Surgery in Motility Disorders

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Paola De Angelis, Fabio Fusaro, Valerio Balassone, Tamara Caldaro, Chiara Imondi, Renato Tambucci, and Luigi Dall'Oglio

Abbreviations

CC	Chicago classification
DES	Diffuse esophageal spasm
EA	Esophageal atresia
EGJ	Esophagogastric junction
ERAS	Enhanced recovery after surgery
ESPGHAN	European Society for Pediatric Gastroenterology, Hepatology, and Nutrition
FI	Faecal incontinence
GER	Gastroesophageal reflux
GERD	Gastroesophageal reflux disease
HAEC	Hirschsprung-associated enterocolitis
HD	Hirschsprung's disease
HRM	High-resolution manometry
IAS	Internal anal sphincter
IFALD	Intestinal failure associated liver disease
JH	Jackhammer esophagus
LES	Lower esophageal sphincter
LHM	Laparoscopic Heller's myotomy
MEN2A	Multiple Endocrine Neoplasia type 2A
NASPGHAN	North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition
NI	Neurological impairment
PEG	Percutaneous endoscopic gastrostomy
PEG-J	Percutaneous endoscopic gastro-jejunostomy
PIPO	Pediatric intestinal pseudo-obstruction
PN	Parenteral nutrition
POEM	Peroral endoscopic myotomy
PPI	Proton pump inhibitor
RAIR	Recto-anal inhibitory reflex
TCA	Total colonic aganglionosis
TLESR	Transient Lower esophageal sphincter relaxation
TPN	Total parenteral nutrition

P. De Angelis · C. Imondi · R. Tambucci
Digestive Endoscopy Unit, Bambino Gesù Children's Hospital, Rome, Italy
e-mail: paola.deangelis@opbg.net; chiara.imondi@opbg.net; renato.tambucci@opbg.net

F. Fusaro
Newborn Surgery Unit, Bambino Gesù Children's Hospital, Rome, Italy
e-mail: fabio.fusaro@opbg.net

V. Balassone · T. Caldaro · L. Dall'Oglio (✉)
Digestive Surgery Unit, Bambino Gesù Children's Hospital, Rome, Italy
e-mail: valerio.balassone@opbg.net; tamara.caldaro@opbg.net; luigi.dalloglio@opbg.net

Introduction

Gastrointestinal motility disorders pose a major clinical challenge because of the limitations of diagnostic tests and the lack of efficacious therapeutic options. Gastrointestinal motility disorders comprise heterogeneous conditions that may affect any area of the digestive tract resulting from abnormality of enteric neuromuscular function. Motility disorders are frequently chronic and may markedly affect patients' quality of life. Despite significant progress has been made over the last years, the exact nature and pathophysiological mechanisms of most gastrointestinal motility disorders remain largely unknown. Unfortunately, most dysmotility disorders cannot be cured and treatment are only offered to relieve symptoms, reduce morbidity and mortality, and improve quality of life. Surgery has a pivotal role in managing patients with motility disorders representing the treatment of choice in different conditions or an important intervention to be associated with medical therapies.

This chapter discusses surgical approaches to the main motility disorders focusing on indications, techniques, and postoperative outcomes. Principal areas of controversy and risks/benefits considerations concerning surgery for motility disorders are debated.

Since the needs of patients with complex medical conditions, as children with gastrointestinal motility disorders are, exceed the boundaries of competence of a single specialist,

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the incorporation of medical and surgical skills is strategic, as suggested by Peter Cotton [1] who firstly described the advantages of the integrated activity of the "digestivists."

Achalasia

Achalasia is a life-long rare debilitating condition characterized by an incomplete lower esophageal sphincter (LES) relaxation and absence of esophageal peristalsis, which leads to slow or absent bolus transit into the stomach (Chap. 22). Diagnosis of achalasia in children is generally made between 7 and 15 years of age, with a mean age of 10.9 years and predominance for male sex. Because of the improved knowledge about achalasia, incidence is constantly increasing and ranges between 0.1 and 0.18/100,000 children per year [2, 3].

Clinical presentation of achalasia in adults and adolescents includes dysphagia (94%), regurgitation (76%), heartburn (52%), chest pain (41%), and weight loss (35%) [2]. Younger children and infants may also present atypically with recurrent pneumonia, nocturnal cough, aspiration, hoarseness, feeding difficulties, and failure to thrive. Achalasia in children is often misdiagnosed as gastroesophageal reflux disease (GERD) or may present in a similar fashion with other conditions, such as eating disorders, eosinophilic esophagitis, or asthma, which often result in a significant diagnostic delay [3, 4].

Clinical history, upper endoscopy, and esophagogram are useful to suspect achalasia and to exclude other conditions such as structural (e.g., peptic stricture, congenital stenosis), and mucosal esophageal disease (e.g., eosinophilic esophagitis). The clinical reference for the diagnosis of achalasia is the high-resolution manometry (HRM) which allows to easily identify impaired relaxation of the lower esophageal sphincter and aberrant peristalsis. Achalasia is categorized by using Chicago Classification 4.0 (CC) into three subtypes according to HRM patterns of esophageal body contractility: type I, minimal/absent contractility in the esophageal body; type II, intermittent periods of panesophageal pressurization; type III (spastic) with premature or spastic esophageal contractions. By using metrics from HRM CCv 4.0 defines other esophageal motility disorders that may benefit from surgical treatment such as esophagogastric junction (EGJ) outflow obstruction (EGJOO), diffuse esophageal spasm (DES), and nutcracker/jackhammer esophagus (JH) [5].

Classifying achalasia subtypes by the Chicago Classification may offer valuable data on prognosis and can be used to direct treatment choice [6].

As no curative treatment is currently available, once the diagnosis is established, the therapeutic aim is the disruption of non-relaxing circular muscle of esophagus and esophagogastric junction (EGJ), in order to facilitate the passage of the bolus into the stomach and to prevent further esophageal dilatation, resulting in an improvement of symptoms [7].

Traditional management of pediatric achalasia includes step-wised esophageal dilation and surgery [6, 8].

The surgical approach in pediatric esophageal achalasia has progressed from an open surgery to a minimally invasive surgery, comprising laparoscopic or robotic Heller's myotomy (LHM) with or without Dor's anti-reflux fundoplication, and peroral endoscopic myotomy (POEM) techniques [9].

In selected patients who are not eligible for definitive surgical management, alternative less effective long-term options include Botulinum toxin injection, calcium channel blockers, and long-acting nitrates, treatments used mainly in adult population, with variable results [10].

Laparoscopic or Robotic Heller's Myotomy with or without Fundoplication

Since satisfactory outcomes occurred in almost 95% of patients, minimally invasive treatments for achalasia are equally effective to open techniques. Laparoscopy is now the preferred approach for Heller's myotomy [9, 11].

The patient is supine in reverse Trendelenburg position. Endotracheal intubation is required for the procedure. A big orogastric tube is generally inserted.

