor for the development of post-sleeve GERD [66]. Most would agree that initial treatment for post-sleeve reflux would be initiation of proton pump inhibitor (PPI) therapy, and previous literature suggests that patients generally have a favorable response to this in the majority of cases [67]. For those patients that do not respond to PPI therapy or prefer alternative options, several interventions exist. The traditional approach has been to convert refractory reflux after sleeve gastrectomy to Roux-en-Y gastric bypass, which still serves as a viable and often-used option with great success. Other interventions that are in variable stages of experience and acceptance include endoscopy radiofrequency ablation to the LES or laparoscopic placement of a magnetic sphincter augmentation device, which seems to have promising early results [68].

Conflict of Interest The authors have no conflict of interest to declare.

References

1. Center for Disease Control and Prevention. Prevalence of obesity among adults and youth: United States, 2015–2016. 2017. Access Dec 2018 from https://www.cdc.gov/nchs/products/databriefs/db288.htm.
2. Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. JAMA Surg. 2014;149(3):275–87.

3. American Society for Metabolic and Bariatric Surgery. Estimate of bariatric surgery numbers, 2011–2017. 2018. Access Dec 2018 from https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers.
4. Chousleb E, Rodriguez JA, O'Leary JP. Chapter 3 – History of bariatric surgery. In: The ASMBS textbook of bariatric surgery, vol. 1. New York: Springer; 2015. p. 44.
5. Talebpour M, Amoli BS. Laparoscopic total gastric placation in morbid obesity. J Laparoendosc Adv Surg Tech A. 2007;17(6):793–8.
6. D'Silva M, Bhasker AG, Kantharia NS, Lakdawala M. High-percentage pathological findings in obese patients suggest that esophago-gastro-duodenoscopy should be made mandatory prior to bariatric surgery. Obes Surg. 2018;28:2753–9.
7. Carabotti M, Avallone M, Cereatti F, Paganini A, Greco F, Scirocco A, et al. Usefulness of upper gastrointestinal symptoms as a driver to prescribe gastroscopy in obese patients candidate to bariatric surgery. A prospective study. Obes Surg. 2016;26(5):1075–80.
8. Tolone S, Limongelli P, del Genio G, Brusciano L, Rossetti G, Amoroso V, et al. Gastroesophageal reflux disease and obesity: do we need to perform reflux testing in all candidates to bariatric surgery? Int J Surg. 2014;12(Suppl 1):S173–7.
9. Tolone S, Savarino E, de Bortoli N, Frazzoni M, Furnari M, d'Alessandro A, et al. Esophagogastric junction morphology assessment by high resolution manometry in obese patients candidate to bariatric surgery. Int J Surg. 2016;28(Suppl 1):S109–13.
10. Georgia D, Stamatina T, Maria N, Konstantinos A, Konstantinos F, Emmanouil L, et al. 24-h multichannel intraluminal impedance PH-metry 1 year after laparocopic sleeve gastrectomy: an objective assessment of gastroesophageal reflux disease. Obes Surg. 2017;27(3):749–53.
11. Pilone V, Tramontano S, Renzulli M, Romano M, Cobellis L, Berselli T, et al. Metabolic effects, safety, and acceptability of very low-calorie ketogenic dietetic scheme on candidates for bariatric surgery. Surg Obes Relat Dis. 2018;14:1013.
12. Holderbaum M, Casagrande DS, Sussenbach S, Buss C. Effects of very low calorie diets on liver size and weight loss in the preoperative period of bariatric surgery: a systematic review. Surg Obes Relat Dis. 2018;14(2):237–44.
13. Parikh M, Issa R, McCrillis A, Saunders JK, Ude-Welcome A, Gagner M. Surgical strategies that may decrease leak after laparoscopic sleeve gastrectomy: a systematic review and meta-analysis of 9991 cases. Ann Surg. 2013;257(2):231–7.
14. Yuval JB, Mintz Y, Cohen MJ, Rivkind AI, Elazary R. The effects of bougie caliber on leaks and excess weight loss following laparoscopic sleeve gastrectomy. Is there an ideal bougie size? Obes Surg. 2013;23(10):1685–91.
15. Demeusy A, Sill A, Averbach A. Current role of staple line reinforcement in 30-day outcomes of primary laparoscopic sleeve gastrectomy: an analysis of MBSAQIP data, 2015–2016 PUF. Surg Obes Relat Dis. 2018;14(10):1454–61.
16. Barreca M, Renzi C, Tankel J, Shalhoub J, Sengupta N. Is there a role for enhanced recovery after laparoscopic bariatric surgery? Preliminary results from a specialist obesity treatment center. Surg Obes Relat Dis. 2016;12(1):119–26.
17. Bevilacqua LA, Obeid NR, Spaniolas K, Bates A, Docimo S Jr, Pryor A. Early postoperative diet after bariatric surgery: impact on length of stay and 30-day events. Surg Endosc. 2018;33:2475–8. https://doi.org/10.1007/s00464-018-6533-1.
18. Benevides ML, Oliveira SS, de Aguilar-Nascimento JE. The combination of haloperidol, dexamethasone, and ondansetron for prevention of postoperative nausea and vomiting in laparoscopic sleeve gastrectomy: a randomized double-blind trial. Obes Surg. 2013;23(9):1389–96.
19. Antor MA, Uribe AA, Erminy-Falcon N, Werner JG, Candiotti KA, Pergolizzi JV, et al. The effect of transdermal scopolamine for the prevention of postoperative nausea and vomiting. Front Pharmacol. 2014;5:55.
20. Telem DA, Gould J, Pesta C, Powers K, Majid S, Greenberg JA, Teixeira A, Brounts L, Lin H, DeMaria E, Rosenthal R. American Society for Metabolic and Bariatric Surgery: care pathway for laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2017;13(5):742–9.
21. Sethi M, Magrath M, Somoza E, Parikh M, Saunders J, Ude-Welcome A, Schwack B, Kurian M, Fielding G, Ren-Fielding C. The utility of radiological upper gastrointestinal series and clinical indicators in detecting leaks after laparoscopic sleeve gastrectomy: a case-controlled study. Surg Endosc. 2016;30(6):2266–75.
22. Diamantis T, Apostolou KG, Alexandrou A, Griniatsos J, Felekouras E, Tsigris C. Review of long-term weight loss results after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2014;10(1):177–83.
23. Pekkarinen T, Mustonen H, Sane T, Jaser N, Juuti A, Leivonen M. Long-term effect of gastric bypass and sleeve gastrectomy on severe obesity: do preoperative weight loss and binge eating behavior predict the outcome of bariatric surgery? Obes Surg. 2016;26(9):2161–7.
24. Juodeikis Ž, Brimas G. Long-term results after sleeve gastrectomy: a systematic review. Surg Obes Relat Dis. 2017;13(4):693–9.
25. Noel P, Nedelcu M, Eddbali I, Manos T, Gagner M. What are the long-term results 8 years after sleeve gastrectomy? Surg Obes Relat Dis. 2017;13(7):1110–5.
26. Himpens J, Dobbeleir J, Peeters G. Long-term results of laparoscopic sleeve gastrectomy for obesity. Ann Surg. 2010;252(2):319–24.
27. Boza C, Daroch D, Barros D, León F, Funke R, Crovari F. Long-term outcomes of laparoscopic sleeve gastrectomy as a primary bariatric procedure. Surg Obes Relat Dis. 2014;10(6):1129–33.

28. Cottam S, Cottam D, Cottam A, Zaveri H, Surve A, Richards C. The use of predictive markers for the development of a model to predict weight loss following vertical sleeve gastrectomy. Obes Surg. 2018;28(12):3769–74.
29. Clapp B, Wynn M, Martyn C, Foster C, O'Dell M, Tyroch A. Long term (7 or more years) outcomes of the sleeve gastrectomy: a meta-analysis. Surg Obes Relat Dis. 2018;14(6):741–7.
30. Lauti M, Lemanu D, Zeng ISL, Su'a B, Hill AG, MacCormick AD. Definition determines weight regain outcomes after sleeve gastrectomy. Surg Obes Relat Dis. 2017;13(7):1123–9.
31. Panunzi S, De Gaetano A, Carnicelli A, Mingrone G. Predictors of remission of diabetes mellitus in severely obese individuals undergoing bariatric surgery: do BMI or procedure choice matter? A meta-analysis. Ann Surg. 2015;261(3):459–67.
32. Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Aminian A, Brethauer SA, Navaneethan SD, Singh RP, Pothier CE, Nissen SE, Kashyap SR, STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes – 5-year outcomes. N Engl J Med. 2017;376(7):641–51.
33. Pucci A, Tymoszuk U, Cheung WH, Makaronidis JM, Scholes S, Tharakan G, Elkalaawy M, Guimaraes M, Nora M, Hashemi M, Jenkinson A, Adamo M, Monteiro MP, Finer N, Batterham RL. Type 2 diabetes remission 2 years post Roux-en-Y gastric bypass and sleeve gastrectomy: the role of the weight loss and comparison of DiaRem and DiaBetter scores. Diabet Med. 2018;35(3):360–7.
34. Aminian A, Brethauer SA, Andalib A, Nowacki AS, Jimenez A, Corcelles R, Hanipah ZN, Punchai S, Bhatt DL, Kashyap SR, Burguera B, Lacy AM, Vidal J, Schauer PR. Individualized metabolic surgery score: procedure selection based on diabetes severity. Ann Surg. 2017;266(4):650–7.
35. Del Genio G, Limongelli P, Del Genio F, Motta G, Docimo L, Testa D. Sleeve gastrectomy improves obstructive sleep apnea syndrome (OSAS): 5 year longitudinal study. Surg Obes Relat Dis. 2016;12(1):70–4.
36. Perysinakis I, Pappis HC, Margaris E. Current controversies in metabolic surgery for nonalcoholic fatty liver disease. Obes Surg. 2019;29:1058. https://doi.org/10.1007/s11695-019-03705-x.
37. Shouhed D, Steggerda J, Burch M, Noureddin M. The role of bariatric surgery in nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. Expert Rev Gastroenterol Hepatol. 2017;11(9):797–811.
38. Esquivel CM, Garcia M, Armando L, Ortiz G, Lascano FM, Foscarini JM. Laparoscopic sleeve gastrectomy resolves NAFLD: another formal indication for bariatric surgery? Obes Surg. 2018;28(12):4022–33.
39. von Schönfels W, Beckmann JH, Ahrens M, Hendricks A, Röcken C, Szymczak S, Hampe J, Schafmayer C. Histologic improvement of NAFLD in patients with obesity after bariatric surgery based on standardized NAS (NAFLD activity score). Surg Obes Relat Dis. 2018;14(10):1607–16.
40. Hanipah ZN, Mulcahy MJ, Sharma G, Punchai S, Steckner K, Dweik R, Aminian A, Schauer PR, Brethauer SA. Bariatric surgery in patients with pulmonary hypertension. Surg Obes Relat Dis. 2018;14(10):1581–6.
41. Ardila-Gatas J, Sharma G, Nor Hanipah Z, Tu C, Brethauer SA, Aminian A, Tolle L, Schauer PR. Bariatric surgery in patients with interstitial lung disease. Surg Endosc. 2019;33:1952. https://doi.org/10.1007/s00464-018-6475-7.
42. Arterburn D, Wellman R, Emiliano A, Smith SR, Odegaard AO, Murali S, Williams N, Coleman KJ, Courcoulas A, Coley RY, Anau J, Pardee R, Toh S, Janning C, Cook A, Sturtevant J, Horgan C, McTigue KM, PCORnet Bariatric Study Collaborative. Comparative effectiveness and safety of bariatric procedures for weight loss: a PCORnet cohort study. Ann Intern Med. 2018;169(11):741–50.
43. Osland E, Yunus RM, Khan S, Alodat T, Memon B, Memon MA. Postoperative early major and minor complications in laparoscopic vertical sleeve gastrectomy (LVSG) versus laparoscopic Roux-en-Y gastric bypass (LRYGB) procedures: a meta-analysis and systematic review. Obes Surg. 2016;26(10):2273–84.
44. Sippey M, Kasten KR, Chapman WH, Pories WJ, Spaniolas K. 30-day readmissions after sleeve gastrectomy versus Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2016;12(5):991–6.
45. Osland E, Yunus RM, Khan S, Memon B, Memon MA. Late postoperative complications in laparoscopic sleeve gastrectomy (LVSG) versus laparoscopic Roux-en-y Gastric Bypass (LRYGB): meta-analysis and systematic review. Surg Laparosc Endosc Percutan Tech. 2016;26(3):193–201.
46. Spaniolas K, Bates AT, Docimo S Jr, Obeid NR, Talamini MA, Pryor AD. Single stage conversion from adjustable gastric banding to sleeve gastrectomy or Roux-en-Y gastric bypass: an analysis of 4875 patients. Surg Obes Relat Dis. 2017;13(11):1880–4.
47. Chaar ME, Lundberg P, Stoltzfus J. Thirty-day outcomes of sleeve gastrectomy versus Roux-en-Y gastric bypass: first report based on Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program database. Surg Obes Relat Dis. 2018;14(5):545–51.
48. Reges O, Greenland P, Dicker D, Leibowitz M, Hoshen M, Gofer I, Rasmussen-Torvik LJ, Balicer RD. Association of bariatric surgery using laparoscopic banding, Roux-en-Y gastric bypass, or laparoscopic sleeve gastrectomy vs usual care obesity management with all-cause mortality. JAMA. 2018;319(3):279–90.
49. Khoursheed M, Al-Bader I, Mouzannar A, Ashraf A, Bahzad Y, Al-Haddad A, Sayed A, Fingerhut A. Postoperative bleeding and leakage after sleeve gastrectomy: a single-center experience. Obes Surg. 2016;26(12):2944–51.

50. El Chaar M, Stoltzfus J. Assessment of sleeve gastrectomy surgical technique: first look at 30-day outcomes based on the MBSAQIP database. J Am Coll Surg. 2018;227(6):564–72.
51. Debs T, Petrucciani N, Kassir R, Sejor E, Karam S, Ben Amor I, Gugenheim J. Complications after laparoscopic sleeve gastrectomy: can we approach a 0% rate using the largest staple height with reinforcement all along the staple line? Short-term results and technical considerations. Surg Obes Relat Dis. 2018;14(12):1804–10.
52. Varban OA, Sheetz KH, Cassidy RB, Stricklen A, Carlin AM, Dimick JB, Finks JF. Evaluating the effect of operative technique on leaks after laparoscopic sleeve gastrectomy: a case-control study. Surg Obes Relat Dis. 2017;13(4):560–7.
53. Gagner M, Buchwald JN. Comparison of laparoscopic sleeve gastrectomy leak rates in four staple-line reinforcement options: a systematic review. Surg Obes Relat Dis. 2014;10(4):713–23.
54. Ageno W, Becattini C, Brighton T, Selby R, Kamphuisen PW. Cardiovascular risk factors and venous thromboembolism: a meta-analysis. Circulation. 2008;117(1):93–102.
55. Stein PD, Matta F. Pulmonary embolism and deep venous thrombosis following bariatric surgery. Obes Surg. 2013;23(5):663–8.
56. Jamal MH, Corcelles R, Shimizu H, Kroh M, Safdie FM, Rosenthal R, et al. Thromboembolic events in bariatric surgery: a large multi-institutional referral center experience. Surg Endosc. 2015;29(2):376–80.
57. Morino M, Toppino M, Forestieri P, Angrisani L, Allaix ME, Scopinaro N. Mortality after bariatric surgery: analysis of 13,871 morbidly obese patients from a national registry. Ann Surg. 2007;246(6):1002–7; discussion 7–9.
58. Winegar DA, Sherif B, Pate V, DeMaria EJ. Venous thromboembolism after bariatric surgery performed by Bariatric Surgery Center of Excellence Participants: analysis of the Bariatric Outcomes Longitudinal Database. Surg Obes Relat Dis. 2011;7(2):181–8.
59. Shoar S, Saber AA, Rubenstein R, Safari S, Brethauer SA, Al-Thani H, et al. Portomesentric and splenic vein thrombosis (PMSVT) after bariatric surgery: a systematic review of 110 patients. Surg Obes Relat Dis. 2018;14(1):47–59.
60. American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. ASMBS updated position statement on prophylactic measures to reduce the risk of venousthromboembolism in bariatric surgery patients. Surg Obes Relat Dis. 2013;9(4):493–7.
61. Althuwaini S, Bamehriz F, Aldohayan A, Alshammari W, Alhaidar S, Alotaibi M, Alanazi A, Alsahabi H, Almadi MA. Prevalence and predictors of gastroesophageal reflux disease after laparoscopic sleeve gastrectomy. Obes Surg. 2018;28(4):916–22.
62. Santonicola A, Angrisani L, Cutolo P, Formisano G, Iovino P. The effect of laparoscopic sleeve gastrectomy with or without hiatal hernia repair on gastroesophageal reflux disease in obese patients. Surg Obes Relat Dis. 2014;10(2):250–5.
63. Burgerhart JS, Schotborgh CA, Schoon EJ, Smulders JF, van de Meeberg PC, Siersema PD, Smout AJ. Effect of sleeve gastrectomy on gastroesophageal reflux. Obes Surg. 2014;24(9):1436–41.
64. Reynolds JL, Zehetner J, Shiraga S, Lipham JC, Katkhouda N. Intraoperative assessment of the effects of laparoscopic sleeve gastrectomy on the distensibility of the lower esophageal sphincter using impedance planimetry. Surg Endosc. 2016;30(11):4904–9.
65. Braghetto I, Csendes A. Prevalence of Barrett's esophagus in bariatric patients undergoing sleeve gastrectomy. Obes Surg. 2016;26(4):710–4.
66. Ece I, Yilmaz H, Acar F, Colak B, Yormaz S, Sahin M. A new algorithm to reduce the incidence of gastroesophageal reflux symptoms after laparoscopic sleeve gastrectomy. Obes Surg. 2017;27(6):1460–5.
67. Hendricks L, Alvarenga E, Dhanabalsamy N, Lo Menzo E, Szomstein S, Rosenthal R. Impact of sleeve gastrectomy on gastroesophageal reflux disease in a morbidly obese population undergoing bariatric surgery. Surg Obes Relat Dis. 2016;12(3):511–7.
68. Desart K, Rossidis G, Michel M, Lux T, Ben-David K. Gastroesophageal reflux management with the LINX® system for gastroesophageal reflux disease following laparoscopic sleeve gastrectomy. J Gastrointest Surg. 2015;19(10):1782–6.

Laparoscopic Duodenal Switch

28

Michel Gagner

The Evolution

Morbid obesity and type-2 diabetes are now recognized as one of the main challenges of the twenty-first century. Although their origin maybe multifactorial, genetic components are probably the main defects, and surgery is now considered an accepted treatment leading to meaningful, life-lasting, favorable impact in this population.

Duodenal switch is the version 2.0 from the intervention proposed by Dr. Nicola Scopinaro, the biliopancreatic diversion with distal gastrectomy BPD performed in Genoa in 1979 [1]. Bile and pancreatic secretions are diverted and shunted away from the stomach, with a duodenal switch, rediscovered to decrease biliary reflux by Tom DeMeester et al. in 1987, an amelioration from the older Mann–Williamson procedure [2]. The gastrectomy technique was modified in 1988–1990, to perform a longitudinal gastrectomy (instead of a distal gastrectomy), in which the greater curvature was removed, leaving the lesser curve and vagal innervation, antrum and pylorus, and at a fair distance from the gastroesophageal junction. On the intestinal side, the common channel length was increased from 50 to 100 cm, [3, 4] therefore leaving an alimentary limb of 150 cm and leaving a length of biliopancreatic limb, anywhere from 100 to 350 cm. Dr. Douglass Hess from Ohio has used a percentage from the total intestinal length, an impractical way to collect data in the long term, basically making the common channel at 10% of the total small bowel, and alimentary limb with common channel at 40%. The first laparoscopic duodenal switch (DS), by Dr. Michel Gagner, was performed on July 2, 1999, at the Mount Sinai Hospital in New York City and published in 2000 [5]. These efforts had been supported prior to that from an animal study, using the porcine model at the research institute of Mount Sinai School of Medicine, with the help of Dr. Gregg Jossart and Dr. John DeCsepel who were clinical and research fellows at the time [6]. We have now reached a worldwide experience of 20 years for the laparoscopic DS.

What was described laparoscopically, included first a sleeve gastrectomy which provided minimal to moderate restriction, maintaining gastric emptying but most importantly decreased acid production to reduce the yield of marginal ulcers frequently seen in classic BPD operations: They had a gastroileostomy with a large gastric pouch of at least 200 ml, which in BPD had no gastric retention leading to severe dumping syndromes [7, 8]. However, gastric emptying and intestinal transit time after laparoscopic sleeve gastrectomy

M. Gagner (✉)
Herbert Wertheim School of Medicine, FIU, Miami, FL, USA

Hôpital du Sacré Coeur, Montreal, QC, Canada

Clinique Michel Gagner, Montreal, QC, Canada

Westmount Square Surgical Center, Westmount, QC, Canada

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_28

have been shown to be accelerated, by 20–50%. Secondly, the 150 cm alimentary limb and 100 cm common channel total an absorption length of 250 cm and decreases overall caloric absorption. Thirdly, the 100 cm common channel, where food mixes with biliopancreatic juices, results in diminished protein and fat absorption, which I like to call hypoabsorption, since the absorption mechanisms are intact, rather than awkwardly stating "malabsorption." Laparoscopic DS has also evolved recently, into a version 3.0, with a simpler procedure called SADI, for single anastomosis duodeno-ileostomy, where a loop of ileum at 250–300 cm is anastomosed at the pylorus, but with out a Roux connection, avoiding an ileoileostomy [9]. This will not be discussed in this chapter, as it is an entirely new set of preliminary data involved.