The key elements of Heller's technique are as follows:

(A) incision of the umbilicus
(B) introduction of the 30° laparoscope through the Hassan trocar and, therefore, of the remaining trocars under direct visualization
(C) exposure of the gastroesophageal junction
(D) section of the phrenoesophageal ligament to expone the anterior esophagus and cardias
(E) myotomy
(F) Dor's fundoplication (optional)
(G) entry points closure

One of the most debated aspects surrounding Heller's myotomy concerns the opportunity to perform an antireflux procedure after the esophageal myotomy to compensate the mobilization of cardias. A prospective randomized trial by Richards et al. showed that the addition of an anterior partial fundoplication significantly decreased the incidence of postoperative gastroesophageal reflux, when compared with no fundoplication. Thus, according with main evidence, routine application of Dor fundoplication is the standard approach. The addition of a Dor fundoplication seems not to affect the postoperative functional outcome of an esophageal myotomy [11, 12]. Similar results are reported with the Toupet technique [13]. We must consider that an impaired esophageal emptying is frequently reported, especially in type I achalasia. The workup or recurrence is often more complicated when a flap valve is associated.

Furthermore, despite laparoscopic myotomy is an overall safe technique with excellent outcomes, complications can occur even in expert hands: rates of esophageal mucosal layer perforation up to 15% have been reported, especially after preoperative treatments (e.g., pneumatic balloon dilatation) [14–16].

The latest technological advances suggest how robotic Heller myotomy, combined with a fundoplication, incorporates all of the advantages of laparoscopic surgery with the added benefits of improved 3-dimensional visualization, increased degree of instrument freedom, human tremor control, and restoration of proper hand-eye coordination. These aspects combine to determine a decreased rate of complications, especially regarding the risk of intraoperative perforation (reduced from 15% to 0%), while maintaining the same effectiveness of traditional laparoscopic myotomy [15–18]. Disadvantages of the robotic approach are the high costs and increased operative times due to the setting of the robot, which can be partially reduced by improving the training of the operative team [16, 17].

PerOral Endoscopic Myotomy (POEM): A New Incisionless Approach to Esophageal Achalasia

POEM Technique

POEM is a well-established treatment for achalasia first described by Pasricha et al. in 2007 in a porcine model, performed by H. Inoue et al. in 2010 in humans [19, 20] and recently introduced into pediatric surgical and gastroenterological practices [10, 21–23].

This technique represents an incisionless approach both to the esophagus and the LES made possible by the ingenious concept of creating a submucosal tunnel preventing mucosal thermal damage during the myotomy. Once submucosal tunnel has reached the gastric side, a myotomy is performed for the total length of the tunnel itself. The mucosal incision is closed by using standard clips.

Thus, the elements of POEM technique are as follows (Fig. 50.1):

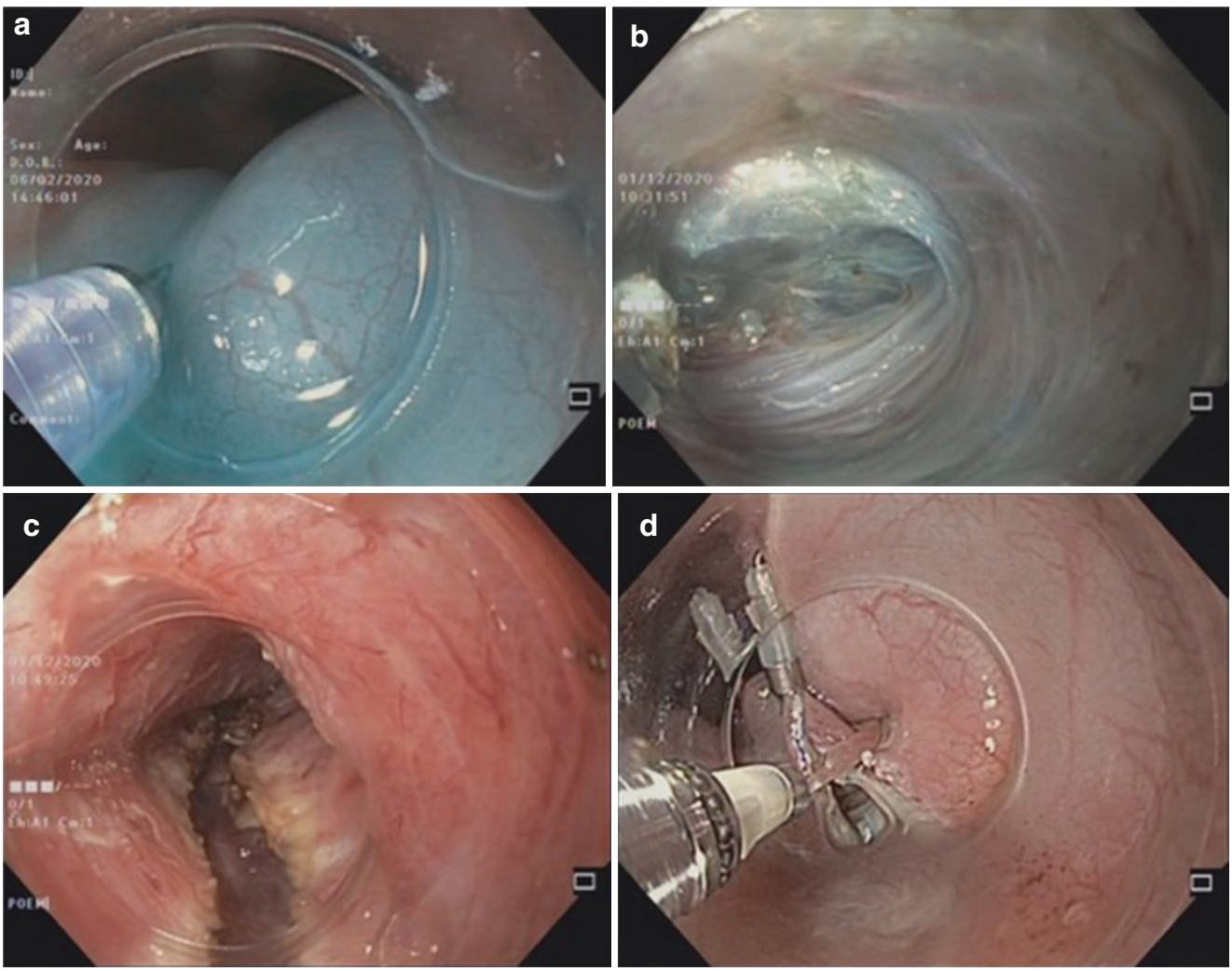

Fig. 50.1 POEM technique. (**a**) Mucosal incision; (**b**) submucosal tunnel creation; (**c**) myotomy; and (**d**) entry point closure

(A) mucosal incision
(B) submucosal tunnel creation
(C) myotomy
(D) entry point closure

The entry point site varies depending on the manometry findings but is typically 10–15 cm proximal to the EGJ.

The tunnel can be created in the anterior (2 o' clock) or posterior (5 o' clock) wall of the esophagus according to the operator's preference and previous treatments in patient's history. This possibility to choose between two alternative tunnel's orientations is particularly profitable in the management of recurrent symptoms after POEM or LHM as it allows to avoid the fibrosis caused by previous myotomy [24].

Risk of GERD and Comparison with LHM

Because no anti-reflux flap valve is generally created, gastroesophageal reflux disease (GERD) after POEM is postulated to be higher than LHM. In a comparative trial, POEM was associated with an increased risk of post-intervention GERD when compared with LHM, with high concordance rates across the three main parameters assessed: reflux- symptoms, abnormal pH-monitoring and endoscopic diagnosis of esophagitis [8]. A recent systematic review estimated a cumulative after-POEM gastroesophageal reflux rate of 17.8% (CI 95%, 14.2–22.0%) [25] compared to a risk between 4% and 16.8% of postoperative GERD in patients undergoing LHM in different studies [8, 26–28]. However, the risk of severe, unresponsive esophagitis is quite low [5]. There are conflicting opinions on the value of adding fundoplication at the time of myotomy. Some authors, in fact, have questioned the real utility to perform an anti-reflux procedure immediately after myotomy, because of the residual impairment of esophageal peristalsis [29]. Furthermore, an outlet obstruction can impair the post-surgical evaluation of a recurrent dysphagia.

Therefore, the management of recurrent dysphagia is easier after POEM comparing to LHM because no flap valve is performed. For this reason, supported by many studies reporting complete GER resolution with medical management[30], many pediatric surgeons perform Heller procedure without flap valve as first choice in children with achalasia and a second anti-reflux procedure only in selected patients with GERD unresponsive to proton pump inhibitor, after the pubertal spurt.

Nevertheless, a diligent follow up with pH-impedance monitoring and endoscopic surveillance of patient underwent POEM is required, to prevent the long-term theoretical risk of chronic esophageal inflammation.

Regardless of the risk of postoperative GERD, because of the different development eras for the two techniques, it remains difficult to compare the effectiveness of POEM and LHM. Both procedures appear to be safe and effective in symptoms relief. The hospitalization is also comparable [31]. The main advantage of POEM over LHM lies in its ability to access the thoracic esophagus, to adapt the length of the myotomy to the manometric findings and to avoid distal inflamed mucosa. POEM is particularly indicated in patients with type III achalasia who benefit from an extended tailored myotomy that involve the entire length of the spastic segment noted on esophageal HRM, which is unfeasible with LHM [6, 32].

Effectiveness and Safety Profile

Clinical success after POEM is most evaluated using the Eckardt score [33]: a score of ≤ 3 is judged to be a clinical success. However, this score only evaluates any weight loss, but does not consider the growth trend and its post-operative recovery, a critical aspect in the evaluation of post-surgical outcome in children.

Other more objective post-procedure efficacy indicators are esophageal HRM and timed barium esophagogram [34].

Mid-term effectiveness results in adults are extremely satisfactory: Eckardt score is less than three points in 98% of patients and post-operative stay is generally around 3–4 days.

Regarding the manometric parameters, a meta-analysis by Akintoye et al. showed that the average LES and IRP measured before the procedure, 33 ± 1.7 and 30 ± 1.4 mmHg, respectively, decreased to 14 ± 1.2 and 13 ± 1.6 mmHg, respectively, 6 months after the POEM. The timed barium esophagogram also recorded equally satisfactory results: prior the procedure the average heights of the barium column were 14 ± 2.3 and 9.7 ± 1.9 cm at 1 and 5 min, respectively; the column heights decreased to 4.2 ± 0.77 and 2.6 ± 0.72 cm at 1 and 5 min, respectively, after the POEM [34] (Fig. 50.2).

Data in pediatric population are quite limited, despite the increasing spread of this technique even in children in the last decade. Recently, a systematic review by Zhong et al. analyzed 11 of the most authoritative studies of last years for a total sample of 385 children undergoing POEM, demonstrating cumulative technical and clinical success rates of 97.4% (CI 95%, 94.7–98.7%) and 92.4% (CI 95%, 89.0–94.8%), respectively. After POEM, the Eckardt score was significantly decreased by 6.76 points (CI 95%, 6.18–7.34, $p < 0.00001$) and the lower esophageal sphincter pressure was significantly reduced by 19.38 mmHg (95% CI, 17.54–21.22, $p < 0.00001$).

Safety profile in expert hands is extremely satisfactory, with a pooled major adverse events rate of 12.8% (CI 95%, 4.5–31.5%) in the meta-analysis of Zhong et al. [25]. Overall, the most common complication is represented by mucosal