The Technical Elements

The surgeon may stand on the right side or between the patient's legs and the assistant to the left side, except for the intestinal part of the procedure where both are on the patient's left. The first 12 mm trocar is then placed in the umbilicus, for a 30° laparoscope. Two 12 mm ports are placed at the same level in the left and right upper quadrants. Additional 5 mm ports are placed, in the epigastria for a liver retractor, one in the left subcostal area for the assistant and one in the left lower quadrant for the intestinal part of the procedure. The short gastric vessels and branches from the gastro-epiploic arcade are divided off from the greater curvature, using ultrasonic shears, from about 6 cm proximal to the pylorus up to the angle of His.

The assistant forceps are placed on the lateral antrum from the left subcostal port, applying a left and upward traction, giving an excellent duodenal exposure. The pylorus is identified, and the peritoneum at the inferior and superior edge of the duodenum is opened, the gastroduodenal artery serving as a lateral limit of the transection and dissection.

This is called the inferior approach, which consists in a complete mobilization of the inferior and posterior attachments of the duodenum. The inferior antrum, pylorus, and first part of the duodenum are isolated using ultrasonic sears and clips. A window is then created on the upper aspect of the duodenum, to accommodate the anvil of a 60 mm linear stapler with a blue cartridge, and most often I use staple line reinforcement using an absorbable membrane, decreasing bleeding and avoiding the need for the duodenal stump oversewing. It also helps in straightening the duodenal wall for suturing during the anastomosis and provides a full opening preventing a stenosis.

A 60-French bougie is introduced, and gastric transection is started 6 cm from the pylorus using black and or green cartridges for the first two to three firings. As the transection progresses toward the fundus, the height of the staples is decreased from green to gold cartridges. The gastrectomy specimen is then extracted trough the umbilical trocar.

The patient is then placed in a Trendelenburg position with the left side down, and measurements are initiated retrograde at the ileocecal junction; a common channel of 100 cm is measured, the future site of the ileoileostomy, using clips on the mesentery. I prefer an umbilical tape of 50 cm for consistent measurement, with flat atraumatic bowel fenestrated forceps. The ileum is then run another 150 cm proximally, and an end-to-side duodeno-ileostomy handsewn is performed, making sure that no twists have occurred (250 cm from the ileocecal valve): It habitually needs a second verification from the ileocecal valve.

The first running posterior layer is made, joining the anti-mesenteric side of the small bowel to the proximal duodenum with 3-0 monofilament absorbable sutures, going from cephalad to caudad. A 2 cm enterotomy, as wide as possible, is made on each intestinal side, and another running suture is used to close the anterior part of the anastomosis, using a similar suture material. The ileum left to the anastomosis is divided with a laparoscopic stapler, and then an ileoileostomy created, side to side joining the end of the biliopancreatic limb with the common cannel at 100 cm from the ileocecal valve. The stump of the biliary limb should be on the left, and an anastomosis is created using a white cartridge of a 60 mm lin-

ear stapler, and the common enterotomy closed a single layer of 3-0 absorbable sutures.

The two mesenteric defects created are closed from the left using a 2-0 silk suture, starting at the ileoileostomy transversely. The patient is then placed head up with the left side up, and the transverse colon is lifted up to expose the Petersen's defect, which is then closed using also 2-0 silk suture on the left side, uniting the transverse mesocolon to the mesentery of the ileum going antecolic. Some surgeons will do a retrocolic passage, and in this case the meso-window, a third mesenteric defect, has to be judiciously closed circumferentially.

Outcomes

The DS has proven to be very effective in achieving and maintaining meaningful weight loss in the morbid and super-obese population (BMI >50 kg/m^2). In Dr. Henry Buchwald's systematic review, comparing weight loss surgical procedures, he suggested that BPD and duodenal switch are the most effective operations giving excess body weight loss (EBWL) of 73% at 2 years, which is maintained for 15–20 years; the Roux-en-Y gastric bypass stays behind in the 50–60% long-term, vertical banded gastroplasty at around similar rates 56% and gastric banding giving the poorest results below 50% [10]. BPD has been abandoned in favor of the DS, due to an unacceptably high rate of revisions for malnutrition, from a too undersized common channel of 50 cm, and to a higher marginal ulceration rate, from a too sizeable gastric pouch. VBGs have also fell tremendously, barely done these days, and replaced by the sleeve gastrectomy, avoiding the foreign body problem (mesh made of polypropylene or PTFE) that frequently eroded into the gastric wall. Sleeve gastrectomy was not part of this Buchwald review, as it started in 2000, but 10-year results show similar findings as the vertical banded gastroplasty, that is, around 50% EWL. This has been confirmed by systematic meta-analysis from a group in Australia [11].

In terms of level I evidence, Sovik et al. performed a randomized study of 60 super-obese patients (BMI 50–60 kg/m^2) to undergo either RYGB or DS and found EBWL to be 22.3, 44.0, and 54.4% following RYGB at 6 weeks, 6 months, and 1 year, respectively, compared to 28.1, 59.9, and 74.8% following DS [12]. This was republished with 5-year results confirming the superiority of DS and its great effect on type-2 diabetes [13].

For large cohorts, especially followed assiduously in countries with national healthcare system, the province of Quebec in Canada has been ideal, where all patients are easily tracked as they rarely move to other provinces or countries. Biertho et al., from Laval University in Quebec City, showed in a study of 810 morbidly obese patients with mean initial BMI of 44.2 + 3.6 kg/m^2 that EBWL plateaued at 76%, with a mean follow-up of 8.6 years [14]. Most US and European surgeons would think that DS is appropriate for super-obese patients, but in Quebec they are also done for the same indication as RYGB. It was concluded that DS was appropriate for morbidly obese patients as well (BMI >40 kgm^2) [14]. Concordantly, Anthone et al. in a review of 701 DS patients with preoperative BMIs ranging from 34–95 kg/m^2 found an EBWL of 69% after 1 year, 73% after 3 years, and 66% after 5 or more years follow-up [15]. Overall, studies examining the outcome of DS suggest analogous results with EBWL ranging from 61% to 85% with moderate term follow-up [16–22].

The DS has also a striking effect on obesity-related comorbidities. Mingrone and Rubino had randomized 60 obese patients with T2DM to receive medical therapy (lifestyle adjustments and hypoglycemic agents) or surgical intervention (RYGB or BPD). They reported no remission of T2DM in the medical therapy group, compared to 75% in the RYGB group and 95% in the BPD group after 2 years of follow-up [23]. That study was followed and reported in Lancet with 5-year results, showing a tremendously maintained effect of the BPD, almost by twofold, when compared to RYGB [24]. Overall, 19 (50%) of the 38 surgical patients (37% of the gastric bypass group and 63% of the biliopancreatic diversion group) maintained diabetes remission at 5 years, compared with none of the

15 medically treated patients ($p = 0{\cdot}0007$). Eight (42%) patients who underwent gastric bypass and 13 (68%) patients who underwent biliopancreatic diversion had an HbA1c concentration of 6.5% or less, compared with 4 (27%) medically treated patients ($p = 0{\cdot}04$) [24].

Iaconelli et al. [25] and Tsoli et al. [26] showed resolution of T2DM in all BPD patients 12 months after surgery. From the Cornell study, no patients had T2DM after 9 years [27]. A systematic review and meta-analysis confirmed that diabetes resolution was greatest for patients undergoing DS, followed by RYGB, and slightest for banding procedures [28]. Bariatric surgery has now been recommended for management of T2DM for selected obese patients (BMI >35 kgm^2) by the International Diabetes Federation; however, no specific surgical procedure was recommended [29, 30]. This panel was overrepresented by surgeons who did only RYGB, and very few DS surgeons were present at the conference, hence biases are such that a DS option was not well defended and represented. This may change in the future with the SADI operation, a version 3.0 of DS [30]. Astiarraga et al. assessed the effect of DS on T2DM in non-obese patients demonstrating amelioration of metabolic control and remission in one-third of patients, suggesting a weight-independent effect of the intervention [31].

Other cardiometabolic parameters, such as hypertension, nonalcoholic fatty liver disease, hypercholesterolemia, and hypertriglyceridemia, have also shown discernable correction ensuing DS [16–22]. Due to the profound lipid hypoabsorption, remission rates for dyslipidemia have been shown to be between 95 and 100% [16, 17, 32]. Furthermore, obstructive sleep apnea and hypopneas resolved in a majority of patients [32].

Treatment of Related Complications

A recent paper by Buchwald and Oien revealed that the proportion of DS procedures in relation to all bariatric surgeries declined from 6.1% to 4.9% to 2.1% in 2003, 2008, and 2011, respectively, and in the USA, it is at about 1% or less [33, 34]. This raises questions on why the procedure with the highest weight loss, lasting effects, and greatest reversal of obesity related comorbidities is the least performed bariatric intervention. The answer is likely multifactorial and complex. Firstly, the technical complexity of this procedure is a consideration, with the procedure being time-consuming and requiring a skilled laparoscopic bariatric surgeon. The laparoscopic approach, introduced by me in 1999, sought the benefits of DS weight loss and reduced morbidity associated with laparoscopic surgery [5]. In many studies, this has proven to be true, with lower postoperative complication rates [35, 36]. Likely, learning curves and operative volumes may be important considerations, with a majority of DS being performed at focused bariatric centers [37, 38]. Many fellowships do not have DS in their armamentarium, and duodenal dissection and transection are seen as a risky procedure for bile duct injury, hepatic arterial injury, or associated with high-leak rate at this upper anastomosis. These fears have not been confirmed. Also, it is the sleeve gastrectomy effect, as more and more bariatric surgeons are doing this procedure, now 70% of all primary bariatric procedures in the USA; it has reduced the use of DS which is now mostly used as a second-stage approach. The last 2 years have seen a resurgence of DS by 60%, mostly due to weight regain after sleeve gastrectomy [39].

In a meta-analysis of 361 studies including 85,048 patients, overall mortality within 30 days of bariatric surgery was found to by 0.28%. DS had the highest early mortality with a rate of 0.29% to 1.23% for open and 0.0% to 2.7% for laparoscopic procedures [40]. But this has changed in the last 20 years, where one sees the mortality of second-stage DS being similar to RYGB, that is, in the range of 0.1–0.2%.

One-year complication rates have been reported in the Bariatric Outcomes Longitudinal Database (BOLD); they are 4.6, 10.8, 14.9, and 25.7%, respectively, after LAGB, LSG, RYGB, and DS [41]. This comprises of minor complications such as gastrointestinal side effects including flatulence, malodorous stools, and major complications like anastomotic leak, the most

common serious early surgical complication, which should be less than 1%. One reason for a higher complication rate in DS is the fact that this procedure is often selected for super-obese patients, notoriously known for a higher complication rate. Avoidance of tension at the anastomosis is paramount, and the intestinal reconstructive part can be deferred as a second stage using good judgement. Hamoui et al. reviewed 701 DS cases performed over a 10-year period and reported that 5% of patients developed complications necessitating revisional surgery [42]. Protein malnutrition was the most common indication for reoperation. A postoperative complication rate of 15% was then seen in their revisional surgery group, with wound infections being the most common complication in this surgical team [42]. This often necessitates an elongation procedure in which the common channel is elongated by at least 100 cm at the expense of the biliopancreatic limb. This is not a complex laparoscopic procedure, as it involves transection of the alimentary limb at the connection and moving this proximally on the BP limb and making a side-to-side anastomosis. The end result is a common channel of 200 cm and a total distance between the duodenum and ileocecal valve of 350 cm.

Biertho et al. analyzed a series of 1000 DS patients, in which major complications occurred in 7% of patients, readmission was required in 12.7% of patients, and reoperations occurred in 6% of patients [36]. My own series from Cornell has shown no operative mortality, a 1.1% leak rate, 2.5% of surgical site infection, and 12.4% of reoperations over 9 years, including cholecystectomy, laparoscopy for bowel obstructions from adhesions or internal hernias, etc. [27] BMI was 30.1 kgm^2 at 1 year and 32.0 kgm^2 at 9 years, a pretty flat line. Body fat was reduced to 26% from >50% after 2 years. Complications requiring surgery were significant, and nutritional problems developed in 29.8% of patients over the course of observation. The baseline Beck Depression Index (BDI) was 13.9 and 7.2 in year 1, and from year 1 through 9, it remained unchanged [27]. There were significant positive changes in quality of life between baseline and year 1 for most domains. These positive changes were maintained for the follow-up cohorts. After surgery the resolution of comorbidities continued for the 9 years. Weight regain is still a possibility, and most would recommend a resleeve resection, not touching any limb lengths, unless a gross error has been done at initial surgery with too long limbs [43].

In a randomized trial, Sovik et al. compared mean operating time, median length of stay, and complication rates between RYGB and DS. On average RYGB required 91 min compared to 206 min for DS. Median length of stay was 2 days post-RYGB and 4 days post-DS. Perioperative complication rates were comparable between the two groups [12, 13]. But one has to mention that Sovik and their groups were not familiar with DS when they started this randomized trial, and equivalent experience might have been lacking. My own practice sees less than 24-hour stay these days, just like gastric bypass or sleeve gastrectomy, with operative time in the range of 2 hours.

DS is the bariatric procedure linked with some of the grandest perioperative malnutrition-/metabolic-related complications [44]. All patients must begin mineral, vitamin, and protein supplementation postoperatively and sometimes preoperatively; however, there should be a standardized approach to replacement to avoid deficiencies using dietary supplements. Following DS, patients may need 3000 Kcal per day and ingest 80 to 120 g of proteins, to overcome the hypoabsorption; otherwise they may become malnourished [45]. Iron-deficiency anemia, protein calorie malnutrition, hypocalcemia, and deficiency of fat-soluble vitamins ADEK, vitamin B1, vitamin B12, and folate are common [46]. DS has proven to be more hypoabsorptive compared to other bariatric surgeries; thus close follow-up is essential. Supplementation is of paramount importance; regrettably in this patient population compliance is lacking [47].

Aasheim et al. randomized 60 super-obese patients to receive either RYGB or DS compared vitamin D, vitamin A, and vitamin B1 levels postoperatively [48]. DS patients had lessened mean vitamin D and A serum concentrations, as well as an abrupt decline in vitamin thiamine compared to RYGB. But in this trial, insufficient

supplements were given to DS patients owing to the early learning curve of this group. Decreased vitamin D and calcium levels with associated secondary hyperparathyroidism have been demonstrated [49–51]. Marceau's group at Laval has confirmed with bone biopsies, with maintained serum PTH, that overall bone mineral density and fracture risks were unchanged 10 years after DS [52]. Clinically there have been case reports of DS-related vitamin A deficiency and associated night-blindness, post-DS peripheral neuropathies associated with B12 deficiencies, although rare, Wernicke's encephalopathy as a result of B1 deficiencies can be seen, especially if there is a stenosis in the sleeve or a stricture at the duodeno-ileostomy anastomosis [53–57]. From my own series of DS patients operated at Cornell, between 1999 and 2010, 274 patients were operated, but 190 patients have been able to be followed through (70% women): age 42.7 years, BMI 53.0 kg/m^2; year 1, 189 were available; year 3–193; year 5–132; year 7–98; year 9–68. BMI was 33.3 kgm^2 at year 1 and 31.5 kgm^2 at year 9. Baseline vitamin D was low and PTH high [58]. All patients took some supplements. Fat-soluble vitamins remained low, and protein deficiency appeared at year 3 and increased to 30% at year 9. At baseline serum zinc was normal, but at year 5, 45% were low. Hematocrit was low for 40% and hemoglobin for 46%. Iron deficiency continued through year 9, more marked in males. Calcium deficiency increased from year 3 and became steady. Half of patients had abnormal PTH at baseline and the percentage increased. Twenty percent had abnormal baseline magnesium values. This fluctuated during yearly observations [58]. I think most groups are not giving enough supplementations, and compliance is a huge problem, but when serum levels are low, it remains an opportunity to educate and correct.

Conclusions

Duodenal switch offers one of the best long-term controls of obesity-related diseases such as type-2 diabetes and is associated with one of the lowest risk of weight regain long-term. It should be part of surgeons' armamentarium, particularly for the management of weight regain following sleeve gastrectomy. Like any advanced surgical procedure, there is a learning curve associated with laparoscopic DS, but standardization of the different surgical steps allows keeping complication rates low. The use of a hand-sewn anastomosis allows keeping the risk of anastomotic leak to the lowest. In case of intraoperative difficulties, the procedure can be aborted to a stand-alone sleeve gastrectomy, and a duodenal switch can be performed 18 months to several years after the initial surgery, without losing its efficacy.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Scopinaro N, Gianetta E, Civalleri D, et al. Biliopancreatic bypass for obesity: II. Initial experience in man. Br J Surg. 1979;66(9):618–20.
2. DeMeester TR, Fuchs K, Ball C, Albertucci M, Smyrk TC, Marcus J. Experimental and clinical results with proximal end-to-end duodenojejunostomy for pathologic duodenogastric reflux. Ann Surg. 1987;206(4):414–26.
3. Marceau P, Biron S, Bourque RA, Potvin M, Hould FS, Simard S. Biliopancreatic diversion with a new type of gastrectomy. Obes Surg. 1993;3(1):29–35.
4. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. Obes Surg. 1998;8:267–82.
5. Ren CJ, Patterson E, Gagner M. Laparoscopic biliopancreatic diversion with duodenal switch: a case series of 40 consecutive patients. Obes Surg. 2000;10:514–23.
6. DeCsepel J, Burpee S, Jossart G, Andrei V, Murakami Y, Benavides S, Gagner M. Laparoscopic biliopancreatic diversion with a duodenal switch for morbid obesity: a feasibility study in pigs. J Laparoendosc Adv Surg Tech A. 2001;11(2):79–83.
7. Gagner M, Matteotti R. Laparoscopic biliopancreatic diversion with duodenal switch. Surg Clin North Am. 2005;85(1):141–9.
8. Feng JJ, Gagner M. Laparoscopic biliopancreatic diversion with duodenal switch. Semin Laparosc Surg. 2002;9(2):125–9.
9. Sánchez-Pernaute A, Rubio MÁ, Cabrerizo L, Ramos-Levi A, Pérez-Aguirre E, Torres A. Single-anastomosis duodenoileal bypass with sleeve gastrectomy (SADI-S) for obese diabetic patients. Surg Obes Relat Dis. 2015;11(5):1092–8.
10. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, Schoelles K. Bariatric sur-

gery: a systematic review and meta-analysis. JAMA. 2004;292:1724–37.
11. O'Brien PE, Hindle A, Brennan L, Skinner S, Burton P, Smith A, Crosthwaite G, Brown W. Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. Obes Surg. 2019;29(1):3–14.
12. Sovik TT, Taha O, Aasheim ET, et al. Randomized clinical trial of laparoscopic gastric bypass versus laparoscopic duodenal switch for superobesity. Br J Surg. 2010;97:160–6.
13. Risstad H, Søvik TT, Engström M, Aasheim ET, Fagerland MW, Olsén MF, Kristinsson JA, le Roux CW, Bøhmer T, Birkeland KI, Mala T, Olbers T. Five-year outcomes after laparoscopic gastric bypass and laparoscopic duodenal switch in patients with body mass index of 50 to 60: a randomized clinical trial. JAMA Surg. 2015;150(4):352–61.
14. Biertho L, Biron S, Hould FS, et al. Is biliopancreatic diversion with duodenal switch indicated for patients with body mass index <50 kg/m^2? Surg Obes Relat Dis. 2010;6:508–14.
15. Anthone GJ, Lord RVN, DeMeester TR, Crookes PF. The duodenal switch operation for the treatment of morbid obesity. Ann Surg. 2003;238:618–27.
16. Strain GW, Gagner M, Inabnet B, et al. Comparison of effects of gastric bypass and biliopancreatic diversion with duodenal switch on weight loss and body composition 1-2 years after surgery. Surg Obes Relat Dis. 2007;3:31–6.
17. Marceau P, Biron S, Hould FS, et al. Duodenal switch improved standard biliopancreatic diversion: a retrospective study. Surg Obes Relat Dis. 2009;5:43–7.
18. Topart P, Becouarn G, Salle A. Five-year follow-up after biliopancreatic diversion with duodenal switch. Surg Obes Relat Dis. 2011;43:205–8.
19. Crea N, Pata G, Di Betta E, et al. Long-term results of biliopancreatic diversion with or without gastric preservation for morbid obesity. Obes Surg. 2011;21:139–45.
20. Papadia FS, Adami GF, Marinari GM, et al. Bariatric surgery in adolescents: a long-term follow-up study. Surg Obes Relat Dis. 2007;3:465–8.
21. Nelson D, Beekley A, Carter P, et al. Early results after introduction of biliopancreatic diversion/duodenal switch at a military bariatric center. An J Surg. 2011;201:678–84.
22. Vage V, Nilsen R, Berstad A, et al. Predictors for remission of major components of the metabolic syndrome after biliopancreatic diversion with duodenal switch (BPDDS). Obes Surg. 2013;23:80–6.
23. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. N Engl J Med. 2012;266:1577–85.
24. Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Nanni G, Castagneto M, Bornstein S, Rubino F. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet. 2015;386(9997):964–73.
25. Iaconelli A, Panuzi S, De Gatetano A, et al. Effects of bilio-pancreatic diversion on diabetic complications: a 10-year follow-up. Diabetes Care. 2011;34:561–7.
26. Tsoli M, Chronaiou A, Kehagias I, et al. Hormone changes and diabetes resolution after biliopancreatic diversion and laparoscopic sleeve gastrectomy: a comparative prospective study. Surg Obes Relat Dis. 2013;9(5):667–77.
27. Strain GW, Torghabeh MH, Gagner M, Ebel F, Dakin GF, Abelson JS, Connolly D, Pomp A. The impact of biliopancreatic diversion with duodenal switch (BPD/DS) over 9 years. Obes Surg. 2017;27(3):787–94.
28. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery systematic review and meta-analysis. Am J Med. 2009;122:248–56.
29. Dixon JB, Zimmer P, Alberti KG, et al. Bariatric surgery: an IDF statement for obese type 2 diabetes. J Diabetes. 2011;3:261–4.
30. Rubino F, Nathan DM, Eckel RH, Schauer PR, Alberti KG, Zimmet PZ, Del Prato S, Ji L, Sadikot SM, Herman WH, Amiel SA, Kaplan LM, Taroncher-Oldenburg G, Cummings DE, Delegates of the 2nd Diabetes Surgery Summit. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Obes Surg. 2017;27(1):2–21.
31. Astiarraga B, Gastaldelli A, Muscelli E, et al. Biliopancreatic diversion in nonobese patients with type 2 diabetes: impact and mechanisms. J Clin Endocrinol Metab. 2013;98(7):2765–73.
32. Pata G, Crea N, Di Betta E, et al. Biliopancreatic diversion with transient gastroplasty and duodenal switch: long-term results of a multicentric study. Surgery. 2013;153:413–22.
33. Buchwald H, Oien D. Metabolic/bariatric surgery worldwide 2011. Obes Surg. 2013;23:427–36.
34. Ponce J, Nguyen NT, Hutter M, Sudan R, Morton JM. American Society for Metabolic and Bariatric Surgery estimation of bariatric surgery procedures in the United States, 2011–2014. Surg Obes Relat Dis. 2015;11(6):1199–200.
35. Kim WW, Gagner M, Kini S, Inabnet W, Quinn T, Herron D, Pomp A. Laparoscopic vs open biliopancreatic diversion with duodenal switch: a comparative study. J Gastrointest Surg. 2003;7(4):552–7.
36. Biertho L, Lebel S, Marceau S, Hould FS, Lescelleur O, Moustarah F, Simard S, Biron S, Marceau P. Perioperative complications in a consecutive series of 1000 duodenal switches. Surg Obes Relat Dis. 2013;9(1):63–8.
37. Nguyen NT, Paya M, Stevens M, et al. The relationship between hospital volume and outcome in bariatric surgery at academic medical centers. Ann Surg. 2004;240:586–93.

38. Ballantyne GH, Belsley S, Stephens D, et al. Bariatric surgery: low mortality at a high-volume center. Obes Surg. 2008;18:660667.
39. English WJ, DeMaria EJ, Brethauer SA, Mattar SG, Rosenthal RJ, Morton JM. American Society for Metabolic and Bariatric Surgery estimation of metabolic and bariatric procedures performed in the United States in 2016. Surg Obes Relat Dis. 2018;14(3):259–26.
40. Buchwald H, Estok R, Fahrbach K, Banel D, Sledge I. Trends in mortality in bariatric surgery: a systematic review and meta-analysis. Surgery. 2007;142(4):621–32; discussion 632–5
41. Demaria EJ, Winegar DA, Pate VW, et al. Postoperative outcomes of metabolic surgery to treat diabetes from sites participating in the ASMBS bariatric surgery center of excellence program as reported in the bariatric outcomes longitudinal database. Ann Surg. 2010;252:559–66.
42. Hamoui N, Chock B, Anthone GJ, Crookes PF. Revision of the duodenal switch: indications, technique and outcomes. J Am Coll Surg. 2007;204:603–8.
43. Gagner M, Rogula T. Laparoscopic Reoperative sleeve gastrectomy for poor weight loss after biliopancreatic diversion with duodenal switch. Obes Surg. 2003;13:649–54.
44. Sekhar N, Gagner M. Complications of laparoscopic biliopancreatic diversion with duodenal switch. Curr Surg. 2003;60(3):279–80.
45. Faintuch J, Matsuda M, Emilia M, et al. Severe protein-calorie malnutrition after bariatric procedures. Obes Surg. 2004;14:175–81.
46. Aills L, Blankenship J, Buffington C, et al. ASMBS allied health nutritional guidelines for the surgical weight loss patient. Surg Obes Relat Dis. 2008;4:S73–S108.
47. Marceau P, Biron S, Hould FS, et al. Duodenal switch: long-term results. Obes Surg. 2007;17:1421–30.
48. Aasheim ET, Bjorkman S, Sovik TT, et al. Vitamin status after bariatric surgery: a randomized study of gastric bypass and duodenal switch. Am J Clin Nutr. 2009;90(1):15–22.
49. Slater GH, Ren CJ, Siegel N, et al. Serum fat-soluble vitamin deficiency and abnormal calcium metabolism after malabsorptive bariatric surgery. J Gastrointest Surg. 2004;8:48–55.
50. Balsa JA, Botella-Carretero JI, Peromingo R, et al. Chronic increase of bone turnover markers after biliopancreatic diversion is related to secondary hyperparathyroidism and weight loss. Relation with bone mineral density. Obes Surg. 2010;20:468–73.
51. Sinha N, Shieh A, Stein EM, Strain G, Schulman A, Pomp A, Gagner M, Dakin G, Christos P, Bockman RS. Increased PTH and 1.25(OH)(2)D levels associated with increased markers of bone turnover following bariatric surgery. Obesity (Silver Spring). 2011;19(12):2388–93.
52. Marceau P, Biron S, Lebel S, et al. Does bone change after biliopancreatic diversion? J Gastrointest Surg. 2002;6:690–8.
53. Primavera A, Brusa G, Novello P, et al. Wernicke-Korsakoff encephalopathy following biliopancreatic diversion. Obes Surg. 1993;3:175–7.
54. Aasheim ET, Sovik TT, Bakke EF. Night blindness after duodenal switch. Surg Obes Relat Dis. 2008;4:685–6.
55. Aasheim ET, Hofso D, Hjelmesaeth J, Sandbu R. Peripheral neuropathy and severe malnutrition following duodenal switch. Obes Surg. 2008;18:1640–3.
56. Aasheim ET. Wernicke encephalopathy after bariatric surgery: a systematic review. Ann Surg. 2008;248:714–20.
57. Stroh C, Weiher C, Hohmann U, et al. Vitamin a deficiency (VAD) after a duodenal switch procedure: a case report. Obes Surg. 2010;20:397–400.
58. Strain GW, Torghabeh MH, Gagner M, Ebel F, Dakin GF, Connolly D, Goldenberg E, Pomp A. Nutrient status 9 years after biliopancreatic diversion with duodenal switch (BPD/DS): an observational study. Obes Surg. 2017;27(7):1709–18.

29 Management of Complications of Bariatric Operations

Aftab Jafri, Emanuele Lo Menzo, Samuel Szomstein, and Raul J. Rosenthal

Introduction

The 1991 National Institutes of Health consensus statement on surgery for obesity stated: "Severe obesity is a chronic intractable disorder; any therapeutic program must, therefore, be lifelong" [1]. The most recent population survey showed an increase in weight over time between the ages of 20 and 60, with the incidence of obesity increasing from 34% before 40 years of age to 41% in patients 40 to 60 years old [2]. Bariatric procedures are highly effective at achieving significant weight loss and improvement in comorbidities associated with obesity. The most recent position statement by the American Society for Metabolic and Bariatric Surgery supports the durability and effectiveness of bariatric procedures in treating morbid obesity and comorbidities when compared to medical management [3].

Along with the increased number of operations, complications will increase. In addition, surgeons performing metabolic surgery, particularly laparoscopic sleeve gastrectomy (LSG), outside of centers of excellence can potentially result in higher complications in the future.

In this chapter we present some of the technical complications encountered after the most common bariatric operations. Other perioperative complications such as cardiovascular, respiratory, renal, peripheral neuropathies, thromboembolic events, and rhabdomyolysis will not be discussed here.

Diagnosis

The diagnosis is mostly based on clinical findings with or without radiological evidence. A high index of suspicion is important since the clinical presentation of some of the complications is often initially subtle. In addition, some of the comorbidities associated with morbid obesity, such as diabetes, autoimmune diseases, or medications for such comorbidities (steroids, immunosuppressive medications), may further alter the clinical presentation of such complications. Vitals signs, particular early and sustained tachycardia, have always been regarded as one of the principal indicators of an intra-abdominal leak. Laboratory evaluation could substantiate the clinical diagnosis but often might be unrevealing. The common radiographic investigations include fluoroscopic gastrointestinal contrast studies and computed tomography (CT) scans. Not uncommonly, the use of both modalities sequentially increases sensitivity in recognizing postoperative complications. Finally, the use of upper endoscopy has assumed a prominent role not only for diagnostic but also for therapeutic purposes.

A. Jafri · E. Lo Menzo · S. Szomstein
R. J. Rosenthal (✉)
Department of General Surgery, The Metabolic and Bariatric Institute, Cleveland Clinic Florida, Weston, FL, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_29

Laparoscopic Adjustable Gastric Banding (LAGB)

LAGB underwent several changes over the years in terms of both design and technique of insertion, and these modifications contributed to the decrease in complications. Overall weight loss is less compared to options like LSG and Roux-en-Y gastric bypass (RYGB). The long-term complications and need for reintervention have contributed to the decrease in utilization of this procedure. Following are some salient complications of the operation [4].

Gastric/Esophageal Perforation

This is a very rare complication arising as a result of retroesophageal or gastric dissection. Another reason for esophageal perforations is the bougie that is inserted by the anesthesiologist while placing the band. It can manifest acutely with peritonitis or later as a port site infection. If recognized, intraoperative placement should be aborted, and the injury should be closed primarily with placement of drains in the vicinity of repair. Late presentation usually requires band removal, incision, and drainage if required and antibiotics for port site infection.

Band Slippage

It is the most common complication that can present in the early or late postoperative period. The reported incidence varies from 3% to 24% [4]. Incidence has dramatically decreased with the adoption of the pars flaccida technique. Another factor that has contributed to the decrease in slippage is the modification of the type of band utilized from the narrow high-pressure systems to the wider low-pressure circumferential balloon-type bands. The location of the slippage is almost exclusively anterior since the implementation of the pars flaccida technique. Patients usually presents with nausea and emesis followed by retching. Abdominal pain can also be present and can be an ominous sign of impending gastric necrosis. The first investigation should be an abdominal X-ray to demonstrate the position and angulation of the band. In fact, a horizontal position of the band, as opposed to the typical oblique, often is diagnostic for anterior prolapse. The first intervention consists of urgent complete emptying of the band. An upper GI contrast study will confirm the diagnosis (Fig. 29.1). Additional imaging with CT scan might be helpful to rule out perforation and abscesses. In the presence of abdominal pain, leukocytosis ischemia or perforation of the prolapsed stomach should be suspected, and intravenous antibiotics and emergent exploration with band removal should be performed.

Band Erosion

This complication is reported with an incidence of 0.3% to 14% [5]. Patients can present with nonspecific epigastric or abdominal pain, cessation of weight loss, gastrointestinal bleeding, abdominal abscess or infected/abscess at the port site, peritonitis, and pneumoperitoneum. The diagnosis is usually made by endoscopic evaluation. The management always entails band removal, which can be accomplished endoscopically when the buckle of the band is intragastric. More commonly the removal is done laparoscopically.

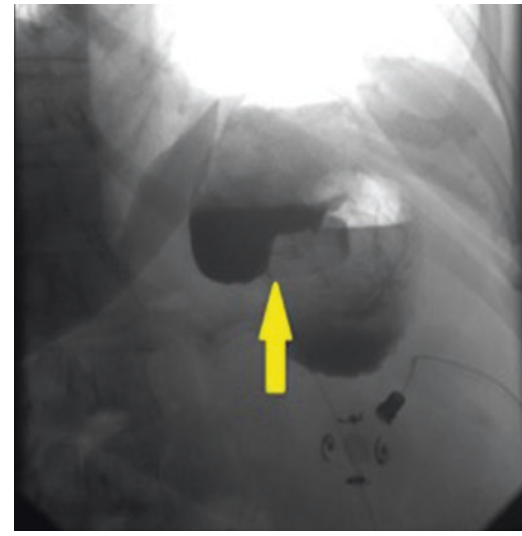


Fig. 29.1 Fluoroscopic image of an anterior band prolapse. The arrow indicates the horizontal position of the band

Esophageal Dilatation (Megaesophagus)

This is mostly seen in patients with slipped or overadjusted bands. The treatment of choice is to completely remove the fluid from the band and, after complete remission of the megaesophagus, slowly initiate readjustment. If tolerated, the band can be kept in place and monitored regularly with UGI series every 3 months. If no remission is encountered after a period of 12 weeks, the band has to be removed and the patient must continue close monitoring of symptoms. Alternative bariatric operations become controversial. Specifically, LSG might be contraindicated since these patients may require a gastric pull up if the megaesophagus does not go into remission.

Port and Catheter Complications

The port can dislocate or flip over. This can result in difficulty in adjusting the band and may require repositioning. Another complication that can occur is if the catheter connecting the port with the band breaks or gets disconnected. In this case, the patient will require a relaparoscopy to reconnect the port. Finally, as mentioned before, a port site infection can be the result of poor technique of adjustment or an early sign of erosion. In this case, the band and port have to be removed.

Sleeve Gastrectomy

Although regarded as one of the safest bariatric operations, it can potentially present with several complications.

Leaks

Leak is the most significant and feared complication of LSG. Reduction of gastric volume by 70–80% with competent pylorus and lower esophageal sphincter with resultant increased intragastric pressure along with a long staple line provides a fertile environment for leaks. Prevention of leaks can be accomplished with adequate mobilization of the greater curvature of the stomach and retrogastric attachment for proper visualization of the stomach to the lesser curvature, utilization of a 36 Fr or larger bougie to prevent strictures, avoiding rotation of the staple line with symmetrical lateral retraction, and consideration being given to the thickness of the stomach and appropriate selection of staple height cartridges. Although it is our routine practice, imbrication of the staple line has not definitively shown to decrease the leak rate [6]. The most common site of leak is the proximal staple line. Time of presentation is of importance, as acute leaks present within 7 days and are often related to technical problems with the staple line, ischemia, or energy source burns. Leaks developing between 1 and 6 weeks are termed as early and after 6 weeks as late—the latter posing a more challenging problem [6]. Diagnostic workup includes a CT abdomen and pelvis with PO and IV contrast. In unstable patients, emergent operative intervention is of paramount importance, with wide drainage and washout carried out in most cases, although direct repair of the leak can be attempted if location is obviously uncovered without risking further damage. Percutaneous image-guided drainage and endoscopic stent placement across the leak are a legitimate option in managing leaks in the acute and early settings in patients who are hemodynamically stable. Another option for mid to distal acute leaks is to convert them into controlled fistulas by placement of a T-tube and performing a feeding jejunostomy (Fig. 29.2) [7]. Chronic leaks are less amenable to the abovementioned techniques, and invasive surgical intervention remains the mainstay. Preoperative planning includes review of operative reports of the index operation and technique and extensive radiological review with upper gastrointestinal contrast studies inclusive of CT abdomen and pelvis. Reoperation is delayed until the patient is nutritionally replenished and the surgical field becomes less hostile (at 12 weeks). Surgical options can include suturing of an antecolic roux limb to the area of leak after adequate debridement of the inflamed gas-

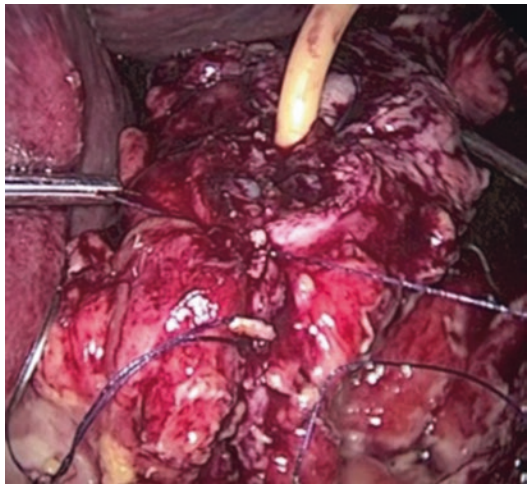


Fig. 29.2 T-tube in gastric sleeve to control leak

tric wall and an NG tube being advanced across the anastomosis or laparoscopic proximal gastrectomy with Roux-en-Y esophagojejunostomy [8]. The success rate of this approach is high, and the leak rate is documented to be 6.6%, requiring NPO for 4 weeks and TPN for its resolution. Endoscopic septotomy has been reported in the literature as a safe and effective technique for the management of LSG-associated leaks and collections, including those refractory to other endoscopic and percutaneous methods [9].

Postoperative Bleeding

The overall incidence of postoperative bleeding is low and rarely requires operative intervention. There are three potential sites of bleeding: intraabdominal, intraluminal, or port site. Postoperative nausea or emesis, melena, and port site hematomas should prompt further radiological investigative workup. Management requires serial vital signs monitoring, urine output monitoring, hemoglobin/hematocrit, and PRBC transfusion for hemodynamic instability or Hb <7.0 and possible operative exploration and hemostasis for intra-abdominal bleeding. Endoscopic evaluation and hemostasis are required and effective in cases where intraluminal bleeding is persistent and causes instability.

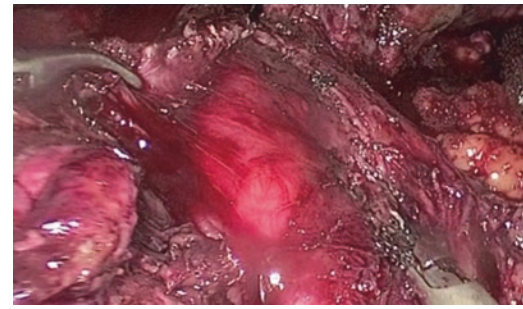


Fig. 29.3 Seromyotomy after stenosis of sleeve gastrectomy

Kinking/Stenosis/Obstruction

There are several points where partial obstruction or kink can be created. Most commonly this occurs while firing the stapling device at the incisura angularis, creating an almost 90° angle. If this sort of narrowing occurs and the patient develops persistent nausea and emesis, a conversion to RYGB may be necessary. Other alternatives include seromyotomy, which has a high leak rate, and central gastric resection with anastomosis (Fig. 29.3) [10].

GERD as a Late Complication After LSG

There are no major long-term complications after LSG, but there is development or worsening of GERD with or without esophagitis. To the authors' knowledge, the literature does not have level 1 evidence studies that demonstrate that LSG is contraindicated in patients with GERD. However, it is the authors' and the literature preference to recommend a gastric bypass in these patients instead. The latter should be supported by pH and manometry studies that demonstrate severe GERD with chronic esophagitis. When patients develop severe GERD after LSG, the initial treatment is proton pump inhibitors and close monitoring of esophagitis with EGD. In the case that GERD becomes intractable or complicated by aspiration pneumonia, gastric bypass is the preferred surgical approach.

Roux-en-Y Gastric Bypass

It induces weight loss by utilizing restrictive and malabsorptive strategies. The alimentary limb can be progressed to the gastric pouch in an antecolic or retrocolic fashion; there are mesenteric defects created during the course of the procedure that are potential sites for internal herniation and postoperative bowel obstruction. The complications of gastric bypass surgery can be divided into acute (7 days), early (7 days to 6 weeks), late (6 to 12 weeks), and chronic (>12 weeks).

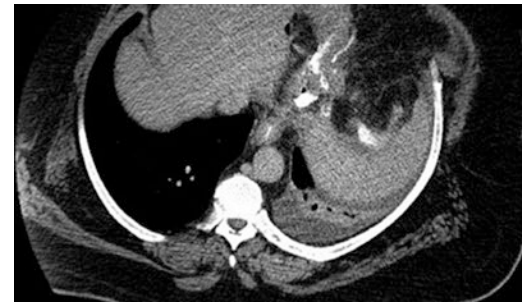


Fig. 29.4 CT scan showing a gastrojejunal anastomotic leak. Note the reactive pleural effusion and left lung atelectasis

Acute and Early Complications

Leaks

Undetected leaks remain the second leading cause of death after RYGB surgery. Potential sites of leaks include the gastrojejunal anastomosis, gastric pouch, gastric remnant, the jejunal blind end, and the jejunojejunal anastomosis. Approximately 70–80% of leaks occur at the gastrojejunal anastomosis, 10–15% at the gastric pouch, 5% at the jejunojejunal anastomosis, and 3–5% at the excluded stomach. Factors involved in the development of these leaks include tension, ischemia, and stapler misfiring. Some of the risk factors associated with higher incidence of leaks include male gender, super morbid obesity, age >55 years, and revisional procedures [11]. Signs and symptoms of leak include sustained tachycardia, abdominal pain, fever, nausea and vomiting, oliguria, and hemodynamic instability. The diagnosis can be confirmed by contrast upper gastrointestinal (UGI) fluoroscopic evaluation or CT scan. CT scan adds sensitivity to the diagnosis of GJ leaks because of the ability to show not only contrast extravasation and extraluminal collections but also indirect signs of leak, such as surrounding inflammatory changes, intraabdominal free air, and left pleural effusion (Fig. 29.4). Also, the CT scan is able to show additional sites of potential leaks, such as gastric remnant, J-J anastomosis, gastric remnant distention, etc. Management includes intravenous antibiotics, bowel rest, control of secretions, wide drainage, and early nutrition. The approach to drainage of the intra-abdominal collection is dictated by the clinical scenario. In the presence of hemodynamic instability, surgical intervention is warranted. During the operation, key steps include extensive irrigation; repair of the leak, if feasible and safe, although often unsuccessful; placement of feeding gastrostomy or enteral access distal to the leak site; and extensive closed-suction drain placement. Based on surgeons' individual skills and experience, these steps can be either accomplished laparoscopically or via an open approach. It is the authors' experience and recommendation to keep the surgical approach as simple as possible in this kind of clinical setting. In an emergency we should always choose the faster and simpler approach and refrain from redo anastomosis. Whenever the patient's hemodynamic status allows, endoscopic stent placement can be considered, and local sepsis control can be accomplished via percutaneous drainage or with the drains previously placed at the time of surgery. Failure of nonoperative management has been reported in 12% of the cases [12]. Regardless of the approach utilized, the mortality of a leak remains high at about 10% [13].