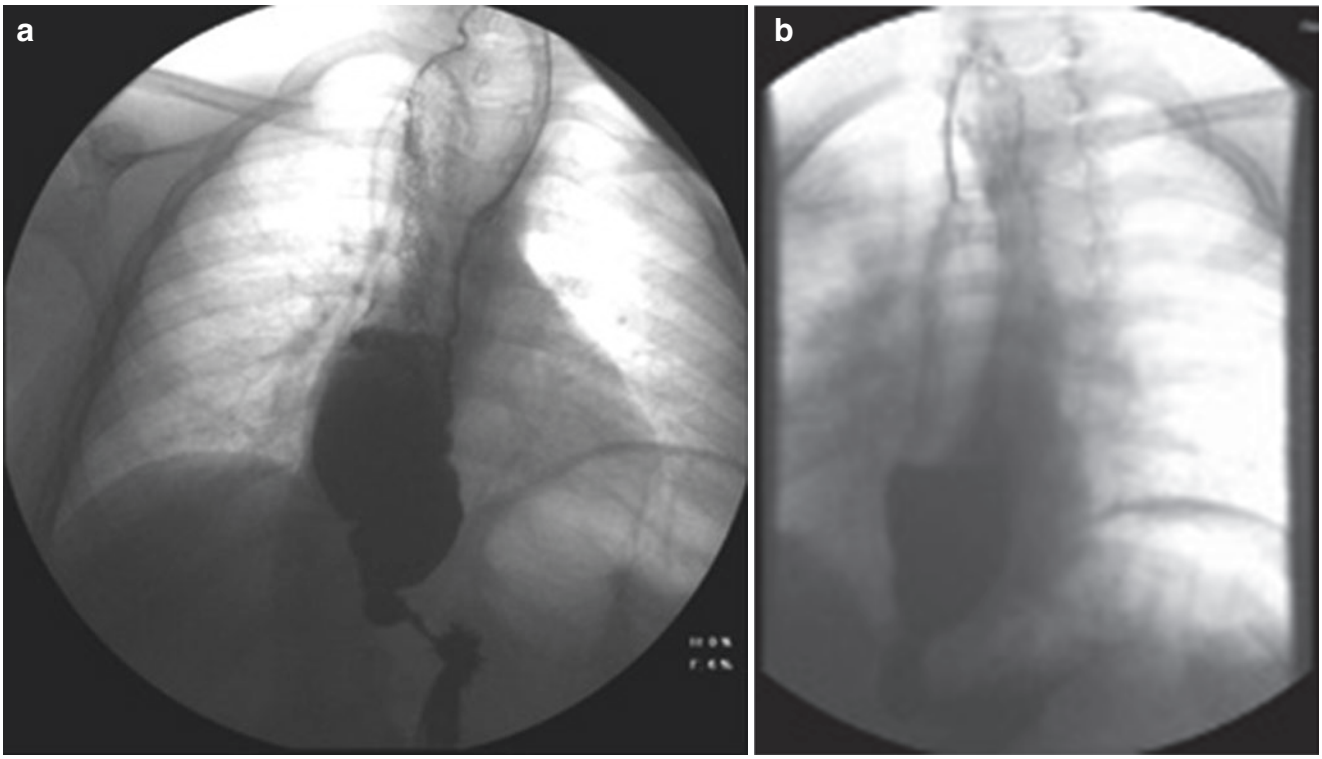

Fig. 50.2 Barium swallow before (**a**) and after(**b**) POEM in a 16-year girl with type I achalasia and a sigmoid esophagus

perforation that is reported in up to 3% of POEMs, and it is generally demonstrated by day after endoscopy or esophagogram. Management of mucosal perforation after POEM is generally conservative (prolonged fasting, antibiotics, and endoscopic treatment). Capnoperitoneum/capnomediastinum requiring decompression, pleural effusion, and submucosal bleeding are also reported as major adverse events. No mortality or emergency surgery after POEM has been reported [35].

Conclusions

In conclusion, a high index of suspicion and prompt investigations are required to detect achalasia in children. Esophageal HRM has a key role in diagnosing achalasia and, by categorizing the disorder in subtypes, it offers important information on prognosis and in driving the choice of treatment.

POEM is a safe and effective emerging technique in the pediatric endoscopy settings with high levels of expertise, according to the most recent literature and to the experience with the adult population. With rates of efficacy, safety and long-term effects largely comparable to those of LHM, POEM could quickly become the first-line therapy of pediatric achalasia when an expert operator is available.

Gastroesophageal Reflux Disease

Although antireflux surgery for gastroesophageal reflux disease (GERD) is one of the most performed procedures in pediatric surgery [36], indications are poorly defined. Therefore, there is a large degree of heterogeneity among centers regarding approaches of surgery for GERD [37]. It should be pointed out that, despite fundoplication has an unquestioned value in preventing reflux-related complications and improving quality of life in many selected children, it is far from an uncomplicated procedure especially when offered to the "wrong" patient. Indeed, the procedure permanently alters gastroesophageal anatomy and function, and may promote a variety of complications [38].

Current guidelines on pediatric gastroesophageal reflux disease (GERD) of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) stated that "*only patients with clearly proven GERD should be considered for surgery*" but they also highlight that obtaining un objective and definitive proof of GERD in children is still an unresolved issue. Indeed, guidelines pointed out also that "*to date no gold standard diagnostic tool exists for the diagnosis of GERD in infants and children*" [39].

Indications for Antireflux Surgery

In clinical practice, children candidate for surgery usually exhibit persistent symptoms despite optimized medical therapy with proton pump inhibitors (PPIs) are suffering from GERD-related complications (e.g., reflux-related pulmonary aspiration or peptic esophagitis) or have predisposing anatomic anomalies (e.g., a large hiatal hernia). Selection of patients for antireflux surgery in pediatrics is traditionally based on a combination of symptoms attributed to reflux, the presence of underlying pathologies that may predispose the development of severe GERD (e.g., neurologic impairment, esophageal atresia), and a preoperative workup that mainly includes upper gastrointestinal endoscopy, esophageal pH monitoring (or pH impedance) and upper gastrointestinal contrast studies [40]. Nonetheless definitive indication for antireflux surgery predominantly relies on individual experience and attitude that greatly varies among centers. Most of the pediatric literature consists of retrospective series in which details concerning diagnosis of GERD and previous medical therapy are lacking [39].

Therefore, recommendations on antireflux surgery in infant and children are only based on expert opinion and suggest that surgery can be considered when GERD is associated with:

1. life-threatening complications (e.g., cardiorespiratory failure) of GERD after failure of optimal medical treatment.
2. symptoms refractory to optimal therapy, after appropriate evaluation to exclude other underlying diseases.
3. chronic conditions (i.e., neurologically impaired) with a significant risk of GERD-related complications.
4. the need for chronic pharmacotherapy for control of signs and/or symptoms of GERD [39].

Over the last years, the number of surgical fundoplication in adults has steadily declined owing to concerns about complications, limited durability, and the need for reoperation in some patients [41]. In line, data collected from a national administrative dataset including 52 children's hospitals across the United States documented a threefold decrease in volume for fundoplication in children with GERD over the last decade [42].

Fundoplication

Different surgical options have been described to treat GERD, but the most common operation is the fundoplication. During fundoplication the gastric fundus is wrapped around the lower part of the esophagus to create a mechanical valve at the level of the esophagogastric junction. This operation decreases the amount of reflux by increasing the baseline tone of the lower esophageal sphincter (LES), decreasing the nadir pressure during swallow induced LES relaxation and the number of transient LES relaxations (TLESRs), and, by lengthening the intra-abdominal portion of the esophagus, accentuates the angle of His, and, when present, reduces a hiatal hernia [38].

Different fundoplication approaches exist, but they can be broadly differentiated in total fundoplication (Nissen procedure), which wraps the fundus 360 degrees around the esophagus, and partial fundoplication, with less than 360-degree wrap (the most common are 270° posterior fundoplication [Toupet procedure] and a 180° anterior fundoplication [Dor and Thal procedure]).

All types of fundoplication can be carried out as either open or laparoscopic surgery [43]. Follow-up studies suggested that laparoscopic fundoplication was associated with improved outcomes (hospital stay, costs, infection and surgical complications, and unplanned readmissions) compared with the open procedure [44, 45]. Therefore, laparoscopic fundoplication is currently regarded as the operation of choice by most pediatric surgeons [46, 47] and considered the gold standard for surgical treatment of severe GERD [47]. However, findings from randomized studies failed to show that laparoscopic fundoplication is superior to open approach with regard to short-term clinical outcomes while, in the long-term children operated with laparoscopy have a higher recurrence rate of GERD. Despite laparoscopic approach leads to a reduced incidence of retching, it shows a higher recurrence rate of GERD than open surgery [48–50]. A meta-analysis comparing open and laparoscopic fundoplication in six studies (four retrospective and two prospective studies) for a total of 721 patients showed no significant differences in GERD recurrence at 12 months, while other outcomes (operative time, hospital stay, start of feeding, and 30-day morbidity) generally favored laparoscopic approach. The significant heterogeneity among studied and the overall poor methodological quality considerably limit the interpretation of these results [51].