Gastrogastric Fistula (GGF)

Gastrogastric fistula refers to an abnormal communication between the gastric pouch and the excluded gastric remnant. The incidence of GGF varies between 0 and 46% in the literature. In our experience the incidence has been 1.2% [14]. Overall the incidence of GGF, similar to other complications after gastric bypass, has been steadily decreasing. Common presenting

symptoms include nausea, vomiting, and epigastric pain, which are present in approximately 80% of the patients. Marginal ulcer and failure to lose weight or weight regain should increase suspicion. The initial management includes radiological evaluation, and medical treatment comprises proton pump inhibitors, with the addition of sucralfate in case of a documented concomitant ulcer. The aim of the treatment is to reduce the acid production in the gastric remnant, which is now enhanced by the presence of food. In the presence of a marginal ulcer responding to medical therapy and in absence of additional symptoms, observation and re-evaluation in 6 weeks are acceptable. The minority of patients that do not respond adequately to medical treatment and present with weight regain or failure of weight loss will require additional interventions. Some authors advocate endoscopy as a first-line therapeutic intervention, claiming no increased complication if a future revisional surgery is necessary. Unfortunately, although often technically feasible, endoscopic closure has a very high recurrence rate. The success rate is inversely proportional to the diameter of the fistula itself. Fistulae larger than 1 cm have a much smaller chance of remaining closed after endoscopic treatment. Endoscopic techniques include injection of fibrin glue, plasma coagulation, clipping, stenting, and various endoscopic suturing techniques [13]. A much more effective treatment is surgical intervention. In the case of acid hypersecretion and chronic marginal ulcer, pouch trimming and redo gastrojejunostomy are fundamental. In the case of refractory marginal ulcer with proven acid hypersecretion in the pouch, a truncal vagotomy might be added. Remnant gastrectomy has also been advocated by our group as a treatment option for GGF [14]. In the cases of fistulae related to the failure of separation of the remnant from the gastric pouch, simple stapling across the previously undivided gastric bridge will be appropriate. This is especially true when the fistula is not in proximity of the gastrojejunal anastomosis.

Postoperative Hemorrhage

Postoperative hemorrhage has been reported in 1.9–4.4% of gastric bypass procedures [15]. The bleeding could be either intraluminal or extraluminal, and it usually originates from the staple lines of the GJ or JJ anastomosis, gastric remnant, or gastric pouch (Fig. 29.5). The signs and symptoms vary from mild tachycardia to signs of hypovolemic shock with hypotension and oliguria. It is important to remember that intraluminal bleeding can also determine intestinal obstruction and devastating complications (anastomotic leak, gastric remnant perforation) even if the bleeding is self-limiting. Although most of the immediate postoperative hemorrhages are self-limiting and can be managed with blood product transfusion, stopping anticoagulation, and aggressively correcting coagulation derangements, the presence of hemodynamic instability or the continuous requirement of blood transfusion is an indication for immediate intervention. In the early postoperative period, the role of endoscopy for the evaluation of intraluminal bleeding is limited to the evaluation and potential treatment of the gastrojejunal anastomosis. More aggressive endoscopic procedures (enteroscopy and double-balloon enteroscopy) to evaluate jejunojejunostomy and gastric remnant should be reserved for late postoperative bleeding. Whenever endoscopic intervention is not feasible or appropriate, operative intervention should not be delayed. The hemodynamic status of the patient along with the

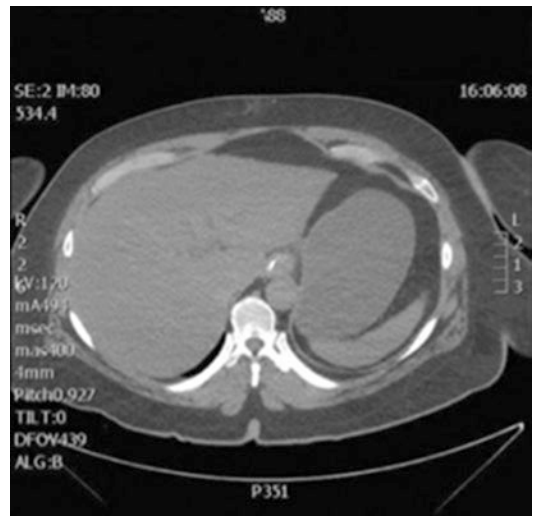


Fig. 29.5 CT scan showing a gastric remnant filled with blood secondary to an intraluminal bleeding after gastric bypass

surgeon's comfort level will determine if a laparoscopic or open approach is chosen. Often the intraabdominal source of bleeding is not found, but hematoma evacuation and washout expedite the patient's recovery. In the presence of an intraluminal bleeding source, the affected anastomosis can be approached directly or intraluminally via an adjacent enterotomy.

Small Bowel Obstruction

Although small bowel obstruction can occur at any time after gastric bypass, up to 48% occur within the first month [16]. Based on the location the obstruction can be classified in type A, when the alimentary limb is affected; type B, when the biliopancreatic limb is obstructed; and type C, common channel obstruction. Early postoperative obstruction can further be divided into mechanical or functional. Stenosis at the anastomotic sites is usually due to postoperative edema and tends to resolve in 24–48 hrs. It is important to avoid vomiting and retching during this phase in order to prevent aspiration and anastomotic disruption. Antiemetics, inhibitors of acid secretions, and possible tube decompression, with nasogastric tubes carefully placed under fluoroscopic guidance, are helpful in the expectant management of these patients. This is especially true if partial obstruction is present. In cases of complete obstruction or whenever the clinical picture does not improve, technical issues are involved, and anastomotic revision is necessary. Intraluminal clots from recent staple line bleeding have also been described as a cause of early mechanical obstruction. Radiographic evaluation is essential in the diagnosis. It is important to evaluate not only the site of obstruction but also the status of the proximal bowel or stomach. The presence of gastric remnant distention has to be carefully evaluated, and it can be the only apparent sign of a distal obstruction. The intervention varies based on the type and degree of distention. Purely air-filled remnant without any bowel dilatation can be observed with sequential X-rays, as long as the patient is asymptomatic. Most of the time, this finding is related to a transient "vagal stunning" and is self-limited. Metoclopramide can be utilized with variable results in this case, as long as distal obstruction has been ruled out. If the patient is symptomatic (left shoulder pain, hiccups, retching), percutaneous or operative decompression is in order. Whenever the gastric remnant is fluid-filled, the most likely cause is the presence of a distal obstruction. Early intervention is usually recommended in this case. Percutaneous decompression is not advised because it will not resolve the distal obstruction and the intraluminal fluid will likely leak around the insertion site, as this is typically not buttressed against the abdominal wall. Acute gastrojejunostomy strictures are rare and they are mostly related to technical errors. The initial treatment is observation to allow edema resolution. If after a reasonable waiting period (4–5 days) there is no improvement, endoscopic dilatation or redo anastomosis is indicated. Early endoscopic dilatation might be necessary but has to be conservative in the immediate postoperative period. There is no data to establish when it is too early to perform endoscopic dilatation and when safe. Endoscopic dilatation has been reported as early as 7 days postoperatively [16]. Usually the patient can, then, be kept on a mostly liquid diet until 4–6 weeks after surgery and be submitted to a more aggressive and safer endoscopic dilatation. Early strictures (7 days to 6 weeks) are usually ischemic in origin or due to foreign bodies (suture or staples extrusion) or marginal ulcers.

Internal hernias can cause mechanical obstruction in the early/acute phase, or more likely, late/chronic after the visceral fat diminishes as a result of effective weight loss. They are the most common cause of bowel obstruction after laparoscopic RYGB. Their incidence has been reported in up to 9% of the cases [17]. The potential mesenteric spaces through which internal hernias occur vary based on the configuration of the bypass reconstruction. Typically, after retrocolic retrogastric bypass, three defects are present: transverse mesocolon, Petersen's (between the Roux limb and the transverse mesocolon), and mesenteric defect at the jejunojejunostomy. One of the advantages claimed by the proponents of the antecolic antegastric reconstruction technique is the decreased incidence of internal hernias, as a mesocolic defect is not created. Other

important factors that likely affect the incidence of internal hernias are the division of the mesentery, the length of the limbs, and the orientation of the jejunojejunostomy. In fact, some authors have suggested that the counterclockwise rotation of the Roux limb reconstruction causes fewer internal hernias (in particular at the Petersen's space) than the clockwise rotation [17]. If the ability to perform gastric bypass laparoscopically has significantly decreased the incidence of wound infection and hernias, it has increased the possibility for potential acute postoperative port site hernia with obstruction. The reported incidence of port site hernias is 0.74% for all laparoscopic procedures and 0.57% after bariatric surgery [18]. Current recommendations call for closure of trocars >10 mm in diameter. However, in obese patients, 12 mm ports from radially dilating nonbladed trocars are not routinely closed, based on level II data, especially if off the midline. Port site hernias are often difficult to diagnose simply by physical exam because of the patient body habitus and the common presence of port site tenderness and occasional seromas. A liberal use of CT scan can reliably identify the condition, which requires prompt re-exploration. Also, reconstruction configuration errors (Roux-en-O) determine mechanical obstruction. This type of configuration error occurs when the biliopancreatic limb is mistakenly anastomosed to the gastric pouch. The typical presentation includes abdominal pain, nausea, bilious vomiting, and rapid weight loss. Although sometimes the clinical presentation is quite dramatic with a picture of proximal small bowel obstruction, at times all the diagnostic modalities (contrast upper GI and CT scan) can be normal. Additional radiographic studies that can assist in the diagnosis are fluoroscopic examination with contrast directly injected in the gastric remnant (with access via a gastrostomy tube if present) and hepatobiliary iminodiacetic acid (HIDA) scan. The latter test can unequivocally show the radionuclide excreted in the duodenum reflux back into the gastric pouch and esophagus. Besides the mild generalized ileus that can be encountered after laparoscopy, the majority of functional obstructions occur at the level of the gastric remnant. The severity varies from just mild dilatation of the remnant in an asymptomatic patient to impending remnant perforation with nausea, hiccups, shoulder pain, and secondary vomiting. Most of the cases are self-limiting and are due to the previously mentioned "vagal stunning." In these cases, medical treatment with metoclopramide and close observation with follow-up imaging are sufficient. In the cases of symptomatic remnant distention, percutaneous or operative drainage is mandatory. As previously mentioned, the drainage method has to be dictated by the clinical scenario and the imaging findings.

Late and Chronic Complications

Marginal Ulcers (MU), Stricture

Marginal ulcers and stricture are analyzed together due to the frequent coexistence and similar etiology. The incidence of marginal ulceration has been reported between 1% and 16%, whereas the incidence of strictures has been estimated in up to 27% [16]. Several factors have been associated with their pathogenesis, including ischemia, acid exposure, a foreign body at the anastomotic site, medications, and tobacco. The treatment of marginal ulcers is primarily medical, with acid suppression with proton pump inhibitors combined with cytoprotective agents (Sucralfate). Approximately one-third of the patients will require surgical intervention either because of intractability or complications (i.e., bleeding, perforation, or stricture). Bleeding should be treated endoscopically, and in case of failure or recurrence, oversewing the ulcer bed is the treatment of choice. In cases of hemodynamic instability, gastrojejunal resection with anastomosis ± vagotomy might play a role. Perforations are usually treated with Graham patch alone or primary closure with omental patch, and only rarely anastomotic resection with new anastomosis is feasible or indicated. Anastomotic strictures are largely managed by endoscopic dilatation (either using through-the-scope balloon dilators or Bougie dilators) with a high success rate. The need for surgical revision has been reported in less than 1% of the cases.

Intussusception

Intussusception is a rare cause of mechanical obstruction after gastric bypass. Its reported inci-

dence is between 0.07% and 0.15%, and it seems to occur with equal frequency after open and laparoscopic approach. Almost invariably the site of intussusception is around the jejunojejunal anastomosis, and no lead points are usually identified. The clinical presentation can be acute or chronic with spontaneous reduction and relapsing crampy abdominal pain. The most reliable imaging study is the CT scan with oral contrast with the typical "target" sign, but its accuracy is only 80%. In the majority of cases, the intussusception will resolve spontaneously, and no surgical intervention will be required. However, in case of recurrent episodes or when the intussusception does not resolve, surgery is the only choice. As far as the preferred surgical approach, the surgeon's experience and comfort should dictate if laparoscopic or open. If the laparoscopic approach is chosen, prompt conversion to open laparotomy is necessary in the presence of vascular compromised bowel or in case of massive bowel dilatation that prevents adequate visualization. If no additional procedures are done, the chance of recurrence is nearly 100%, whereas plication of the common channel to the biliopancreatic limb and resection and reconstruction of the jejunostomy decrease the recurrence rates to 40% and 12%, respectively [19].

Conclusions

Complications can be expected to be seen more frequently as the number of patients who undergo weight loss surgery rises. It is therefore important for general surgeons to have an understanding of the common bariatric procedures and their complications.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Gastrointestinal surgery for severe obesity. Consens Statement. 1991;9(1):1–20. Review.
2. Grabovac I, Smith L, Stefanac S, Haider S, Cao C, Waldhoer T, Jackson SE, Yang L. Healthcare providers' advice on lifestyle modification in the US population: results from the National Health and Nutrition Examination Survey 2011–2016. Am J Med. 2018;132(4):489–497.e1.
3. Azagury D, Papasavas P, Hamdallah I, Gagner M, Kim J. ASMBS Position Statement on medium- and long-term durability of weight loss and diabetic outcomes after conventional stapled bariatric procedures. Surg Obes Relat Dis. 2018;14:1425–41.
4. Lo Menzo E, Szomstein S, Rosenthal R. Update on treatment of morbid obesity with adjustable gastric banding. Surg Clin North Am. 2016;96(4):795–813. https://doi.org/10.1016/j.suc.2016.03.010. Review.
5. Cherian PT, Goussous G, Ashori F, Sigurdsson A. Band erosion after laparoscopic gastric banding: a retrospective analysis of 865 patients over 5 years. Surg Endosc. 2010;24(8):2031–8.
6. Noel P, Nedelcu M, Gagner M. Impact of the surgical experience on leak rate after laparoscopic sleeve Gastrectomy. Obes Surg. 2016;26(8):1782–7.
7. Court I, Wilson A, Benotti P, Szomstein S, Rosenthal RJ. T-tube gastrostomy as a novel approach for distal staple line disruption after sleeve gastrectomy for morbid obesity: case report and review of the literature. Obes Surg. 2010;20(4):519–22.
8. Sasson M, Ahmad H, Dip F, Lo Menzo E, Szomstein S, Rosenthal RJ. Comparison between major and minor surgical procedures for the treatment of chronic staple line disruption after laparoscopic sleeve gastrectomy. Surg Obes Relat Dis. 2016;12(5):969–75.
9. Mahadev S, Kumbhari V, Campos JM, Galvao Neto M, Khashab MA, Chavez YH, Bessler M, Gonda TA. Endoscopic septotomy: an effective approach for internal drainage of sleeve gastrectomy-associated collections. Endoscopy. 2017;49(5):504–8.
10. Dapri G, Cadière GB, Himpens J. Laparoscopic seromyotomy for long stenosis after sleeve gastrectomy with or without duodenal switch. Obes Surg. 2009;19(4):495–9.
11. Ballesta C, Berindoague R, Cabrera M, Palau M, Gonzales M. Management of anastomotic leaks after laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2008;18(6):623–30.
12. Gonzalez R, Sarr MG, Smith CD, Baghai M, Kendrick M, Szomstein S, et al. Diagnosis and contemporary management of anastomotic leaks after gastric bypass for obesity. J Am Coll Surg. 2007;204(1):47–55.
13. Cucchi SG, Pories WJ, MacDonald KG, Morgan EJ. Gastrogastric fistulas. A complication of divided gastric bypass surgery. Ann Surg. 1995;221(4):387–91.
14. Salimath J, Rosenthal RJ, Szomstein S. Laparoscopic remnant gastrectomy as a novel approach for treatment of gastrogastric fistula. Surg Endosc. 2009;23(11):2591–5.
15. Cho M, Kaidar-Person O, Szomstein S, Rosenthal RJ. Laparoscopic remnant gastrectomy: a novel approach to gastrogastric fistula after Roux-en-Y gastric bypass for morbid obesity. J Am Coll Surg. 2007;204(4):617–24.
16. Rosenthal RJ. Dilating the stenotic gastrojejunostomy after laparoscopic Roux-en-Y gastric bypass for morbid obesity: when things go wrong. J Gastrointest Surg. 2009;13(9):1561–3.

17. Nimeri AA, Maasher A, Al Shaban T, Salim E, Gamaleldin MM. Internal hernia following laparoscopic Roux-en-Y gastric bypass: prevention and tips for intra-operative management. Obes Surg. 2016;26(9):2255–6. Ver Steeg K
18. Owens M, Barry M, Janjua AZ, Winter DC. A systematic review of laparoscopic port site hernias in gastrointestinal surgery. Surgeon. 2011;9(4):218–24.
19. Edwards MA, Grinbaum R, Ellesmere J, Jones DB, Schneider BE. Intussusception after Roux-en-Y gastric bypass for morbid obesity: case report and literature review of rare complication. Surg Obes Relat Dis. 2006;2(4):483–9.

Tailoring Surgical Treatment for the Individual Patient

30

Verónica Gorodner, Marco Di Corpo, and Francisco Schlottmann

Introduction

Certainly, bariatric surgery numbers in the USA have changed over the years. Not only the amount of surgeries has increased, but also the type of elected operation has shifted. In 2011, the most frequent operation performed was the Roux-en-Y gastric bypass (RYGB) accounting for almost 37% of the total, while sleeve gastrectomies (SGs) occupied 18% of the procedures. In 2017, the inverse phenomenon was observed. RYGB accounted for 18% of the cases, while SG scaled up to nearly 60% [1]. Clearly, there are several reasons that might explain this occurrence. SG supporters might argue that this operation has no anastomosis, no mesenteric defects, and no malabsorption. In addition, there is less incidence of dumping syndrome, the stomach can be accessed by endoscopy, and for sure SG is a less complex technique. The objective of this chapter was to clarify real advantages and disadvantages of the two most popular procedures, in order to assist the surgeon in tailoring the surgical treatment to the individual patient. Outcomes related to type 2 diabetes, weight loss, complications, and gastroesophageal reflux disease (GERD) will be analyzed.

Roux-en-Y Gastric Bypass

RYGB was introduced in Iowa by Mason in 1967 [2]. The original technique has experienced several modifications. The current one includes division of the stomach with the consequent creation of a small gastric pouch, followed by jejunal transection and posterior Roux-en-Y reconstruction. This operation is considered as a mixed procedure, because it combines restriction and malabsorption (Figs. 30.1 and 30.2).

Sleeve Gastrectomy

The sleeve gastrectomy is a purely restrictive procedure, although resection of the fundus of the stomach might decrease temporarily ghrelin levels, one of the hormones involved in the regulation of the appetite. The

V. Gorodner (✉)
Programa Unidades Bariátricas,
Buenos Aires, Argentina

M. Di Corpo
Department of Surgery, University of North Carolina,
Chapel Hill, NC, USA

University of North Carolina at Chapel Hill,
Chapel Hill, NC, USA
e-mail: marco_dicorpo@med.unc.edu

F. Schlottmann
Department of Surgery, Hospital Alemán of Buenos Aires, University of Buenos Aires,
Buenos Aires, Argentina

Department of Surgery, University of North Carolina,
Chapel Hill, NC, USA

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_30

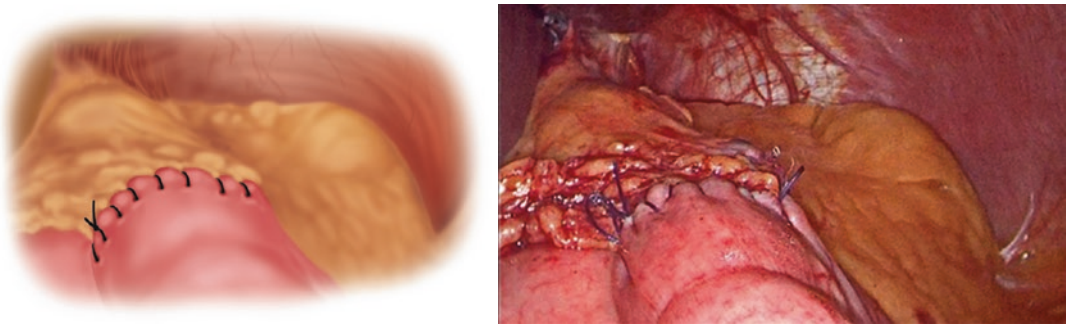


Fig. 30.1 Roux-en-Y gastric bypass, gastrojejunostomy

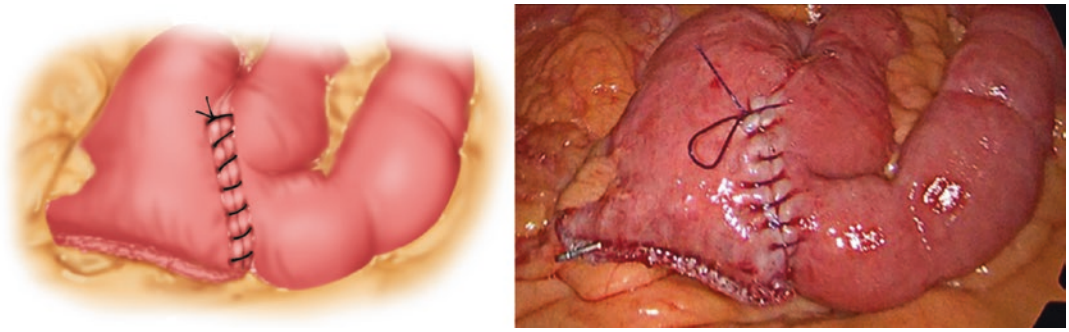


Fig. 30.2 Roux-en-Y gastric bypass, jejuno-jejunostomy

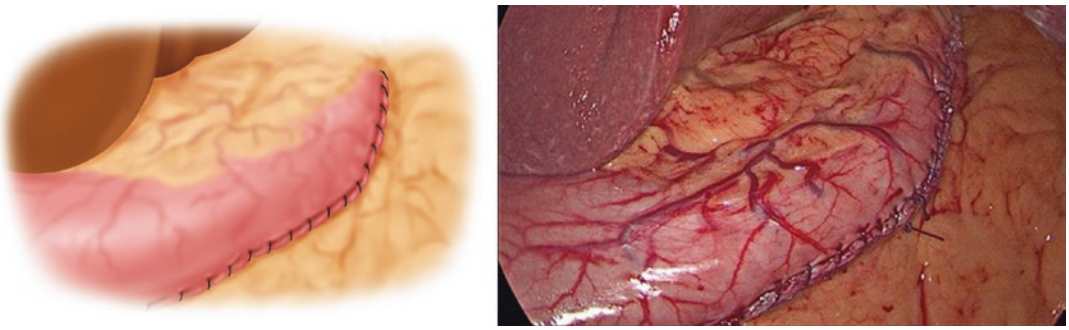


Fig. 30.3 Sleeve gastrectomy

operation includes removal of approximately three-fourth of stomach, with the subsequent reduction in gastric volume (Fig. 30.3). The first SG was performed in 2000, by Michel Gagner in New York. This operation emerged as an attempt in decreasing complications after duodenal switch in super–super-obese patients. The SG was designed as a first step of a two-stage procedure, which included a SG followed by a RYGB. The idea was to complete the second step of the procedure once the patient had lost enough weight in order to decrease the risk of complications [3]. Years later, the American Society for Metabolic and Bariatric Surgery (ASMBS) recognized SG as a primary bariatric procedure, due to its effectiveness and safety already demonstrated during several consensuses [4–6].

Classification of Obesity

Body mass index (BMI) calculation is the most utilized method to diagnose and classify obesity. BMI results from the ratio between weight (kg) and height (m^2). Obesity is categorized as follows:

- Obesity Class I: BMI 30–34.9 kg/m^2
- Obesity Class II: BMI 35–39.9 kg/m^2
- Obesity Class III: BMI ≥40 kg/m^2

Selection Criteria

According to the NHI consensus, patients with BMI >40 kg/m^2 or between 35 and 40 with comorbidities such as type 2 diabetes, cardiovascular disease, or physical alterations that interfere with normal life are considered candidates for bariatric surgery [7]. Patients should be motivated and well informed, and they must understand benefits and risks of surgery.

Results

So far, both procedures have been briefly introduced, and selection criteria have been exposed. Advantages and disadvantages according to published results will be discussed next.

Effect on Type 2 Diabetes

One of the most classic publications approaching this topic is the STAMPEDE trial. In this study, 150 obese patients with type 2 diabetes were randomized to either medical or surgical treatment. Surgical treatment comprised SG and RYGB; patients were followed-up for 5 years. Primary outcome was HbA1c ≤6, with or without diabetes medications. At the end of the trial, 5.3% of the patients in the medical treatment (MT) group, 28.6% in the RYGB, and 23.4% in the SG group were able to achieve this goal. The statistical analysis showed that there was no difference between both surgical procedures; however, the difference was evident after comparison between MT versus RYGB ($p = 0.01$) and MT versus SG ($p = 0.03$).

The key part came after analyzing the need for any type of medication for type 2 diabetes control. Almost half of the patients (45%) in the RYGB group were not taking any medications. Remarkably, this number decreased to 25% in the SG group ($p < 0.05$). This means that type 2 diabetes was better controlled, with fewer medications after RYGB than after SG [8].

An interesting meta-analysis including five randomized controlled trials (RTC), with 396 patients (RYGB = 196 and SG = 200), was performed by Li et al. Remission was defined as fasting plasma glucose levels <126 mg/dL with HbA1c <6.5% without oral medications or insulin. Authors concluded that both procedures were effective in the treatment of type 2 diabetes. However, the remission rate was much higher in the RYGB group ($p = 0.001$) [9].

Conversely, the following two studies did not find any statistically significant difference. Peterli conducted a randomized multicenter study in Switzerland, analyzing results from 217 patients who were appointed either to SG ($n = 107$) or RYGB ($n = 110$). At 5-year follow-up, complete remission was observed in 61.5% of the patients of the SG group versus 67.9% in the RYGB group (p = NS) [10].

Similarly, the SLEEVEPASS randomized Clinical Trial performed in Finland included 238 patients who were assigned to undergo either SG or RYGB. At 5-year follow-up, complete remission of diabetes was observed in 12% of patients undergoing SG and 25% of patients after RYGB (p = NS). No differences were found either in fasting plasma glucose or HA1c levels among both procedures at the same follow-up period. Authors attributed this disparity respect to other studies to possible differences in preoperative diabetes duration [11].

Weight Loss

Schauer et al. also compared weight loss among groups. Change in BMI from baseline was −5,

−23, and −18 for MT, RYGB, and SG, respectively. Statistical analysis showed significant differences among all comparisons (surgical vs. MT p <0.05 and RYGB vs. SG p = 0.01), being RYGB the best treatment option in terms of weight loss [8].

The following data comes from an attractive meta-analysis of 14 comparative studies (RYGB vs. SG), with 5264 patients. There were 2782 RGYB (53%) and 2482 SG (47%). The primary end point was to compare mid- (3–5 years) and long-term (>5 years) weight loss between both procedures. Authors did not find any difference in weight loss at midterm follow-up. However, RYGB patients presented a clear superior weight loss in the long run (p <0.05) [12].

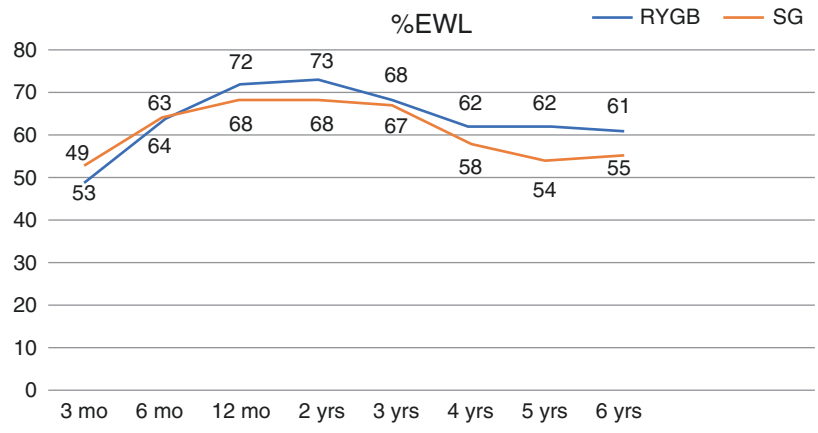
Furthermore, the study from Finland found superiority of RYGB over SG in terms of weight loss. At 5-year follow-up, mean excess weight loss (EWL) for SG was 49%, whereas that number scaled up to 57% for the RYGB group. Authors concluded that there was not equivalence, based on their predefined margins of equivalence [11].

Contrariwise, Peterli et al. did not find any statistically significant difference in percentage excess BMI loss for SG compared with RYGB (61.1 vs. 68.3%, p = NS) at 5-year follow-up. Moreover, they found no difference in the proportion of patients being able to reach a percentage excess BMI loss greater than 50% at 5 years (68.3% in the SG group vs. 76% in the RYGB group, p = NS) [10].

The subsequent numbers come from our own experience, not published yet. A total of 2839 patients were operated. There were 2383 (84%) RYGB and 456 SG (16%). Interestingly, SG showed superior weight loss at 3 months. After that period of time, RYGB demonstrated better results steadily. At 6-year follow-up, the percentage of EWL was 61% for RYGB and 55% for the SG group (p <0.05); %EWL at every point in time are shown in Fig. 30.4.

Complications

Zellmer et al. published a remarkable meta-analysis that included 84 articles comparing risks associated to both procedures. The study involved 11,000 RYGB and 5000 SG. Leak, bleeding, deep venous thrombosis (DVT), pulmonary embolism (PE), stomal stenosis/stricture, reoperation, and mortality rates were investigated. Complication rate was higher for RYGB in every category,



p	3 months	6 months	12 months	2 years	3 years	4 years	5 years	6 years
	<0.001	<0.05	<0.001	<0.001	NS	<0.05	<0.001	<0.05

Fig. 30.4 % Estimated weight loss (EWL): Roux-en-Y gastric bypass (RGYB) vs. sleeve gastrectomy (SG)

except for leaks. Nevertheless, statistical analysis showed significance only for bleeding and stomal stenosis/stricture (Table 30.1). They concluded that there is a generalized misconception about lesser risk after SG. They recommended choosing the operation based on individual patients' characteristics and institutional experience, instead of basing the decision only on risks associated with the procedure [13].

Conversely, Kumar et al. investigated about 30-day complication rate using the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) data registry. This database included 150,000 operations performed across the USA and Canada during 2015. They found that leak rate and morbidity and mortality rates were significantly higher for RYGB than for SG (Table 30.2). Again, they concluded that in spite of this, RYGB should not be abandoned and that the short-term complications needed to be weighed against differences in the mid- and long-term outcomes [14].

Authors from the SM-BOSS (Swiss Multicenter Bypass or Sleeve Study) did not observe any statistical significant difference in either early (SG, 0.9% vs. RYGB, 4.5%, p = NS) or late complications (SG, 14.9% vs. RYGB, 17.3%, p = NS) occurrence among the two procedures. Also, the need for reoperation or endoscopic revision was evaluated. Again, no difference was found between both operations. De Novo GERD or worsening of preexisting GERD was the most frequent cause of reoperation after SG, while insufficient weight loss was the second one. Instead, the most common reason for reoperation after RYGB was internal hernia. Of note, they explained that closure of mesenteric defects was not mandatory during the trial, so the incidence of internal hernias could have been reduced by adding that step to the operation [10].

The group conducting the SLEEVEPASS trial did not detect any differences in terms of early or late complications either. Specifically, late complications were reported in 19% of cases after SG and 26% of patients after RYGB (p = NS). Remarkably, their observations were concurrent with those coming from the Swiss study. The most frequent cause of reoperation after SG was intractable GERD, while internal hernia was the most common after RYGB. Again, mesenteric defects were not closed during this trial [11].

Outcomes coming from our experience were also analyzed in terms of complications (Gorodner V, Matucci A, Grigaites A. (2018), data unpublished yet). Complication rate was 9% for RYGB and 5% for SG (p <0.05). It is worth mentioning that when complications were divided into mild and severe; the difference remained significant only for mild complications (Table 30.3).

Table 30.1 Complication rate; comparison between RYGB and SG [11]

Complication (%)	RYGB	SG	p
Leak	1.9	2.3	NS
Bleeding	3.1	2	0.001
DVT/pulmonary embolism	0.7	0.6	NS
Stomal stenosis/stricture	3.4	1.3	0.001
Reoperation	4.4	3.4	NS
Mortality	0.4	0.2	NS

DVT deep venous thrombosis, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

Table 30.2 Complication rate; comparison between RYGB and SG [12]

Complication (%)	RYGB	SG	p
Leak	1.5	0.7	<0.001
Comorbidities	11.6	5.7	<0.001
Mortality	0.2	0.1	<0.001

RYGB Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

Gastroesophageal Reflux Disease

Before presenting the different experiences, the correct approach for diagnosing GERD should be briefly reminded. Unfortunately, there is a generalized misunderstanding, since diagnosis of GERD is usually based only on symptoms which are not completely reliable for this type of disease [15]. All the steps are complementary, and none of them should be avoided. Symptom assessment, upper gastrointestinal series (UGI), esoph-

Table 30.3 Complication rate; comparison between RYGB and SG (our experience, Gorodner V, Matucci A, Grigaites A. (2018), data unpublished)

	RYGB (2383)	Reoperation	LSG (456)	Reoperation	*p*
Severe complications					
Leak	4 (0.1%)	4	–	–	–
Intra-abdominal bleeding	20 (0.8%)	8	10 (2%)	6	–
GI bleeding	24 (1%)	3	1 (0.2%)	–	–
Internal hernia	36 (1.5%)	36	–	–	–
SBO	9 (0.4%)	9	–	–	–
SBO + intestinal necrosis	2 (0.08%)	2	–	–	–
Portal-splenic thrombosis	1 (0.04%)	–			
Pulmonary embolism	–		1 (0.2%)	–	
Total severe	96 (4%)	62	12 (2.6%)	6	NS
Mild complications					
Abdominal pain	7 (0.3%)	4	–	–	–
Pneumonia	3 (0.1%)		3 (0.6%)	–	–
Stenosis G-J	67 (2.8%)		–	–	–
Wound infection	24 (1%)		7 (1.5%)	–	–
Ulcer	23 (1%)		–	–	–
Pancreatitis	1 (0.04%)		–	–	–
Total mild	125 (5%)	4	10 (2%)	–	0.007

RYGB Roux-en-Y gastric bypass, *SG* sleeve gastrectomy, *SBO* small bowel obstruction, *G-J* gastro-jejunum

agogastroduodenoscopy (EGD), and esophageal function tests (esophageal manometry and 24-h pH monitoring or Bravo™ pH monitoring) should all be ordered to achieve an accurate diagnosis. The importance of the last two tests should be mentioned apart. The esophageal manometry provides information about the motility of the esophagus allowing to exclude primary esophageal motility disorders. It also allows to locate precisely the lower esophageal sphincter (LES), for posterior correct placement of the pH monitoring catheter. The 24-h pH/Bravo™ pH monitoring are the only objective elements available for this process, allowing to rule out/confirm the presence/absence of GERD. Clarification of the former concepts should be useful at the time of interpreting the literature. Next, data published based on objective studies will be presented.

Sleeve Gastrectomy

Bugherhart et al. published their results on 20 patients undergoing SG. Esophageal manometry showed that LES pressure significantly decreased from 18.3 to 11 mmHg (p = 0.03) (normal value 14–24 mmHg). Remarkably, the 24-h pH monitoring demonstrated that esophageal acid exposure increased significantly, with % time with pH <4 going from 4.1 to 12 (p = 0.004) (normal value <4.5) [16]. In another study conducted by del Genio et al., results from 25 patients before and after SG were analyzed. LES pressure did not show major changes: 21.3 vs. 22 mmHg before and after SG, respectively (p = NS). However, the DeMeester score rose from 9 to 18.4 (p = 0.041) (normal value 14.7) [17]. Thereaux et al. studied 50 patients under the same circumstances. They divided patients into two groups: group 1 = normal preoperative pH monitoring and group 2 = abnormal preoperative pH monitoring. They found that 69% of patients in group 1 had the novo GERD, although 33% of patients in group 2 were able to resolve their preexisting GERD [18].

Our group studied 14 patients before and after SG. LES pressure dropped from 17.1 to 12.6 mmHg after the surgery (p <0.05). Moreover, the DeMeester score increased from 12.6 to 28.4 (p <0.05). Analyzing GERD status after SG, 21% of patients showed worsening of their disease, while 36% of patients had de novo GERD. Interestingly enough, one-third of patients with documented GERD after SG did

not report any symptoms. This means that based on symptoms, these patients would have been considered reflux-free [19].

Conversely, Rebecchi et al. found a beneficial effect of SG on GERD. They described a significant reduction in the DeMeester score, which went from 39.5 to 10.6. However, the incidence of de novo GERD was still 5.4% [20].

This issue becomes more worrisome when data about Barrett's esophagus (BE) were analyzed. Genco et al. reported their experience on 110 patients. EGD was performed before SG and repeated at 5-year follow-up. None of the patients had BE before SG. At last follow-up, the incidence of BE was 17.2% (p <0.001) [21].

Roux-en-Y Gastric Bypass

The opposite effect was observed after RYGB. Mejia-Rivas et al. investigated the effect of RYGB on GERD in 20 patients. On esophageal manometry, LES pressure was slightly increased postoperatively, going from 18 to 20.1 mmHg (p = NS). On pH monitoring, the DeMeester score significantly decrease from 48.3 to 7.7 (p <0.001). Only one patient (5%) had abnormal esophageal acid exposure with heartburn as the main symptom [22]. In another interesting publication, Madalosso et al. studied the effect of banded RYGB on 53 patients preoperatively, at 6 and 39 months postoperatively. On EGD, the prevalence of reflux esophagitis decreased from 45% preoperatively to 19% in the last follow-up (p = 0.001). Nevertheless, de novo esophagitis appeared in 17% of the patients at 6 months, although this number decreased to 7% at 39 months follow-up. DeMeester score fell from 28.6 preoperatively to 1.2 at 39 months follow-up (p <0.001). They supposed that reduction in abdominal pressure, improvement in gastric emptying after weight loss, and reduced gastric output might explain these findings [23].

Our group examined the effect of RYGB on GERD in 13 patients. Esophageal manometry demonstrated almost no difference in pre- and postoperative LES pressure (15 vs. 14 mmHg, respectively, p = NS). The difference became evident when analyzing the DeMeester score, which dropped from 36 preoperatively to 11 after the operation (p <0.001). When evaluating the GERD status, 69% of patients were able to resolve their GERD, 23% showed improvement, and 8% remained the same (Gorodner V, Matucci A, Grigaites A. (2018), data unpublished). This became even more interesting when the effect on Barrett's esophagus was assessed. From 1681 patients who underwent RYGB in our group, 19 (0.9%) were diagnosed with BE preoperatively. Of those, 11 were ready to be included in our analysis; there were 9 short-segment BE (SSBE) and 2 long-segment BE (LSBE). None of them had dysplasia. At 41 months follow-up, four patients (36%) showed regression of BE (three SSBE and one LSBE). Of note, none of the remaining seven patients showed progression of the disease [24].

Discussion

Analyzing the Arguments That Might Explain the Rise in SG Numbers

No Anastomosis

It is well known that an anastomosis performed at any segment of the digestive tract might be related to complications such as leaks, marginal ulcers, bleeding, and stomal stenosis. The fact that SG does not comprise any anastomosis in its technique might be considered as an advantage. However, stenosis at the gastrojejunostomy is one of the most frequent complications reported after RYGB, at a rate of 4 to 6% approximately [25]. Fortunately, stenosis is successfully treated with pneumatic dilatation, which is considered a relatively simple procedure. For instance, Caro et al. published their experience on 200 endoscopic balloon dilatations in 111 patients; 75% of the patients required only one session to treat the stenosis. The remaining patients demanded two or more sessions [26].

No Mesenteric Defects

Internal hernias due to mesenteric defects might become a worrisome complication. There is a wide range of presentation that goes from a noncom-

plicated small bowel partial obstruction to small bowel necrosis. An incidence as high as 14% has been reported [27]. The lack of mesenteric defects is an unquestionable benefit that SG has. Geubbels et al. performed a meta-analysis of 45 articles including 31,320 patients. They concluded that the incidence of internal hernias can be lowered down to 1% if the antecolic route is used, adding mesenteric and Petersen's defects closure [28].

No Malabsorption

Although the bypassed segment of small bowel might be short, the RYGB has been traditionally associated to nutritional deficiencies. Saltzman et al. described several mechanisms that might contribute to this phenomenon. Among them, reduced food intake, suboptimal dietary quality, altered digestion and absorption, and nonadherence to supplementation regimens can be enumerated. The most common clinically relevant micronutrient deficiencies after RYGB include thiamine, vitamin B12, vitamin D, iron, and copper. They confirmed that severe sequelae of nutrient deficiencies are uncommon and that they are preventable by appropriate supplementation [29].

The fact that SG is a purely restrictive procedure makes this operation an appealing alternative. However, nutritional deficiencies involving iron, folate, vitamin B12, and vitamin D had been reported in the literature, even at a long-term follow-up. Authors concluded that patients had low adherence to nutritional supplementation regimen, and as a consequence, long-term follow-up and supplementation were crucial for SG [30].

Lower Incidence of Dumping Syndrome

While any kind of gastric resection carries the risk of dumping syndrome (DS), the incidence of this complication seems to be much higher after RYGB than after SG. Ramadan et al. compared the incidence of DS after SG (Group A = 268 patients), RYGB with mechanical gastrojejunostomy with 30-mm linear stapler (Group B = 229 patients) and RYGB with 15-mm hand-sewn gastrojejunostomy (Group C= 44 patients). At 6 months, the rate of DS for group A was 1.12%, for Group B was 18.78%, and for Group C was 0%. They concluded that the lesser the anastomosis diameter, the fewer the chances of experiencing DS. Moreover, dietary modifications are key to avoid this uncomfortable syndrome [31]. In summary, even though the incidence of DS is higher for the RYGB, the SG is not free of this complication, and patients should be instructed in order to avoid it.

The Stomach Can Be Accessed by Endoscopy

The impossibility of accessing the gastric remnant and the duodenum after RYGB constitutes one of the most real disadvantages of this procedure. Consequently, patient's characteristics should be carefully evaluated before choosing this operation. For instance, special attention should be paid to patients receiving anticoagulation. Also, a regular endoscopic retrograde cholangiopancreatography (ERCP) to access the biliary tract would not be possible after RYGB. Patients who need surveillance of certain pathologies, such as incomplete intestinal metaplasia, should not undergo RYGB, unless removal of the gastric remnant is performed.

A Less Complex Technique

There is no question that SG demands less surgical dexterity than RYGB. RYGB, instead, requires advanced skills in laparoscopic suturing and stapling. In addition, all these tasks must be performed in obese individuals, making every task more challenging. It is well known that complications after any type of surgery decrease after the learning curve is overcome. Several years ago, Schauer et al. investigated the effect of operative experience on perioperative outcomes after laparoscopic RYGB. They found that operative time and complication rate decreased after 100 cases [32]. It is evident that RYGB is associated with an extensive learning curve. Hence, surgeons willing to perform RYGB should be adequately trained before starting their practice.