Data comparing the fundoplication technique and in particular outcomes of partial versus complete fundoplication in children are even more scarce. A single randomized controlled trial compared outcomes between partial (Thal) versus complete fundoplication in children found that in the long-term Nissen fundoplication had a significantly lower recurrence rate of symptoms than a Thal fundoplication in patients with neurological disorders while no significant difference between them was observed in non-neurologically impaired children. However, patients undergoing partial fundoplication have a statistically significant lower risk of postoperative dysphagia requiring endoscopic dilation compared to children undergoing complete fundoplication [52].

Other Anti-Reflux Operations

Esophagogastric Disconnection or Dissociation

Total esophagogastric disconnection is a radical procedure that has been developed to treat children with neurological impairment (NI) with intractable GERD unresponsive to other approaches. It involves the disconnection of the esophagus from the stomach and anastomosis with the jejunum. The patient is then fed through a permanent gastrostomy without risk of reflux [53].

This procedure has been advocated for NI children with severe neurological compromise with inability or contraindication (unsafe swallowing) to be orally fed [54, 55].

Prolonged postoperative care and occurrence of possible complications including malabsorption, need for prolonged enteral feeding, dumping syndrome, and Barrett's esophagus have been reported after total esophagogastric disconnection [56–60].

ESPGHAN guidelines recommend restricting the indication for total esophagogastric disconnection, as an alternative of classical antireflux surgery, to selected cases in children with NI [61].

Jejunal Feeding

Post-pyloric feeding has been proposed as an alternative to antireflux surgery in patients with severe GERD. Indeed, it represent a less invasive and reversible procedure compared with fundoplication. Gastrojejunostomy (PEG-J) is preferred procedure to gain jejunal access, alternatives are naso-jejunal tube placement or surgical transcutaneous jejunostomy. To minimize the risk of dislodgement in the stomach, the tube needs to be ideally passed beyond the ligament of Treitz. When PEG-J is in place, the gastric port can be used to give medications, vent air, and drain fluids while jejunal nutrition can be simultaneously given through the jejunal port. Main drawbacks are the need of continuous feeding regimes and the risk of frequent jejunal tube dislodgement requiring replacement, while major surgical complications have recently been identified in 6% of patients [62]. A metanalysis comparing outcomes for fundoplication and PEG-J in children with NI failed to show significant superiority of one over the other approach [63]. In another study, neither treatment option is clearly superior in preventing the subsequent aspiration pneumonia or improving overall survival for NI children [64].

Considering the risks and benefits associated with the therapeutic options, it is advisable that the choice of one over the other should involve a decision-making process fully shared with families.

Surgical Techniques

As stated, laparoscopic technique via transabdominal is preferred over open surgery for most patients undergoing fundoplication.

The basic laparoscopic equipment includes insufflation with CO_2, monitors, laparoscopic instruments (30-degree angled laparoscope, four trocars ranging from 3–5 to 10 mm, liver retractor, laparoscopic needle holder, laparoscopic grasper, electrosurgery hook, scissors), suction/irrigation system, electrocautery, and/or laparoscopic ultrasonic energy device dissector.

To perform laparoscopic fundoplication, the patient is placed supine in the reverse Trendelenburg position, with the legs abducted on straight leg boards, with the surgeon between the patient's legs, the assistant surgeon on the patient's right, and the camera holder to the left.

The initial port (5 or 10 mm) is placed at the level of the umbilicus, using a closed or open technique, and three additional ports are placed under direct vision of the laparoscope.

The laparoscopic procedure ensures a meticulous dissection and full mobilization of the lower esophagus (Fig. 50.3). These preconditions are of great importance in performing safely a floppy wrap.

Thal Fundoplication

Thal fundoplication is a simple intervention which fixes the distal esophagus within the abdomen and produces an acute angle of His. It is a 90-degree anterior wrap.

The procedure involves three steps:

1. Dissection of the abdominal esophagus and crura, then ligation of the esophageal hiatus on the dorsal side of the esophagus with non-absorbent sutures.

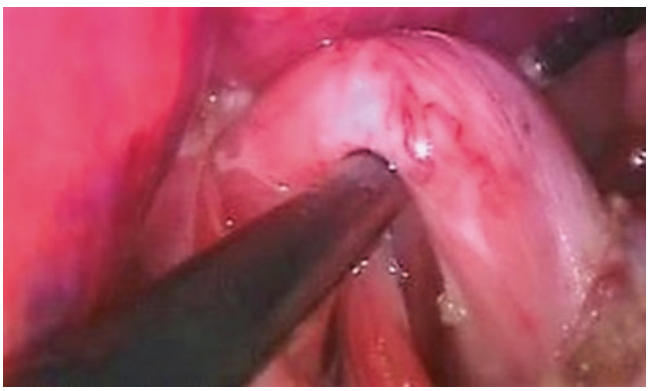

Fig. 50.3 Laparoscopic view of dissection and mobilization of the intra-abdominal segment of the esophagus. A retroesophageal window is created bluntly to perform a floppy wrap

2. Reconstruction of His angle through two more sutures between the left wall of the abdominal esophagus and the fundus of the stomach. Anchoring suture is added to the left crus of the diaphragm.
3. Anterior wrapping: The greater curvature of the stomach dome is sutured to both the right wall of the abdominal esophagus and the right crus of the diaphragm to prevent wrap migration. The stomach and the right wall of the esophagus are sutured with two more sutures and wrapping it over 180° anterior [65].

Dor Fundoplication

Dor fundoplication is an anterior 180-degree wrap originally described by the surgeon Dor in 1962.

The technique implicates the dissection of the hiatus using a vessel sealer or an electro-cautery shears or hook. The gastro-hepatic ligament is opened to find the right crus, then the dissection is continued across the apex of the hiatus to expose the left crus to the base of the angle of His. The esophagus is dissected until the anterior mediastinum in order to ensure adequate intra-abdominal esophageal length. Any herniation is repaired with two to three interrupted not absorbable stitches between the right and left crura. Approximation of the crura is usually performed posterior to the esophagus, although anterior closure may be appropriate.

An anterior 180-degree Dor fundoplication is created by suturing the anterior wall of the gastric fundus to the left and right crura and the diaphragmatic hiatus (Fig. 50.4). Stitches are placed through the right side of the fundus and through the adjacent left crus to recreate the angle of His. An apex suture is placed through the top of the fundus and the apex of the diaphragmatic hiatus. The posterior left fundus is then sutured to the right crus to complete the 180-degree fundoplication [66].

Toupet Fundoplication

Toupet fundoplication is first devised in 1963 by Andre Toupet.

It is a 270-degree posterior wrapping of the stomach around the esophagus, that leave the anterior esophageal hemicircumference free to avoid the inability to belch.