Summarizing Effects of Both Procedures on Type 2 Diabetes, Weight Loss, Complications, and GERD

Effect on Type 2 Diabetes

Data in the literature are diverse. The least that could be said is that both procedures are effective in controlling type 2 diabetes. However, it seems that RYGB would be more effective in achieving disease control with the need of fewer medications.

In summary, after reading the literature, the following conclusions could be drawn:

1. Some publications state that RYGB achieves better diabetes control.
2. Some publications state that RYGB and SG are equally effective.
3. None of the articles mentioned SG as a better option for the treatment of diabetes.

Therefore, we recommend choosing RYGB for the treatment of obese patients with type 2 diabetes.

Weight Loss

Weight loss appears to be superior after RYGB. Nevertheless, differences between both procedures do not seem to be categorical at the time of electing the type of surgery, although they do play a role. We recommend favoring the election of RYGB for those patients that need to lose more weight.

Complications

Undoubtedly, RYGB carries a higher complication rate than SG. However, some studies were not able to find such difference.

Analyzing the type of complication in detail is critical before judging this aspect. For instance, special attention should be turned to leaks after bariatric operations, since they are one of the most feared complications. It is well known that the management of a leak after SG results more challenging, due to the presence of a long staple line. In addition, the existence of stenosis along the SG should be ruled out, since this might perpetuate the leak. Even the pylorus that increases the intragastric pressure could play a role making the leak persistent. Therefore, complication rate should not be the main factor to consider when selecting the correct operation for each patient.

Gastroesophageal Reflux Disease

After careful evaluation of objective data published in the literature, it is evident that SG is clearly related to GERD and that RYGB would be the best option for the treatment of obesity associated with GERD. The same concept applies for obesity and BE.

Possible factors associated with GERD after SG include the construction of a narrow conduct with the consequent increase in intragastric pressure, decrease in gastric volume, and compliance. Also, the distortion of the angle of His with the subsequent damage of one of the components of the anti-reflux barrier certainly plays a role. Instead, RYGB comprises the construction of a small gastric pouch, the exclusion of the fundus, most part of the body, and the antrum and the Roux-en-Y configuration resulting in decreased GERD, independently of weight loss occurrence. Several studies confirmed this observation [23, 33].

Therefore, we strongly recommend performing esophageal functions tests for SG candidates. If GERD is documented, RYGB would be the best treatment option. Moreover, patients undergoing SG should be warned that they might develop GERD, requiring long-term use of proton pump inhibitors or even conversion to a RYGB. They also should know that EGD should be performed periodically to look for possible esophagitis and/or BE.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers.
2. Mason EE, Ito C. Gastric bypass in obesity. Surg Clin North Am. 1967;47(6):1345–51.
3. Regan JP, Inabnet WB, Gagner M, Pomp A. Early experience with a two-stage laparoscopic Roux-en-Y gastric bypass as an alternative in the super-super obese patient. Obes Surg. 2003;13(6):861–4.
4. Clinical Issues Committee of the American Society for Metabolic and Bariatric Surgery. Updated position statement on sleeve gastrectomy as a bariatric procedure. Surg Obes Relat Dis. 2010;6(1):1–5.
5. Clinical Issues Committee of the American Society for Metabolic and Bariatric Surgery. Updated position statement on sleeve gastrectomy as a bariatric procedure. Surg Obes Relat Dis. 2012;8(3):e21–6.
6. American Society for Metabolic and Bariatric Surgery Clinical Issues Committee. American Society for Metabolic and Bariatric Surgery updated position statement on sleeve gastrectomy as a bariatric procedure. Surg Obes Relat Dis. 2017;13(10):1652–7.
7. Gastrointestinal Surgery for Obesity. National Institutes of Health consensus development conference statement. Am J Clin Nutr. 1992;55:615S–9S.
8. Schauer P, Bhatt D, Kirwan J, Wolski K, Aminian A, Brethauer S, et al. Bariatric surgery versus intensive medical therapy for diabetes — 5-year outcomes. N Engl J Med. 2017;376(7):641–51.
9. Li JF, Lai DD, Ni B, Sun KX. Comparison of laparoscopic Roux -en- Y gastric bypass with laparoscopic sleeve gastrectomy for morbid obesity or type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. Can J Surg. 2013;56(6):E158–64.
10. Peterli R, Wölnerhanssen BK, Peters T, Vetter D, Kröll D, Bornély Y, Schultes B, Beglinger C, Drewe J, Schiesser M, Nett P, Bueter M. Effect of laparoscopic sleeve gastrectomy vs. laparoscopic Roux-en- Y gastric bypass on weight loss in patients with morbid obesity: the SM-BOSS Randomized Clinical Trial. JAMA. 2018;319(3):255–65.
11. Salminen P, Helmiö M, Ovaska J, Juuti A, Leivonen M, Peromaa-Haavisto P, Hurme S, Soinio M, Nuutila P, Victorzon M. Effect of laparoscopic sleeve gastrectomy vs. laparoscopic Roux -en- Y gastric bypass on weight loss at 5 years among patients with morbid obesity: the SLEEVEPASS randomized clinical trial. JAMA. 2018;319(3):241–54.
12. Shoar S, Saber A. Long-term and midterm outcomes of laparoscopic sleeve gastrectomy versus Roux-en-Y gastric bypass: a systematic review and meta-analysis of comparative studies. Surg Obes Relat Dis. 2017;13(2):170–80.
13. Zellmer JD, Mathiason MA, Kallies KJ, Kothari SN. Is the laparoscopic sleeve gastrectomy a lower risk bariatric procedure compared with laparoscopic Roux-en- Y gastric bypass? A meta-analysis. Am J Surg. 2014;208(6):903–10.
14. Kumar SB, Hamilton BC, Wood SG, Rogers SJ, Carter JT, Lin MY. Is the laparoscopic sleeve gastrectomy safer that laparoscopic gastric bypass? A comparison of 30-day complications using the MBSAQIP data registry. Surg Obes Relat Dos. 2018;14(3):264–9.
15. Galvani C, Fisichella PM, Gorodner MV, Perretta S, Patti MG. Symptoms are poor indicator of reflux disease after fundoplication for gastroesophageal reflux disease: role of esophageal function tests. Arch Surg. 2003;138(5):514–8.
16. Burgerhart JS, Charlotte AI, Schotborgh SEJ, Smulders JF, van de Meeberg PC, Siersema PD, Smout AJ. Effect of sleeve gastrectomy on gastro-esophageal reflux. Obes Surg. 2014;24:1436.
17. Del Genio G, Tolone S, Limongelli P, Brusciano L, D'Alessandro A, Docimo G, Rossetti G, Silecchia G, Ianelli A, del Genio A, del Genio F, Docimo L. Sleeve gastrectomy and development of "de novo" gastro-esophageal reflux. Obes Surg. 2014;24(1):71–7.
18. Thereaux J, Barsamian C, Bretault M, Dusaussoy H, Lamargue D, Bouillot JL, Czernichow S, Carette C. pH monitoring of gastro-oesophageal reflux before and after laparoscopic sleeve gastrectomy. Br J Surg. 2016;103(4):399–406.
19. Gorodner V, Buxhoeveden R, Clemente G, Sole L, Caro L, Grigaites A. Does laparoscopic sleeve gastrectomy have any influence on gastroesophageal reflux disease? Preliminary results. Surg Endosc. 2015;29(7):1760–8.
20. Rebecchi F, Allaix ME, Giaccone C, Ugliono E, Morino M. Gastroesophageal reflux disease and laparoscopic sleeve gastrectomy: a physiopathologic evaluation. Ann Surg. 2014;260(5):909–14; discussion 914–5
21. Genco A, Soricelli E, Casella G, Maselli R, Catagneto-Gissey L, Di Lorenzo N, Basso N. Gastroesophageal reflux disease and Barrett's esophagus after laparoscopic sleeve gastrectomy: a possible, underestimated long-term complication. Surg Obes Relat Dis. 2017;13(4):568–74.
22. Mejia-Rivas MA, Herrera-Lopez A, Hernandez-Calleros J, Herrera MF, Valdovinos MA. Gastroesophageal reflux disease in morbid obesity: the effect of Roux-en-Y gastric bypass. Obes Surg. 2008;18(10):1217–24.
23. Madalosso CA, Gurski RR, Callegari-Jacques SM, Navarini D, Mazzini G, Pereira MS. The impact of gastric bypass on gastroesophageal reflux disease in morbidly obese patients. Ann Surg. 2016;263(1):110–6.
24. Gorodner V, Buxhoeveden R, Clemente G, Sanchez C, Caro L, Grigaites A. Barrett's esophagus after Roux-En- Y gastric bypass: does regression occur? Surg Endosc. 2017;31(4):1849–54.
25. Bendewald FP, Choi JN, Blythe LS, Selzer DJ, Ditslear JH, Mattar SG. Comparison of hand-sewn, linear-stapled, and circular-stapled gastrojejunostomy in laparoscopic Roux-en-Y gastric bypass. Obes Surg. 2011;21(11):1671–5.
26. Caro L, Sanchez C, Rodriguez P, Bosch J. Endoscopic balloon dilatation of anastomosis strictures occurring

after laparoscopic gastric bypass for morbid obesity. Dig Dis. 2008;26(4):314–7.
27. Rodríguez A, Mosti M, Sierra M, Pérez-Johnson R, Flores S, Dominguez G, Sanchez H, Zarco A, Romay K, Herrera MF. Small bowel obstruction after antecolic and antegastric laparoscopic Roux-en-Y gastric bypass: could the incidence be reduced? Obe Surg. 2010;20(10):1380–4.
28. Geubbels N, Lijftogt N, Fiocco M, van Leersum NJ, Wouters MW, de Brauw LM. Meta-analysis of internal herniation after gastric bypass surgery. Br J Surg. 2015;102(5):451–60.
29. Saltzman E, Karl JP. Nutrient deficiencies after gastric bypass surgery. Annu Rev Nutr. 2013;33:183–203.
30. Ben-Porat T, Elazary R, Goldenshluger A, Sherf Dagan S, Mintz Y, Weiss R. Nutritional deficiencies four years after laparoscopic sleeve gastrectomy-are supplements required for a lifetime? Surg Obes Relat Dis. 2017;13(7):1138–44.
31. Ramadan M, Loureiro M, Laughlan K, Caizazzo R, Iannelli A, Brunaud L, Czernichow S, Nedelcu M, Nocca D. Risk of dumping syndrome after sleeve gastrectomy and Roux-en- Y gastric bypass: early results of a multicentre prospective study. Gastroenterol Res Pract. 2016;2016:2570237.
32. Schauer P, Ikramuddin S, Hamad G, Gourash W. The learning curve for laparoscopic Roux-en-Y gastric bypass is 100 cases. Surg Endosc. 2003;17(2):212–5.
33. Nelson LG, Gonzalez R, Haines K, Gallagher SF, Murr MM. Amelioration of gastroesophageal reflux symptoms following Roux-en-Y gastric bypass for clinically significant obesity. Am Surg. 2005;71:950–3; discussion 953–4

31

Evaluation and Treatment of the Patient Who Is Regaining Weight

A. Daniel Guerron and Ranjan Sudan

Introduction

Obesity is a significant worldwide problem. This emerging healthcare epidemic affects millions of people in the United States [1]. Moreover, increasing BMI is associated with greater comorbidity burden affecting a patient's quality of life and results in greater cost burden to the nation [2, 3]. A similar pattern is seen all over the world in both industrialized and developing countries [4]. Likewise, bariatric surgery offers the best long-term outcomes regarding weight loss and comorbidities resolution [5]. Accordingly, the number of bariatric operations has increased during recent years. According to the last IFSO worldwide survey, 685.874 operations were performed during 2016, of which 92.6% were primary and the rest were revisional operations [6]. Sleeve gastrectomy (SG) was the most performed operation worldwide (53.6%), followed by the Roux-en-Y gastric bypass (RYGB) (30.1%), and one-anastomosis gastric bypass (OAGB) (4.8%) [6].

A. D. Guerron
Department of Surgery, Duke University, Durham, NC, USA

R. Sudan (✉)
Department of Surgery, Duke University, Durham, NC, USA

Psychiatry & Behavioral Sciences, Department of Surgery, Duke University, Duke University Health System, Durham, NC, USA
e-mail: Ranjan.sudan@duke.edu

Morbidity and mortality related to bariatric procedures have improved due to developments in technology and training of surgeons. Currently, mortality is less than 1%, and morbidity is under 10% [7–9]. However, one long-term concern is weight regain and may represent one of the most important long-term considerations after bariatric surgery [10]. Moreover, weight regain can be associated with either development or return of previously resolved or well-controlled obese-related comorbidities such as type 2 diabetes [11]. Weight regain has been described as the most common reason for revisional surgery accounting for 52.2% of these operations [12]. In addition, the reported incidences vary depending on the primary operation and follow-up. Braghetto et al. reported 40% of patients regaining weight after SG at 5-year follow-up, [13] and Torquati et al. reported a weight regain of 17.1% for RYGB at 2-year follow-up [14].

Weight recidivism is recognized as a significant problem, but there is no consensus now on the correct nomenclature. Some terms that are in common use include weight regain, weight recidivism, and insufficient weight loss. Generally, there is agreement in the bariatric community that obesity is a chronic disease, that weight regain may be related to multiple etiologies, and a multifactorial approach to its treatment, is critical. Options for treatment include behavioral modifications, pharmacological intervention, endoscopic revision, and surgical operations. Surgical revisional operations are deemed safe

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1_31

but are associated with statistically significant higher morbidity and mortality that is acceptable from a clinical perspective [15].

This chapter describes the current definitions of weight recidivism in RYGB and LSG, initial diagnosis and management, and up-to-date interventions. Different endoscopic and surgical interventions with their respective outcomes, technical tips and pitfalls, and their outcomes are explored.

Definition of Weight Regain After Bariatric Surgery

Currently, there is no consensus to report success in bariatric surgery. Different authors have used various methods to describe success of weight loss operations in the literature. In order to avoid misinterpretation, ASMBS has proposed a standardization of terms and calculations to report surgical weight-related outcomes [16]. These definitions are important in understanding the literature on weight regain. However, success of weight loss after reoperations is reported variously as either from the time of the index operation or from the time of revision. It is also clear that body mass index (BMI) is a poor indicator of the percent of body fat since it does not capture information on the fat mass in different body sites [17]. Hence, BMI and those values that use BMI for their calculation as percentage of the excess of weight loss (%EWL) may not be the best way to describe weight regain. For this reason, percentage of total weight loss (%TWL) after the primary operation and after revision may be the best indicator of body mass loss after bariatric surgery and for description of weight regain. Historically, a successful bariatric operation was defined by Brolin as loss of 50% EWL or more [18], and this criterion has been used by several authors to publish their outcomes. Success can also be described using Reinhold's criteria [19], which were modified by Christou [20], in which a good outcome is defined as postoperative BMI of less than 35 kg/m^2 and excellent when it is less than 30 kg/m^2.

Weight regain also needs to be differentiated from the failure to lose adequate weight after a primary bariatric operation. The most common definition of weight regain is an increase of body weight of more than 10 kg from the nadir [21], although other definitions can be found in the literature. Weight regain rates for SG have been reported as high as 75.6% at 6 years follow-up [22], but unfortunately, these authors did not report the definition that was used for this purpose. Recently, Casella et al. reported their SG outcomes at 10 years [23] and found that out of 182 patients, 10.4% had weight regain using the definition mentioned. Lauti et al. analyzed a cohort of 96 patients and applied 6 different types of definition of weight regain [24]. Using these different definitions, the proportion of patients with weight regain ranged from 9% to 91%, depending on the definition used. These data show that reports can vary due to a lack of standardization of nomenclature. Weight regain after RYGB operations over long-term follow-up has also been reported [25]. Christou et al. [20] reported a failure rate of 20.4 and 34.9% at 10 years based on final BMI ≥35 kg/m^2 for morbidly obese and BMI ≥40 kg/m^2 for super obese, respectively. Cooper et al. [26] reported a 23% mean weight regain from nadir over an average of 7 years of follow-up among 276 respondents, via a self-administered questionnaire. Recently, Kothari et al. published their 10-year results after RYGB [27]. Patients had a mean 79% EWL at 18 months, but that number decreased to 50% at 12-year follow-up [27].

Factors Involved in Weight Regain

Many etiologies have been proposed to explain weight regain. The success of treatment of obesity lies in multiple factors, each playing an important role. There must be a perfect balance between the characteristics of the patient, management by the multidisciplinary team, and the chosen surgical technique. Currently, there is no perfect way to do this, and surgeons and patients often choose the simplest operation that is associated with the least likelihood of complica-

tions. This accounted for the previous popularity of the LAGB and the current rise of the sleeve gastrectomy. For these reasons, the causes for weight loss failure or weight regain are grouped according to those dependent on the patient, the multidisciplinary team, and the surgery. The multidisciplinary management should aim their efforts in maximizing weight loss while preventing nutritional problems.

Patients Demographic

Preoperative BMI is one of the strongest predictors of weight loss after bariatric surgery, and higher initial BMI (>60) predicts inadequate weight loss at 12 months [28]. Younger patients are more likely to experience significant weight regain. In a study of 244 previously successful patients, younger patients were more likely to experience significant weight regain both at 96 and 120 months of follow-up [29]. Multivariate analysis revealed that younger age was a significant predictor of weight regain even after adjusting for duration after RYGB [14]. Conversely, some authors have reported that older age (>60) predict poor weight loss [28]. Recently, Keith Jr. et al. found that white race, male sex, and higher socioeconomic status were risk factors for weight regain after surgery [30]. Interestingly, patients who waited longer than 18 months for surgery and had preoperative weight gain also had inadequate weight loss [28].

Behavioral Evaluation

The adoption of preoperative behavioral evaluation is important when deciding on bariatric surgery. Patients who lack compliance with follow-up appointments after surgery and increase their calorie intake are at increased risk of weight regain [31]. Patients must clearly understand the objectives of the surgery and agree on expectations in conjunction with the surgeon and the multidisciplinary team. Detecting and treating eating disorders before surgery are mandatory because it can influence weight loss and subsequent weight regain. Kofman et al. described patients that have eating disturbances and uncontrolled desire to eat are more predisposed to regain weight after their surgeries [32, 33]. Rutledge et al. evaluated 60 patients who underwent a RYGB [34] and found that two or more psychiatric disorders were associated with less weight loss and more weight regain at 1 year after surgery.

Biological Factors

After bariatric surgery hormonal patterns change drastically, and that may explain many of surgery's effects and benefits. Moreover, hormonal pathways have been suggested to explain poor weight loss and weight regain [35]. Santo et al. described a study in which they found that patients who had weight regain also had less elevation of GIP and GLP-1 levels after meals [36], and this was predictable on preoperative evaluation. Tamboli et al. described that high preoperative levels of ghrelin might identify patients who have weight regain after surgery [37]. However, these findings have not been corroborated by other authors [38].

Another interesting argument is the set point theory that postulates that the body will defend a predetermined set point to preserve body mass and function. A disproportionate reduction of fat-free mass may suppress the resting metabolic rate in order to preserve muscle mass. This translates in less efficient calorie consumption and decrease in caloric requirements, thus promoting weight gain [39].

Multidisciplinary Team

Compliance with follow-up positively influences weight loss after bariatric surgery [40]. Nutritional and psychological counseling after bariatric surgery is mandatory. The team must arrange the postoperative visits according to the resources available locally. It is important for the patient to understand that after bariatric surgery, lack of nutritional counseling and compliance during postoperative status will determine poor

outcomes [41]. Early detection of weight regain can be appropriately managed by the dietary team in order to avoid future weight issues [42]. Psychological evaluation for bariatric patients must be individualized [43]. Closer follow-up by the mental health team is mandatory in order to treat preoperative conditions or detect new psychological disorders that might affect outcomes [44]. In addition, physical therapy after bariatric surgery is important [45]. Exercise can improve a patient's metabolic profile and provide benefits in addition to the metabolic effects of bariatric surgery [46] and can help maintain weight and avoid future weight regain [47].

Technical Factors

Several factors related to the primary bariatric operation can be potential reasons for weight recidivism. These anatomical changes can arise from inappropriate surgical technique or be an evolution in the natural history of the postoperative course. Several authors have proposed mechanisms to explain weight regain after bariatric surgery [21, 35] and are presented separately for RYGB and SG.

Factors Associated for RYGB

Weight regain has been attributed to certain anatomical factors such as the size of gastrojejunal (G-J) stoma, size of the pouch, and gastrogastric (G-G) fistula. Previously, the Cleveland clinic group defined an enlarged stoma as one that measured more than 2 cm, and the pouch was considered to be enlarged or dilated if it was >6 cm in length or >5-cm-wide [48]. Later, Haneghan et al. analyzed a population for weight regain patients and found that a dilated stoma (>2 cm) was an independent predictor for weight regain but could not find any statistical difference related to pouch dimensions [49]. Abu Dayyeh et al. showed that stoma diameter was significantly associated with weight regain after RYGB. At 5 years after the RYGB, each 10-mm dilatation in the G-J stoma diameter was associated with a substantial weight regain [50].

The results regarding pouch size have been unclear. Roberts et al. studied 320 patients who underwent a RYGB at Yale University Hospital and found that pouch size has a direct effect on weight loss at 6 and 12 months after surgery [51]. However, other experiences have not found any relation between pouch size and weight regain [49, 52]. In addition, gastrogastric (G-G) fistula must be ruled out as a cause of weight regain. The restrictive and hormonal effect of the gastric pouch can be diminished if there is a communication with the excluded stomach. If a G-G fistula is found during investigations for weight regain, revisional surgery to eliminate the G-G fistula may be helpful.