The procedure includes the division of the gastro-hepatic ligament using the ultrasonic shears oh hook, the diaphragmatic crura dissection and the mobilization of the abdominal esophagus. A retroesophageal window is created bluntly from the right side with care not to injure the posterior vagus nerve. After that, the posterior wall of the fundus is pulled behind the esophagus to the right side and it is fixed to the esophagus and to the right crus with three to five not absorbable sutures. The same procedure is performed on the left side, where the fundus is fixed to the esophagus and the left crus (Fig. 50.5). The vagus nerve should be identified and preserved at all steps of the operation. The hiatus should be closed by one or two stitches when it is very enlarged (Fig. 50.6) [67].

Nissen Fundoplication

Nissen fundoplication, a total (360°) wrap fundoplication, is the most common antireflux operation, performed by Rudolph Nissen [68].

Fig. 50.4 Dor anterior 180-degree wrap: the fundus is wrapped halfway around the front of the abdominal esophagus and attached to part of the diaphragm tissue

Fig. 50.5 Toupet 270-degree posterior wrap: the fundus is wrapped about two-thirds of the way around the back side of the bottom of the distal esophagus

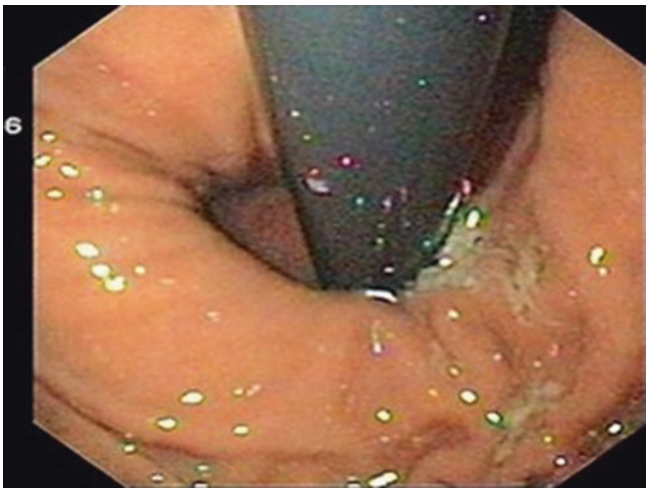

Fig. 50.6 Retroflexed endoscopic view of hiatal hernia

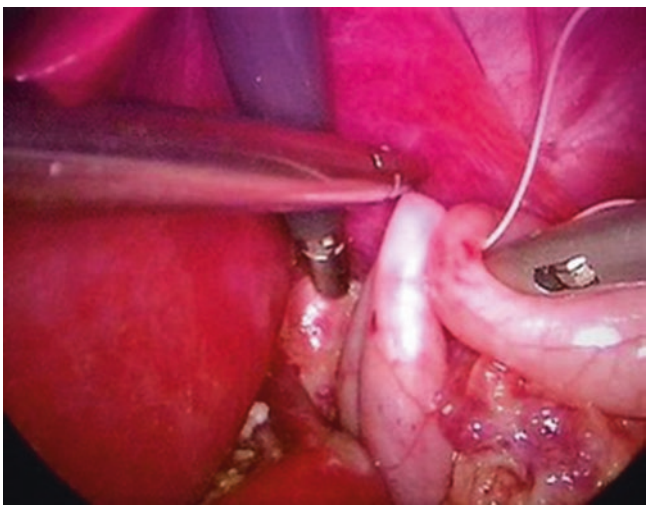

Fig. 50.7 Laparoscopic Nissen 360-degree fundoplication: the fundus is passed behind the esophagus from left to right and it is closed anteriorly using two or three non absorbable sutures

The first steps of the procedure are the same as the Toupet fundoplication and consist mainly of left and right crural dissection, mobilization of the intra-abdominal esophagus, and division of the short gastric vessels. Preservation of vagus nerves is recommended to ensure a better functional outcome. In cases of hiatal hernia, in which the fundus may slide up through the enlarged esophageal hiatus of the diaphragm, the right and left crura should be reapproximated posteriorly, utilizing two or three permanent sutures. To conclude, the posterior fundus is passed behind the esophagus from left to right and it is closed anteriorly using two or three non absorbable sutures (Figs. 50.7, 50.8, and 50.9). The most superior suture can incorporate a small piece of anterior esophagus and right crus to help secure the wrap. An orogastric tube can also be used to calibrate the wrap and prevents excessive narrowing of the esophagus.

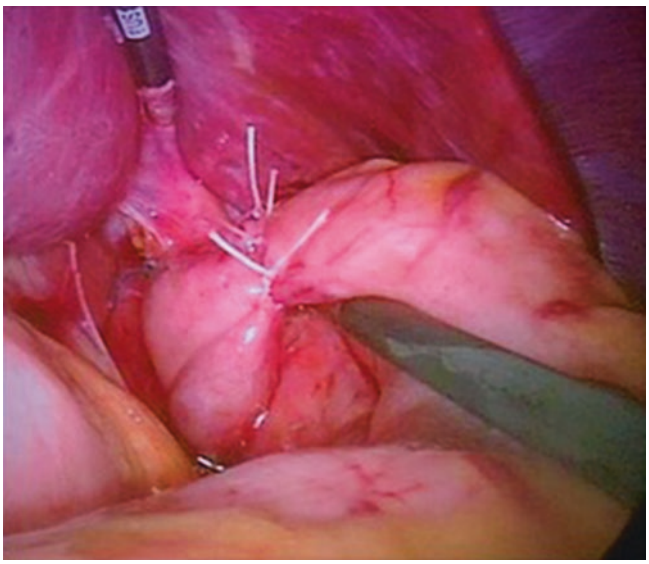

Fig. 50.8 Floppy Nissen fundoplication: laparoscopic view

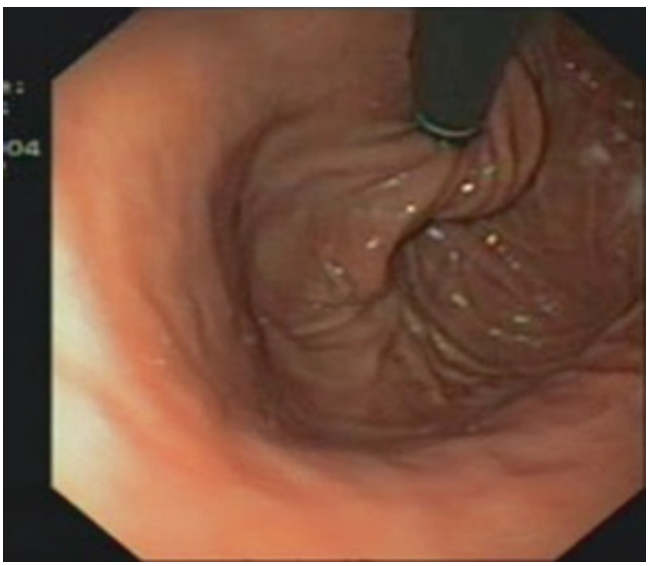

Fig. 50.9 Retroflexed endoscopic view of Nissen fundoplication

Esophago-Gastric Dissociation

The esophago-gastric dissociation is an alternative antireflux surgery for neurologically impaired children, described in 1997 by Adrian Bianchi.

The original technique (Fig. 50.10) involved a fully mobilization of the distal esophagus that was transected above the gastroesophageal junction; the gastric end was over sewn. An isoperistaltic Roux-en-Y loop of jejunum on a convenient mesenteric vascular pedicle was brought without tension through the transverse mesocolon, passing behind the stomach to anastomose with the lower esophagus. An end-to-side jejuno-jejunostomy restored the bowel continuity at 40 cm from the esophago-jejunal anastomosis. When possi-

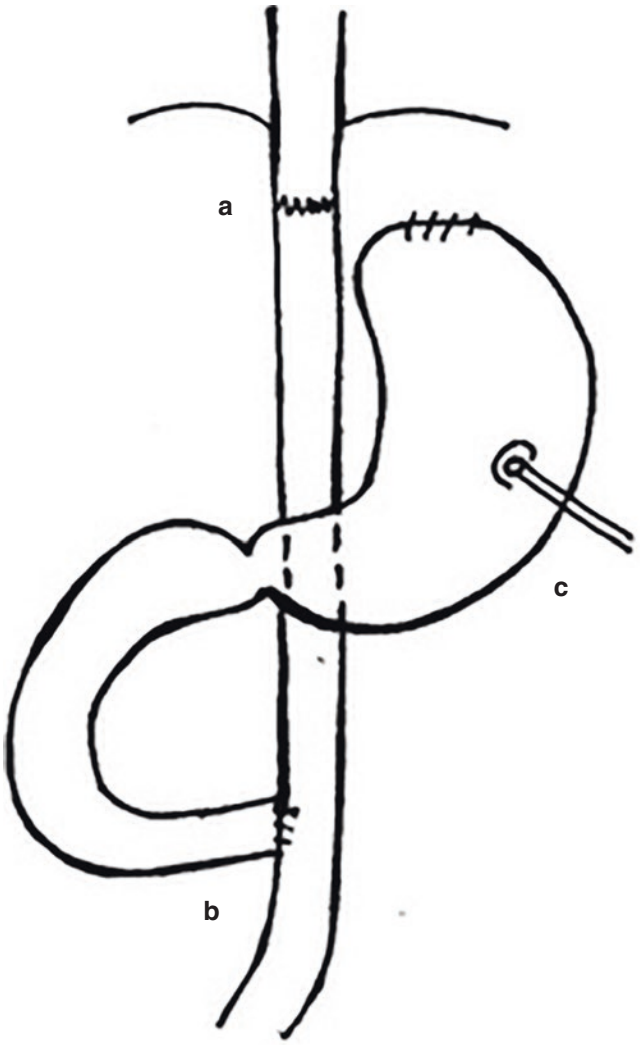

Fig. 50.10 Esophago-gastric dissociation: (**a**) end-to-end esophago-jejunal anastomosis; (**b**) end-to-side jejuno-jejunostomy anastomosis (isoperistaltic Roux-en-Y loop); and (**c**) gastrostomy

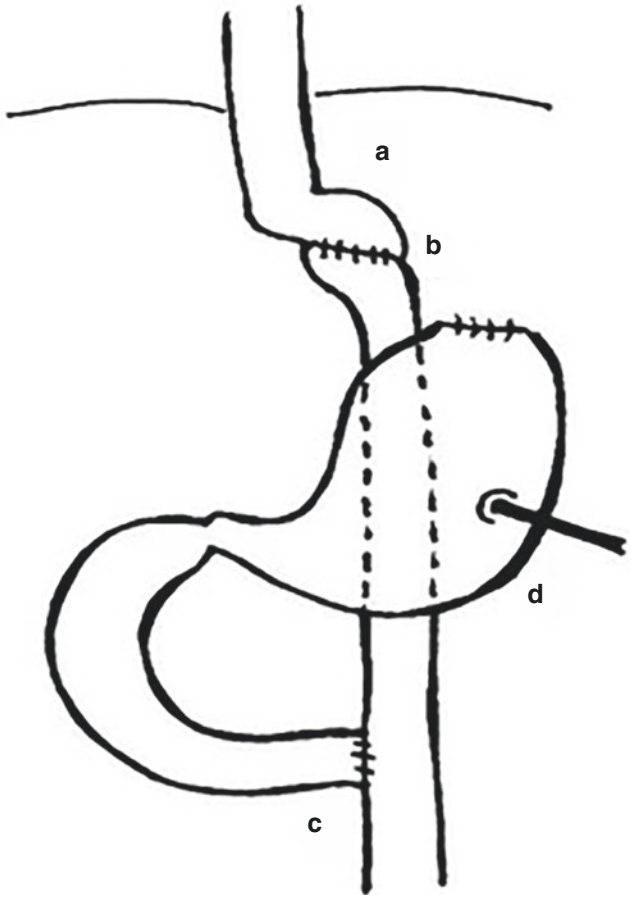

Fig. 50.11 Technical modification of the esophago-gastric dissociation procedure: the oesophageal-gastric stump (**a**) and the isoperistaltic jejunal roux loop are stapled together (anastomosed) (**b**); (**c**) end-to-side jejuno-jejunostomy anastomosis; and (**d**) gastrostomy

ble, a preexisting gastrostomy was preserved; otherwise, a new gastrostomy was fashioned [53, 59].

Recently, a technical modification of the technique has been proposed towards a more secure esophago-jejunal anastomosis (Fig. 50.11). It consists in the creation of an esophago-gastric stump using an articulated 5 mm laparoscopic Endo-GIA stapler; afterwards, a mechanical anastomosis between the esophago-gastric stump and the isoperistaltic jejunal roux loop is created [69].

Complications

The benefit/risk ratio of performing antireflux surgery even in patients with severe GERD is not clear.

Beyond the early post-operative complications (e.g., infection, bleeding, and perforation) that can happen after any gastrointestinal surgery, different complications directly related to the procedure of fundoplication may significantly impair or worsen quality of life.

Despite most long-term follow-up studies report successful outcome in more than 90% of children undergoing fundoplication, data on the true incidence of patients experiencing complications are very limited and derived from studies of poor methodological quality. Therefore, they would not seem to reflect what happens in real life. Indeed, complications are probably underreported in the literature as a result of the common tendency in clinical studies to publish positive results, and in this context, interpretation of results should consider that the great majority of papers are published by experienced and successful surgeons reporting their results of retrospective series [38]. Existing data show that complications are more common in children with underlying diseases as NI and previous esophageal atresia repair [70] that are, unfortunately, in exactly those conditions considered at high-risk for severe GERD accounting for the majority of indications for pediatric fundoplication [71].

Post-surgery issues can be due either to the persistence of symptoms prompting fundoplication, or to the side effects of surgery [72].

Former post-fundoplication complications may be related to a "bad diagnosis" in which the symptoms are incorrectly attributed to GERD. Guidelines on pediatric GERD and those specifically designed for the management of both children with NI and esophageal atresia recommend to objectively measure GERD before surgery [61, 73]. However, due to difficulties in obtaining an objective diagnosis of GERD, and due to the establish belief that most of symptoms experienced in these specific population are GERD-related, in clinical practice indication for surgery are often empirical and only based on center attitude and experience.