Factors Associated for SG

SG is the most commonly performed procedure in the world because of excellent weight loss, resolution of comorbidities, and technical simplicity. However, SG has technical steps that must be followed to avoid poor weight loss and decreased comorbidity resolution, as well as lower morbidity and mortality. Several anatomical factors have been described as a cause for weight regain after SG [21]. The volume of the resected stomach has been suggested as a predictor of failure or weight regain [53]. Bougie size is directly related to the amount of stomach that is resected during a SG. However, Parikh et al. did not find any association between smaller bougie size and better weight loss [54], and small bougie size has been described as a risk factor for complications such as more nausea, vomiting, strictures, and perhaps reflux symptoms [55]. Typical bougie size ranges from 32 to 40 Fr. Experts tend to use larger bougie size. It is more important to perform an appropriate resection of the gastric fundus to avoid its dilatation and subsequent decrease in the restrictive effect of the SG than simply focus on the bougie size [56].

Nonetheless, Braghetto et al. could not find a direct relation between sleeve dilatation and weight regain at 5-year follow-up [13]. Large antral remnant has also been described as a risk factor for weight regain [57, 58]. Recently, a

meta-analysis showed that antral resection has better weight loss compared with patients with antral preservation, without differences in complications rate [59]. Nevertheless, the impact of the antral remnant in long-term weight loss and or weight regain is unknown and needs further investigation.

Predictors for Weight Regain

Patients must be evaluated carefully starting at their first postoperative visit to identify those who are at risk of suffering weight failure. For patients with weight regain, anatomical factors described in the previous section must be evaluated to identify a cause for weight gain as a G-G fistula or a dilated pouch or stoma.

Currently, a postoperative scoring system to define patients at risk for future weight regain does not exist. Weight loss nomograms to identify patients who fail to lose adequate weight after the initial operation have been described [60]. Evaluating patients with these nomograms can indicate those at risk for suboptimal weight loss during the first year after surgery. Weight loss velocity greater than 2%/week, during the first 14 weeks after surgery, is a good indicator of optimal weight loss at 12-months [60]. Another study by Shantavasinkul et al. identified longer interval and younger age as preoperative predictors for weight regain after RYGB [14], but additional factors are also likely involved in weight regain.

Initial Assessment

Initial evaluation starts begins with obtaining previous bariatric history with particular emphasis on initial weight, the presence of comorbidities, nutritional history, complications from prior operations, and interventions. For RYGB, it is imperative to obtain operative notes of the index operation in order to understand limb lengths, and anatomic relationships, as well technique for pouch formation and G-J anastomosis. In addition, for SG the bougie size, and technique for dissection of the proximal stomach, is important. Any potential intraoperative complications encountered in the initial operation will further help in operative planning. With these details, an organized approach can be followed, to discern if weight gain is related to a complication from the previous operation or an abnormal eating pattern. It is essential to ask if patients feel a sensation of restriction, dumping, or other gastrointestinal symptoms. Most of the time, several factors may play a role in weight regain, and it is difficult to find only one cause. As was stated previously, a multidisciplinary approach is mandatory, and surgeons should be cognizant that weight regain is often not purely a technical issue, which can be resolved by more surgery. Communication with the previous surgeon is encouraged but not always possible. Finally, a complete anatomical study of the digestive tract is needed using an UGI and EGD. It is essential to evaluate the patients for anatomical alterations already described such as dilatation of the gastric pouch, dilatation of the G-J anastomosis, neo-fundus, G-G fistula, etc., by an endoscopist experienced in the evaluating bariatric patients. More complex studies like CT scan or abdominal MRI are obtained, if necessary.

Management

Medications

Several studies have been conducted to study the effect of adding medications to patients with weight regain in order to achieve better outcomes [61–63]. Medication prescription could be an exciting approach for patients who are not candidates for revisional surgery due to their high surgical risk [61]. Different medications have been used as an adjunct, but phentermine and its combinations with topiramate are the most studied [61–63]. Likewise, RYGB patients have shown the best weight loss when a medication is used as an adjunct for inadequate weight loss or weight regain [61, 62]. Although, pharmacotherapy for supplementing weight loss seems is promising, future investigations are needed to clarify which patients are most suited for medication treatment.

Revisional Procedures for RYGB

Gastric Pouch Banding

Adding a gastric band in order to improve restriction might be an alternative to treating weight regain after RYGB. This option can offer additional weight loss and has shown good outcomes [64–66]. In a systematic review made by Vijgen et al., the authors found that adding a salvage band around the failed pouch could provide additional weight loss in cases of weight regain [67]. This approach has become less common as band usage, in general, has fallen out of favor due to concerns of slippage and erosion.

Pouch Reduction

If investigation of the digestive tract shows a dilated pouch, that is, a volume greater than 30–50 cc, and the patient reports a loss of restrictive feeling when eating, some investigators propose pouch reduction. This can be performed laparoscopically and may include narrowing of the stoma. Ianelli et al. reported their experience with this procedure in 20 patients [68]. EWL at 20-month follow-up was 69.1%, although a 30% complication rate was also reported. Conversely, Parikh et al. did not show any benefit to reducing the pouch size with regard to weight loss [69]. Al-Bader et al. showed their experience with laparoscopic pouch resizing [70]. Authors reported %EWL of 29.1%, with a median follow-up of 14.1 ± 6.2 months, and complication rate of 15.6% [70]. Therefore, longer follow-ups are necessary in order to evaluate the real impact of pouch resizing.

Stoma Reduction and Endoscopic Procedures

Trans-oral outlet reduction (TORe), restorative obesity surgery endoscopic (ROSE), endoscopic sclerotherapy, and endoscopic gastric plication (EGP) have been described for the management of stoma and pouch dilatation. TORe consists of placing different suture patterns (i.e., interrupted or purse-string pattern) to surround the dilated stoma and to reduce stoma size. Recently, Jiranpinyo et al. explored the feasibility of this procedure in 252 patients. The authors demonstrated the safety and feasibility of the technique and demonstrated additional weight loss [71]. Schulman et al. compared the two suture patterns. The purse-string technique offered better %EWL at 12 months compared to interrupted suture (19.8 vs. 11.7, p <0.001) [72].

ROSE is also an endoscopic approach used to decrease the size of the gastric pouch and stoma by placement of anchors to create tissue folds at the stoma and around the pouch wall. Horgan et al. published a multicenter experience using this endoscopic technique in 116 patients [73]. The procedures were performed safely, with no significant complications. At 6-month follow-up, patients reported an increase in satiety and mean %EWL of 18% [73]. Ryou et al. described the use of ROSE in five patients with weight regain. The procedure was successfully carried out in all patients, and mean weight loss at 3 months was 7.8 kg [74].

Sclerotherapy also has been demonstrated to reduce the size of the dilated stoma [75]. By injecting the sclerosing agent into the G-J anastomosis, a scar forms that leads to a decrease in the diameter of the stoma. This procedure seeks to increase the feeling of fullness after meals, but it is not widely used.

Endoscopic gastric plication (EGP), using StomaphyX (EndoGastric Solutions, Redwood City, CA), has been developed to create gastric plications or folds that are held together using polypropylene fasteners placed under endoscopic visualization to reduce the size of the pouch and the G-J anastomosis. Ong'uti et al. described a series of 27 patients using this endoscopic procedure, and they found that patients reached weight loss during the first 6 months after EGP, but they regained beyond that [76]. In a randomized study, StomaphyX was not able to show any difference when compared to a sham procedure, and on account of this, the study was stopped [77].

Conversion to Distal RYGB

RYGB revisional surgery may be challenging technically. Lysis of adhesions must be carried out carefully in order to identify the underlying anatomy precisely. Identifying, measuring, and marking the various bowel limbs by running the

bowel both antegrade from the gastric pouch and retrograde from the ileocecal are critical. Distal RYGB is a good option for weight loss, but it not offered as a primary procedure due to its risk of protein-calorie malnutrition [78]. In order to convert a RYGB to a distal RYGB, two different operations can be performed. In the first technique, the alimentary limb is divided next to the jejunojejunal anastomosis, and it is moved distally to create a new anastomosis with a longer biliopancreatic limb and a shorter common channel. The new anastomosis can be created according to a surgeon's preferences [79–82]. In the other technique, the biliopancreatic limb is divided next to the jejunojejunal anastomosis and moved distally to create a new anastomosis 75 cm proximal to the ileocecal valve resulting in a longer Roux limb [83]. In a recent systematic review, both techniques were demonstrated to be safe; however, the first modification (making a longer biliopancreatic limb) showed better results with regard to additional weight loss but also had the highest protein-calorie malnutrition [84]. Ghiassi et al. [85] reported a retrospective review of 96 patients who underwent conversion to distal RYGB during 5 years. In the first 11 patients, the RYGB was modified by dividing the Roux limb at the jejunojejunostomy and transposing it distally to create a shortened total alimentary limb length (TALL) of 250 to 300 cm. Of these, seven patients developed protein calorie malnutrition and diarrhea requiring a second operation to lengthen the common channel by an additional 100 to 150 cm (TALL 400–450 cm), leading to resolution of all symptoms. The subsequent 85 patients were converted to distal RYGB with TALL 400 to 450 in a single-stage operation. The authors reported a mean body mass index and mean excess weight loss at the time of distalization of 40.6 kg/m^2 and 33.6%. At 1, 2, and 3 years after distalization, the mean body mass index was reduced to 34.4, 33.1, and 32.2 kg/m^2, respectively, and excess weight loss improved to 41.9, 53.7, and 65.7%, respectively. Diabetes resolved in 66.7%, hypertension resolved in 28.6%, hyperlipidemia resolved in 40%, and sleep apnea resolved in 50% at 1 year. The 30-day complication rate and reoperation rates were 6.3 and 5.2%; an additional 7.3% (7/96) required reoperation for limb lengthening. Hypoalbuminemia developed in 21% at 3 years, but no increase in iron deficiency was observed. Calcium metabolism was affected by distalization to a greater degree as 21% of patients demonstrated low corrected calcium levels, 77% were deficient in vitamin D, and parathyroid hormone levels were above normal in 64% at 3 years.

The variations in techniques described to perform revisional distal RYGB makes it challenging to conclude which technique is better in order to obtain additional weight loss. However, a surgeon experienced in revisional surgery with a multidisciplinary team that is attentive to postoperative nutritional management can optimize results and reduce chances of technical and nutritional complications.

RYGB Conversion to Biliopancreatic Diversion/Duodenal Switch

Primary biliopancreatic diversion/duodenal switch (BPD-DS) is a challenging operation, and the revision of RYGB to BPD-DS is even more so. The conversion can be done as a single- or two-staged procedure depending on surgeon expertise or technical issues encountered during surgery (i.e., anesthesia time, cardiovascular events, etc.). Briefly, the gastrojejunostomy is first taken down, and the continuity of the stomach is established. Then, a modified sleeve gastrectomy is performed, which typically comprises of a fundectomy and transecting the duodenum beyond the pylorus and just above the gastroduodenal artery. A duodenoilelal anastomosis is then constructed using a stapler or is hand-sewn. Finally, the ileo-ileostomy is constructed with a 150 cm alimentary limb and 100 cm common channel. Keshishian et al. published their experience with open BPD-DS as a revisional operation in a cohort of patients with previous vertical banded gastroplasty and RYGB [86]. Twenty-six RYGB patients underwent a BPD-DS, 4 (15%) had leaks related to the gastro-gastrostomy anastomosis, and the %EWL was 67% at 30-month follow-up [86]. Parikh et al. performed BDP-DS in 12 patients [87]. They reported no leaks, and %EWL at 11 months was 63%. Both studies described

good weight loss outcomes with acceptable morbidity. Nevertheless, given the small number of patients, it is difficult to draw conclusions about the safety, effectiveness, and indications for converting RYGB to BPD-DS.

Revisional Operations for SG

Sleeve gastrectomy patients may develop loss of early satiety sensation after surgery. Likewise, weight regain can be a manifestation of this problem. If a dilated stomach is demonstrated, an additional restrictive procedure could be offered. Many patients will have a normal anatomic study, so these cases may benefit from adding a malabsorptive component, to improve weight loss and resolution of comorbidities.

Re-sleeve Gastrectomy

The first report of this operation was published in 2003. A female patient, who experienced weight regain after a BPD-DS 3 years prior, underwent a re-sleeve procedure with no postoperative complications and significant weight reduction [88]. Baltasar et al. also described the same concept [89]. Iannelli et al. reported a series of 13 patients with poor weight loss or weight regain. Initial mean pre-sleeve BMI was 44.6 kg/m^2 with a lowest BMI at 18 months of 31 kg/m^2 after SG and subsequently increased to a mean BMI of 34.9 (28–41) at 23-month follow-up. At 12 months follow-up post-revision, %EWL of 71.4 was achieved. No intraoperative or postoperative complications were reported [90]. Nedelcu et al. reported 61 patients with poor weight loss (28 pts.), weight regain (29 pts.), and gastroesophageal reflux (4 pts.). Preoperative workup demonstrated a neo-fundus or gastric dilatation in all cases. The mean BMI before the primary LSG was 43.2 kg/m^2 (range 33.8–67.1). The lowest mean BMI recorded after the primary LSG was 34.6 kg/m^2 (range 31.9–59.8), representing %EWL of 51.2% (±26.2) at 19.2-month follow-up. The sleeve revision was performed after a mean of 37.4 months with a mean BMI of 38.1 kg/m^2 (range 35.2–59.8). After re-sleeve, the mean BMI and %EWL was 29.8 kg/m^2 (range 20.2–41) and 62.7% (±29.2), respectively, at a mean follow-up of 19.9 months [91]. Therefore, re-sleeve seems to be safe and reproducible if a dilated stomach can be demonstrated.

SG to RYGB

Conversion from SG to RYGB is often utilized for the management of GERD, and some surgeons have used it for poor weight loss or weight regain. Technically, it is not as complex, but the surgeon must be aware of adhesions, especially to segments 2 and 3 of the liver and the presence of a hiatal hernia. Casillas et al. reported 48 patients who were converted from SG to RYGB, due to GERD, weight recidivism, or both. The mean pre-SG BMI was 45.9 kg/m^2 [92]. RYGB conversion for weight loss or weight regain was performed in 27 patients. In this subgroup of patients, the average preoperative BMI was 40.8 kg/m^2; and at 36 months of follow-up, mean %EWL was 16.4%, whereas %TWL was 7.5%. The complication rate was as high as 31% in the entire cohort [92]. Quezada et al. reported 50 SG patients who underwent a conversion to a RYGB [93]. In this cohort, 28 out of 50 patients underwent revision due to weight regain. The lowest BMI after SG ranged from 27 to 31 kg/m^2, and the median BMI prior to the revision to RYGB was 33.9–37.9 kg/m^2. Post-revision, a of BMI of 24–36 kg/m^2 was achieved at 3 years [93]. Iannelli et al. studied 40 patients of whom 29 were due to weight loss failure [94]. The pre-SG BMI mean was 47.7 kg/m^2, whereas the mean pre-conversion BMI was 39.2 kg/m^2. Post-conversion mean BMI of 30.7 kg/m^2 was achieved, representing an additional %TWL of 21.8% (calculated from the weight before conversion). A complication rate of 16% was reported in this series [94]. Carmelli et al. [95] and Gautier et al. [96] also showed %EWL of 66% (16-month follow-up) and 59% (15.5-month follow-up) with a low complication rate. However, both studies had few patients and short follow-up, so it is difficult to accurately analyze the long-term impact on weight loss.

Landreneau et al. presented a retrospective review of 89 patients with previous SG who underwent conversion to RYGB. Eleven patients underwent revision of SG to RYGB for either inadequate weight loss or weight regain following SG. The median pre-revision BMI in this

cohort was 48.6 kg/m^2 with a change in BMI of 2.3 kg/m^2 at 30 days and 7.9 kg/m^2 at 12 months. Twelve months following revision, this subgroup experienced percent TWL of 16.1% and percent EWL of 32.7%. Interestingly, the cohort of patients that required revision to RYGB due to complications associated with SG had a median pre-revision BMI of 30.4 kg/m^2 and had a post-revision change in median BMI of 2.2 kg/m^2 at 30 days and 4.5 kg/m^2 at 12 months. This corresponded to a 12-month percent TWL of 11.9%. The group concluded conversion of SG to RYGB is safe and feasible to enhance weight loss [97]. Therefore, RYGB can be an alternative for patients who had weight regain after SG, especially when accompanied by GERD. Future studies with more subjects and long-term follow-up are needed to help us better understand outcomes after these conversions.

SG to BPD-DS

BPD-DS has the best long-term results for weight loss and resolution of many comorbid diseases. SG is one of the steps when performing a BPD-DS, so in sleeve-alone patients "completing" the BPD-DS is a valid option. The BPD-DS, compared to RYGB, after SG, has shown better outcomes. Homan et al. [98] compared both BPD-DS and RYGB. BPD-DS was significantly more successful than RYGB (%EWL 59% and 23%, $p = 0.0008$, respectively) at a median follow-up of 34 months. In addition, BPD-DS exhibited high complication and nutritional deficiencies rates, but these were not significant [98]. These results were consistent with previous data reported by Weiner et al. [99], who showed better weight loss after a BPD-DS compared to RYGB. In the study of Carmelli et al. [95], BPD-DS was also superior to RYGB and did not show significant complications. Therefore, BPD-DS seems to be a reasonable option to treat SG patients with weight regain and maybe more reasonable for those patients with higher starting BMI (i.e., >50 kg/m^2) before SG who did not achieve sufficient weight loss after SG alone. Like primary BPD-DS, these revisional patients need close monitoring in order to detect nutritional deficiencies.

SG to Single Anastomoses Procedures

Recently several investigators have proposed single anastomosis procedures as an alternative operation on the theoretical basis of fewer complications including internal hernias from one less anastomosis. Most data pertaining to single anastomosis operations are for primary surgery [100–102], and only a few publications investigate their role as a second stage or revisional surgery. Sanchez-Pernatute et al. showed results of single anastomosis duodenoileal (SADI) bypass as a second step after SG [103]. Sixteen patients underwent a SADI procedure and showed a mean %EWL of 72% at 2 years. They also reported remission of diabetes in the eight patients that had diabetes. No intraoperative, postoperative or nutritional deficiency were reported [103]. These findings are similar to those reported by other authors that have described weight loss after SADI [104, 105]. However, these patients also need close surveillance after surgery due to the risk of malnutrition. To date, only a few publications are available about mini-gastric bypass as a revisional operation [106, 107]; therefore, no conclusions can yet be made about its effectiveness as a revisional operation.

Endoscopic Revision of SG

Endoscopic approach is attractive to address complications because it is less invasive. There are reports about endoscopic management of dilated stomach after SG. Endoscopic suturing or plication can be performed to reduce the sleeve diameter [108]. However, more definitive literature about this topic is needed before it can be recommended as a revision operation after SG.

Conclusions

Weight regain after bariatric surgery is challenging. The key to success is technical expertise and multidisciplinary team management is to identify all the possible variables that play a role in weight failure or regain after a primary operation. Professional societies must arrive at a consensus and define weight regain or failure accurately.

Conflicts of Interest The authors have no conflicts of interest to declare.

References

1. Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007–2008 to 2015–2016. JAMA. 2018;319(16):1723–5.
2. Upadhyay J, Farr O, Perakakis N, Ghaly W, Mantzoros C. Obesity as a disease. Med Clin North Am. 2018;102(1):13–33.
3. Dee A, Kearns K, O'Neill C, Sharp L, Staines A, O'Dwyer V, et al. The direct and indirect costs of both overweight and obesity: a systematic review. BMC Res Notes. 2014;7:242.
4. Lanas F, Bazzano L, Rubinstein A, Calandrelli M, Chen CS, Elorriaga N, et al. Prevalence, distributions and determinants of obesity and central obesity in the southern cone of America. PLoS One. 2016;11(10):e0163727.
5. Courcoulas AP, Yanovski SZ, Bonds D, Eggerman TL, Horlick M, Staten MA, et al. Long-term outcomes of bariatric surgery: a National Institutes of Health symposium. JAMA Surg. 2014;149(12):1323–9.
6. Angrisani L, Santonicola A, Iovino P, Vitiello A, Higa K, Himpens J, et al. IFSO Worldwide Survey 2016: primary, endoluminal, and revisional procedures. Obes Surg. 2018;28(12):3783–94.
7. Longitudinal Assessment of Bariatric Surgery C, Flum DR, Belle SH, King WC, Wahed AS, Berk P, et al. Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med. 2009;361(5):445–54.
8. Stenberg E, Szabo E, Agren G, Naslund E, Boman L, Bylund A, et al. Early complications after laparoscopic gastric bypass surgery: results from the Scandinavian obesity surgery registry. Ann Surg. 2014;260(6):1040–7.
9. Helmio M, Victorzon M, Ovaska J, Leivonen M, Juuti A, Jaser N, et al. SLEEVEPASS: a randomized prospective multicenter study comparing laparoscopic sleeve gastrectomy and gastric bypass in the treatment of morbid obesity: preliminary results. Surg Endosc. 2012;26(9):2521–6.
10. Sjostrom L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683–93.
11. Brethauer SA, Aminian A, Romero-Talamas H, Batayyah E, Mackey J, Kennedy L, et al. Can diabetes be surgically cured? Long-term metabolic effects of bariatric surgery in obese patients with type 2 diabetes mellitus. Ann Surg. 2013;258(4):628–36; discussion 36–7
12. Park JY, Song D, Kim YJ. Causes and outcomes of revisional bariatric surgery: initial experience at a single center. Ann Surg Treat Res. 2014;86(6):295–301.
13. Braghetto I, Csendes A, Lanzarini E, Papapietro K, Carcamo C, Molina JC. Is laparoscopic sleeve gastrectomy an acceptable primary bariatric procedure in obese patients? Early and 5-year postoperative results. Surg Laparosc Endosc Percutan Tech. 2012;22(6):479–86.
14. Shantavasinkul PC, Omotosho P, Corsino L, Portenier D, Torquati A. Predictors of weight regain in patients who underwent Roux-en-Y gastric bypass surgery. Surg Obes Relat Dis. 2016;12(9):1640–5.
15. Sudan R, Nguyen NT, Hutter MM, Brethauer SA, Ponce J, Morton JM. Morbidity, mortality, and weight loss outcomes after reoperative bariatric surgery in the USA. J Gastrointest Surg. 2015;19(1):171–8; discussion 8–9
16. Brethauer SA, Kim J, el Chaar M, Papasavas P, Eisenberg D, Rogers A, et al. Standardized outcomes reporting in metabolic and bariatric surgery. Surg Obes Relat Dis. 2015;11(3):489–506.
17. Nuttall FQ. Body mass index: obesity, BMI, and health: a critical review. Nutr Today. 2015;50(3):117–28.
18. Brolin RE, Kenler HA, Gorman RC, Cody RP. The dilemma of outcome assessment after operations for morbid obesity. Surgery. 1989;105(3):337–46.
19. Reinhold RB. Critical analysis of long term weight loss following gastric bypass. Surg Gynecol Obstet. 1982;155(3):385–94.
20. Christou NV, Look D, Maclean LD. Weight gain after short- and long-limb gastric bypass in patients followed for longer than 10 years. Ann Surg. 2006;244(5):734–40.
21. Lauti M, Kularatna M, Hill AG, MacCormick AD. Weight regain following sleeve Gastrectomy-a systematic review. Obes Surg. 2016;26(6):1326–34.
22. Himpens J, Dobbeleir J, Peeters G. Long-term results of laparoscopic sleeve gastrectomy for obesity. Ann Surg. 2010;252(2):319–24.
23. Castagneto Gissey L, Casella Mariolo JR, Genco A, Troisi A, Basso N, Casella G. 10-year follow-up after laparoscopic sleeve gastrectomy: outcomes in a monocentric series. Surg Obes Relat Dis. 2018;14(10):1480–7.
24. Lauti M, Lemanu D, Zeng ISL, Su'a B, Hill AG, MacCormick AD. Definition determines weight regain outcomes after sleeve gastrectomy. Surg Obes Relat Dis. 2017;13(7):1123–9.
25. Sjostrom L. Review of the key results from the Swedish obese subjects (SOS) trial – a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273(3):219–34.
26. Cooper TC, Simmons EB, Webb K, Burns JL, Kushner RF. Trends in weight regain following Roux-en-Y gastric bypass (RYGB) bariatric surgery. Obes Surg. 2015;25(8):1474–81.
27. Kothari SN, Borgert AJ, Kallies KJ, Baker MT, Grover BT. Long-term (>10-year) outcomes after laparoscopic Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2017;13(6):972–8.
28. Al-Khyatt W, Ryall R, Leeder P, Ahmed J, Awad S. Predictors of inadequate weight loss after laparo-

scopic gastric bypass for morbid obesity. Obes Surg. 2017;27(6):1446–52.
29. Monaco-Ferreira DV, Leandro-Merhi VA. Weight regain 10 years after Roux-en-Y gastric bypass. Obes Surg. 2017;27(5):1137–44.
30. Keith CJ Jr, Gullick AA, Feng K, Richman J, Stahl R, Grams J. Predictive factors of weight regain following laparoscopic Roux-en-Y gastric bypass. Surg Endosc. 2018;32(5):2232–8.
31. Sarwer DB, Wadden TA, Moore RH, Baker AW, Gibbons LM, Raper SE, et al. Preoperative eating behavior, postoperative dietary adherence, and weight loss after gastric bypass surgery. Surg Obes Relat Dis. 2008;4(5):640–6.
32. Kofman MD, Lent MR, Swencionis C. Maladaptive eating patterns, quality of life, and weight outcomes following gastric bypass: results of an internet survey. Obesity (Silver Spring). 2010;18(10):1938–43.
33. Sudan R, Sudan R, Lyden E, Thompson JS. Food cravings and food consumption after Roux-en-Y gastric bypass versus cholecystectomy. Surg Obes Relat Dis. 2017;13(2):220–6.
34. Rutledge T, Groesz LM, Savu M. Psychiatric factors and weight loss patterns following gastric bypass surgery in a veteran population. Obes Surg. 2011;21(1):29–35.
35. Maleckas A, Gudaityte R, Petereit R, Venclauskas L, Velickiene D. Weight regain after gastric bypass: etiology and treatment options. Gland Surg. 2016;5(6):617–24.
36. Santo MA, Riccioppo D, Pajecki D, Kawamoto F, de Cleva R, Antonangelo L, et al. Weight regain after gastric bypass: influence of gut hormones. Obes Surg. 2016;26(5):919–25.
37. Tamboli RA, Breitman I, Marks-Shulman PA, Jabbour K, Melvin W, Williams B, et al. Early weight regain after gastric bypass does not affect insulin sensitivity but is associated with elevated ghrelin. Obesity (Silver Spring). 2014;22(7):1617–22.
38. Abu Dayyeh BK, Jirapinyo P, Thompson CC. Plasma ghrelin levels and weight regain after Roux-en-Y gastric bypass surgery. Obes Surg. 2017;27(4):1031–6.
39. Knuth ND, Johannsen DL, Tamboli RA, Marks-Shulman PA, Huizenga R, Chen KY, et al. Metabolic adaptation following massive weight loss is related to the degree of energy imbalance and changes in circulating leptin. Obesity (Silver Spring). 2014;22(12):2563–9.
40. Kim HJ, Madan A, Fenton-Lee D. Does patient compliance with follow-up influence weight loss after gastric bypass surgery? A systematic review and meta-analysis. Obes Surg. 2014;24(4):647–51.
41. Freire RH, Borges MC, Alvarez-Leite JI, Toulson Davisson Correia MI. Food quality, physical activity, and nutritional follow-up as determinant of weight regain after Roux-en-Y gastric bypass. Nutrition. 2012;28(1):53–8.
42. Faria SL, de Oliveira KE, Lins RD, Faria OP. Nutritional management of weight regain after bariatric surgery. Obes Surg. 2010;20(2):135–9.
43. Kinzl JF, Schrattenecker M, Traweger C, Mattesich M, Fiala M, Biebl W. Psychosocial predictors of weight loss after bariatric surgery. Obes Surg. 2006;16(12):1609–14.
44. Marek RJ, Ben-Porath YS, Dulmen M, Ashton K, Heinberg LJ. Using the presurgical psychological evaluation to predict 5-year weight loss outcomes in bariatric surgery patients. Surg Obes Relat Dis. 2017;13(3):514–21.
45. Onofre T, Carlos R, Oliver N, Felismino A, Fialho D, Corte R, et al. Effects of a physical activity program on cardiorespiratory fitness and pulmonary function in obese women after bariatric surgery: a pilot study. Obes Surg. 2017;27(8):2026–33.
46. Coen PM, Tanner CJ, Helbling NL, Dubis GS, Hames KC, Xie H, et al. Clinical trial demonstrates exercise following bariatric surgery improves insulin sensitivity. J Clin Invest. 2015;125(1):248–57.
47. Coen PM, Goodpaster BH. A role for exercise after bariatric surgery? Diabetes Obes Metab. 2016;18(1):16–23.
48. Brethauer SA, Nfonsam V, Sherman V, Udomsawaengsup S, Schauer PR, Chand B. Endoscopy and upper gastrointestinal contrast studies are complementary in evaluation of weight regain after bariatric surgery. Surg Obes Relat Dis. 2006;2(6):643–8.. discussion 9-50
49. Heneghan HM, Yimcharoen P, Brethauer SA, Kroh M, Chand B. Influence of pouch and stoma size on weight loss after gastric bypass. Surg Obes Relat Dis. 2012;8(4):408–15.
50. Abu Dayyeh BK, Lautz DB, Thompson CC. Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. Clin Gastroenterol Hepatol. 2011;9(3):228–33.
51. Roberts K, Duffy A, Kaufman J, Burrell M, Dziura J, Bell R. Size matters: gastric pouch size correlates with weight loss after laparoscopic Roux-en-Y gastric bypass. Surg Endosc. 2007;21(8):1397–402.
52. Topart P, Becouarn G, Ritz P. Pouch size after gastric bypass does not correlate with weight loss outcome. Obes Surg. 2011;21(9):1350–4.
53. Weiner RA, Weiner S, Pomhoff I, Jacobi C, Makarewicz W, Weigand G. Laparoscopic sleeve gastrectomy--influence of sleeve size and resected gastric volume. Obes Surg. 2007;17(10):1297–305.
54. Parikh M, Gagner M, Heacock L, Strain G, Dakin G, Pomp A. Laparoscopic sleeve gastrectomy: does bougie size affect mean %EWL? Short-term outcomes. Surg Obes Relat Dis. 2008;4(4):528–33.
55. Hawasli A, Jacquish B, Almahmeed T, Vavra J, Roberts N, Meguid A, et al. Early effects of bougie size on sleeve gastrectomy outcome. Am J Surg. 2015;209(3):473–7.
56. Gagner M, Hutchinson C, Rosenthal R. Fifth International Consensus Conference: current status of sleeve gastrectomy. Surg Obes Relat Dis. 2016;12(4):750–6.
57. Abdallah E, El Nakeeb A, Youssef T, Abdallah H, Ellatif MA, Lotfy A, et al. Impact of extent of antral

resection on surgical outcomes of sleeve gastrectomy for morbid obesity (a prospective randomized study). Obes Surg. 2014;24(10):1587–94.
58. Obeidat F, Shanti H, Mismar A, Albsoul N, Al-Qudah M. The magnitude of Antral resection in laparoscopic sleeve gastrectomy and its relationship to excess weight loss. Obes Surg. 2015;25(10):1928–32.
59. McGlone ER, Gupta AK, Reddy M, Khan OA. Antral resection versus antral preservation during laparoscopic sleeve gastrectomy for severe obesity: systematic review and meta-analysis. Surg Obes Relat Dis. 2018;14(6):857–64.
60. Mor A, Sharp L, Portenier D, Sudan R, Torquati A. Weight loss at first postoperative visit predicts long-term outcome of Roux-en-Y gastric bypass using Duke weight loss surgery chart. Surg Obes Relat Dis. 2012;8(5):556–60.
61. Nor Hanipah Z, Nasr EC, Bucak E, Schauer PR, Aminian A, Brethauer SA, et al. Efficacy of adjuvant weight loss medication after bariatric surgery. Surg Obes Relat Dis. 2018;14(1):93–8.
62. Stanford FC, Alfaris N, Gomez G, Ricks ET, Shukla AP, Corey KE, et al. The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: a multi-center study. Surg Obes Relat Dis. 2017;13(3):491–500.
63. Schwartz J, Chaudhry UI, Suzo A, Durkin N, Wehr AM, Foreman KS, et al. Pharmacotherapy in conjunction with a diet and exercise program for the treatment of weight recidivism or weight loss plateau post-bariatric surgery: a retrospective review. Obes Surg. 2016;26(2):452–8.
64. Bessler M, Daud A, DiGiorgi MF, Olivero-Rivera L, Davis D. Adjustable gastric banding as a revisional bariatric procedure after failed gastric bypass. Obes Surg. 2005;15(10):1443–8.
65. Chin PL, Ali M, Francis K, LePort PC. Adjustable gastric band placed around gastric bypass pouch as revision operation for failed gastric bypass. Surg Obes Relat Dis. 2009;5(1):38–42.
66. Irani K, Youn HA, Ren-Fielding CJ, Fielding GA, Kurian M. Midterm results for gastric banding as salvage procedure for patients with weight loss failure after Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2011;7(2):219–24.
67. Vijgen GH, Schouten R, Bouvy ND, Greve JW. Salvage banding for failed Roux-en-Y gastric bypass. Surg Obes Relat Dis. 2012;8(6):803–8.
68. Iannelli A, Schneck AS, Hebuterne X, Gugenheim J. Gastric pouch resizing for Roux-en-Y gastric bypass failure in patients with a dilated pouch. Surg Obes Relat Dis. 2013;9(2):260–7.
69. Parikh M, Heacock L, Gagner M. Laparoscopic "gastrojejunal sleeve reduction" as a revision procedure for weight loss failure after roux-en-y gastric bypass. Obes Surg. 2011;21(5):650–4.
70. Al-Bader I, Khoursheed M, Al Sharaf K, Mouzannar DA, Ashraf A, Fingerhut A. Revisional laparoscopic gastric pouch resizing for inadequate weight loss after Roux-en-Y gastric bypass. Obes Surg. 2015;25(7):1103–8.
71. Jirapinyo P, Kroner PT, Thompson CC. Purse-string transoral outlet reduction (TORe) is effective at inducing weight loss and improvement in metabolic comorbidities after Roux-en-Y gastric bypass. Endoscopy. 2018;50(4):371–7.
72. Schulman AR, Kumar N, Thompson CC. Transoral outlet reduction: a comparison of purse-string with interrupted stitch technique. Gastrointest Endosc. 2018;87(5):1222–8.
73. Horgan S, Jacobsen G, Weiss GD, Oldham JS Jr, Denk PM, Borao F, et al. Incisionless revision of post-Roux-en-Y bypass stomal and pouch dilation: multicenter registry results. Surg Obes Relat Dis. 2010;6(3):290–5.
74. Ryou M, Mullady DK, Lautz DB, Thompson CC. Pilot study evaluating technical feasibility and early outcomes of second-generation endosurgical platform for treatment of weight regain after gastric bypass surgery. Surg Obes Relat Dis. 2009;5(4):450–4.
75. Abu Dayyeh BK, Jirapinyo P, Weitzner Z, Barker C, Flicker MS, Lautz DB, et al. Endoscopic sclerotherapy for the treatment of weight regain after Roux-en-Y gastric bypass: outcomes, complications, and predictors of response in 575 procedures. Gastrointest Endosc. 2012;76(2):275–82.
76. Ong'uti SK, Ortega G, Onwugbufor MT, Ivey GD, Fullum TM, Tran DD. Effective weight loss management with endoscopic gastric plication using StomaphyX device: is it achievable? Surg Obes Relat Dis. 2013;9(1):113–7.
77. Eid GM, McCloskey CA, Eagleton JK, Lee LB, Courcoulas AP. StomaphyX vs a sham procedure for revisional surgery to reduce regained weight in Roux-en-Y gastric bypass patients: a randomized clinical trial. JAMA Surg. 2014;149(4):372–9.
78. Kellum JM, Chikunguwo SM, Maher JW, Wolfe LG, Sugerman HJ. Long-term results of malabsorptive distal Roux-en-Y gastric bypass in superobese patients. Surg Obes Relat Dis. 2011;7(2):189–93.
79. Rawlins ML, Teel D 2nd, Hedgcorth K, Maguire JP. Revision of Roux-en-Y gastric bypass to distal bypass for failed weight loss. Surg Obes Relat Dis. 2011;7(1):45–9.
80. Srikanth MS, Oh KH, Fox SR. Revision to malabsorptive Roux-en-Y gastric bypass (MRNYGBP) provides long-term (10 years) durable weight loss in patients with failed anatomically intact gastric restrictive operations: long-term effectiveness of a malabsorptive Roux-en-Y gastric bypass in salvaging patients with poor weight loss or complications following gastroplasty and adjustable gastric bands. Obes Surg. 2011;21(7):825–31.
81. Fox SR, Fox KS, Oh KH. The gastric bypass for failed bariatric surgical procedures. Obes Surg. 1996;6(2):145–50.
82. Sugerman HJ, Kellum JM, DeMaria EJ. Conversion of proximal to distal gastric bypass for failed gas-

tric bypass for superobesity. J Gastrointest Surg. 1997;1(6):517–24; discussion 24–6
83. Brolin RE, Cody RP. Adding malabsorption for weight loss failure after gastric bypass. Surg Endosc. 2007;21(11):1924–6.
84. Tran DD, Nwokeabia ID, Purnell S, Zafar SN, Ortega G, Hughes K, et al. Revision of Roux-en-Y gastric bypass for weight regain: a systematic review of techniques and outcomes. Obes Surg. 2016;26(7):1627–34.
85. Ghiassi S, Higa K, Chang S, Ma P, Lloyd A, Boone K, et al. Conversion of standard Roux-en-Y gastric bypass to distal bypass for weight loss failure and metabolic syndrome: 3-year follow-up and evolution of technique to reduce nutritional complications. Surg Obes Relat Dis. 2018;14(5):554–61.
86. Keshishian A, Zahriya K, Hartoonian T, Ayagian C. Duodenal switch is a safe operation for patients who have failed other bariatric operations. Obes Surg. 2004;14(9):1187–92.
87. Parikh M, Pomp A, Gagner M. Laparoscopic conversion of failed gastric bypass to duodenal switch: technical considerations and preliminary outcomes. Surg Obes Relat Dis. 2007;3(6):611–8.
88. Gagner M, Rogula T. Laparoscopic reoperative sleeve gastrectomy for poor weight loss after biliopancreatic diversion with duodenal switch. Obes Surg. 2003;13(4):649–54.
89. Baltasar A, Serra C, Perez N, Bou R, Bengochea M. Re-sleeve gastrectomy. Obes Surg. 2006;16(11):1535–8.
90. Iannelli A, Schneck AS, Noel P, Ben Amor I, Krawczykowski D, Gugenheim J. Re-sleeve gastrectomy for failed laparoscopic sleeve gastrectomy: a feasibility study. Obes Surg. 2011;21(7):832–5.
91. Nedelcu M, Noel P, Iannelli A, Gagner M. Revised sleeve gastrectomy (re-sleeve). Surg Obes Relat Dis. 2015;11(6):1282–8.
92. Casillas RA, Um SS, Zelada Getty JL, Sachs S, Kim BB. Revision of primary sleeve gastrectomy to Roux-en-Y gastric bypass: indications and outcomes from a high-volume center. Surg Obes Relat Dis. 2016;12(10):1817–25.
93. Quezada N, Hernandez J, Perez G, Gabrielli M, Raddatz A, Crovari F. Laparoscopic sleeve gastrectomy conversion to Roux-en-Y gastric bypass: experience in 50 patients after 1 to 3 years of follow-up. Surg Obes Relat Dis. 2016;12(8):1611–5.
94. Iannelli A, Debs T, Martini F, Benichou B, Ben Amor I, Gugenheim J. Laparoscopic conversion of sleeve gastrectomy to Roux-en-Y gastric bypass: indications and preliminary results. Surg Obes Relat Dis. 2016;12(8):1533–8.
95. Carmeli I, Golomb I, Sadot E, Kashtan H, Keidar A. Laparoscopic conversion of sleeve gastrectomy to a biliopancreatic diversion with duodenal switch or a Roux-en-Y gastric bypass due to weight loss failure: our algorithm. Surg Obes Relat Dis. 2015;11(1):79–85.
96. Gautier T, Sarcher T, Contival N, Le Roux Y, Alves A. Indications and mid-term results of conversion from sleeve gastrectomy to Roux-en-Y gastric bypass. Obes Surg. 2013;23(2):212–5.
97. Landreneau JP, Strong AT, Rodriguez JH, Aleassa EM, Aminian A, Brethauer S, et al. Conversion of sleeve gastrectomy to Roux-en-Y gastric bypass. Obes Surg. 2018;28(12):3843–50.
98. Homan J, Betzel B, Aarts EO, van Laarhoven KJ, Janssen IM, Berends FJ. Secondary surgery after sleeve gastrectomy: Roux-en-Y gastric bypass or biliopancreatic diversion with duodenal switch. Surg Obes Relat Dis. 2015;11(4):771–7.
99. Weiner RA, Theodoridou S, Weiner S. Failure of laparoscopic sleeve gastrectomy–further procedure? Obes Facts. 2011;4(Suppl 1):42–6.
100. Sanchez-Pernaute A, Herrera MA, Perez-Aguirre ME, Talavera P, Cabrerizo L, Matia P, et al. Single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S). One to three-year follow-up. Obes Surg. 2010;20(12):1720–6.
101. Neichoy BT, Schniederjan B, Cottam DR, Surve AK, Zaveri HM, Cottam A, et al. Stomach intestinal pylorus-sparing surgery for morbid obesity. JSLS. 2018;22(1):e2017.00063.
102. Rutledge R. The mini-gastric bypass: experience with the first 1,274 cases. Obes Surg. 2001;11(3):276–80.
103. Sanchez-Pernaute A, Rubio MA, Conde M, Arrue E, Perez-Aguirre E, Torres A. Single-anastomosis duodenoileal bypass as a second step after sleeve gastrectomy. Surg Obes Relat Dis. 2015;11(2):351–5.
104. Dijkhorst PJ, Boerboom AB, Janssen IMC, Swank DJ, Wiezer RMJ, Hazebroek EJ, et al. Failed sleeve gastrectomy: single anastomosis duodenoileal bypass or Roux-en-Y gastric bypass? A Multicenter Cohort Study. Obes Surg. 2018;28(12):3834–42.
105. Balibrea JM, Vilallonga R, Hidalgo M, Ciudin A, Gonzalez O, Caubet E, et al. Mid-term results and responsiveness predictors after two-step single-anastomosis duodeno-Ileal bypass with sleeve gastrectomy. Obes Surg. 2017;27(5):1302–8.
106. Greco F. Conversion of vertical sleeve gastrectomy to a functional single-anastomosis gastric bypass: technique and preliminary results using a non-adjustable ring instead of stapled division. Obes Surg. 2017;27(4):896–901.
107. Noun R, Slim R, Chakhtoura G, Gharios J, Chouillard E, Tohme-Noun C. Resectional one anastomosis gastric bypass/mini gastric bypass as a novel option for revision of restrictive procedures: preliminary results. J Obes. 2018;2018:4049136.
108. Sharaiha RZ, Kedia P, Kumta N, Aronne LJ, Kahaleh M. Endoscopic sleeve plication for revision of sleeve gastrectomy. Gastrointest Endosc. 2015;81(4):1004.

Index

M. G. Patti et al. (eds.), *Foregut Surgery*, https://doi.org/10.1007/978-3-030-27592-1