Upper gastrointestinal symptoms following fundoplication might be directly produced by the wrap that causes an antegrade obstruction that generates dysphagia, and/or a retrograde obstruction that produces inability to vent gas from the stomach and to vomiting that causes gas-bloat syndrome [72]. Moreover, fundoplication changes the morphology of the stomach by reducing its volume to create the wrap but it may also be potential cause of a variety of changes in gastric sensorimotor functions such as altered afferent input and development of visceral afferent hypersensitivity, gastrointestinal dysmotility, and changes in reflex pathways, including the gastric accommodation reflex and the emetic reflex [74, 75].

Mechanisms leading to disturbances in the gastric accommodation are not clear. Proximal gastric wall dysfunction, vagal injury, or mechanical effects have been reported as a cause of reduced gastric accommodation after surgery [76, 77].

Decreased gastric accommodation leads to impaired distribution of intragastric contents with the foods reaching and distending the distal stomach earlier than physiologically expected; reduced gastric compliance may lead to stimulation of visceral afferents producing visceral hypersensitivity and retching [78]. The rapid gastric emptying may also cause postprandial diarrhea, reactive hypoglycemia and dumping syndrome, reported in 30% of children after fundoplication [79].

Animal model showed that there is evidence that emetic sensitivity is increased post fundoplication [74]. Moreover, the operation may induce gastric dysrhythmia and loss of central inhibition of the gastric emetic reflex [80]. The activation of the emetic reflex leads to retching. Since fundoplication acts as a mechanical impediment to the final act of vomiting, gastric contents remain retained in the stomach, emetic reflex stimulus persists, and the retching continues [81].

Patients with fundoplication may experience gas-bloat syndrome that is characterized by abdominal bloating, postprandial fullness, inability to burp and vomit, and abdominal discomfort. It is more common in patients who have undergone complete laparoscopic Nissen fundoplication than partial fundoplication [82]. The inability to vent gas from the stomach due to the obstructive effect of the wrap may result in gastric distension with air that, if there is impaired accommodation of the fundus, may also lead in symptoms of retching and gagging. Venting gastrostomy between feeds will remove this accumulation of air, reduce overall gastric volume and help to prevent the resultant bloating [83].

Dysphagia is the most frequently reported postoperative complication [52]. Post-operative dysphagia is caused by outlet obstruction created by the wrap at the level of the esophagogastric junction. Early post-operative dysphagia generally resolves in the short term [84]. However, a subset of patient may develop long-term post-operative dysphagia that can mar otherwise successful GERD treatment [85, 86].

The risk of post-fundoplication dysphagia is significantly increased in patients with esophageal dysmotility since it may arise from insufficient esophageal peristaltic vigor to overcome the obstructive effect of the fundoplication [87]. Therefore, the integrity of esophageal motility is an important factor predicting outcomes following fundoplication. Preoperative and postoperative evaluation of the motility pattern on esophageal manometry could be useful to predict post-surgery outcome and to guide management of patients, even though existing data does not demonstrate a strong correlation between manometric changes and post-operative dysphagia [88, 89]. In this context, novel esophageal pressure-flow variables on high-resolution esophageal manometry with impedance demonstrates a high degree of prognostic value for prediction of postoperative new-onset dysphagia [86, 90].

Wrap failure due to a loose or disrupted wrap, or hiatal herniation, and recurrence of reflux, occurs in approximately 5–15% of children [47, 71]. Risk factors for fundoplication failure include younger age, preoperative hiatal hernia, postoperative retching, postoperative esophageal dilation; underlying disorder, such as esophageal atresia and NI, increased the risk of failure [71, 91, 92]. Wrap failure most occurs 1–3 years after fundoplication and is typically diagnosed due to recurrent GERD symptoms [71, 93].

Specific Patient Populations

Children with Neurological Impairment

Patients with NI are suffering from esophageal motor dysfunction directly related to central nervous system damage [94] that together with other predisposing condition, such as prolonged supine position and the increased intra-abdominal pressure secondary to spasticity, scoliosis or seizures, contribute to the risk of severe GERD [95]. In children with central nervous system disease, the incidence of GERD has been reported to be as high as 70% [61]. Even though children with NI account for the great majority requiring antireflux surgery in the pediatric surgical field, there have been very

few studies that have evaluated the GERD of NI patients before surgery in relation to the outcome [96].

Pharyngo-esophageal motility dysfunctions in NI children may also produce a misdiagnosis of GERD and predispose to post-fundoplication complication.

For example, fundoplication is often pursued for NI patients with intractable aspiration with the idea they are at greater risk of aspirating gastroesophageal reflux contents. However, evidence failed to show a consistent benefit of fundoplication for the treatment of aspiration pneumonias, and, in some cases, aspiration can even worsen after fundoplication due to pooling of saliva and food above the wrap [64, 97, 98].

It has been reported that NI children undergoing feeding gastrostomies placement are at greater risk of development or worsening of GERD [99–101] and therefore "prophylactic" antireflux surgery has been historically advocated in this specific population. However, fundoplication is associated with a high occurrence rate post-operative morbidity (up to 50%) with a 1% to 3% mortality rate [74, 100–103]. Moreover, data on infants with NI who underwent fundoplication at the time of gastrostomy placement demonstrated that reflux-related hospitalizations were comparable with those of patients who underwent gastrostomy placement alone [104] and several studies evaluating the relationship between gastrostomy and GERD using pH/impedance monitoring failed to evidence a significant aggravation of GERD after placement of gastrostomy [99, 105]. Owing these data, ESPGHAN guidelines suggest that routine fundoplication at the time of gastrostomy would unnecessarily expose a large proportion of children with NI to antireflux surgery complications and recommends that it should not be performed [61].

ESPGHAN guidelines recommend that fundoplication be considered in cases of failure of optimized medical therapy for GERD in children with NI, and despite the overall limited predicting value of testing [106] extensive evaluation of GERD with endoscopy, contrast studies, gastric emptying studies, and pH-impedance should be always performed before performing surgery.

In general, it is important to highlight that, due to the considerable unpredictability of the surgery for GERD in NI children, surgeon should ensure that parents are fully informed as to the risks and benefits of the procedure.

Children with Esophageal Atresia

GERD is considered the most frequent gastrointestinal complication after surgical repair of esophageal atresia (EA) [73] responsible for several short- and long-term sequelae such as peptic complications (erosive esophagitis, gastric metaplasia, Barrett's esophagus, and adenocarcinoma), anastomotic stricture formation and pulmonary complications (aspiration pneumonia, increased airway reactivity, chronic lung disease, and worsened tracheomalacia) [107–110]. Based on that, all EA patients are systematically treated with PPIs since surgical repair until 1 year of age, and most of them continue the treatment in the long term [73].

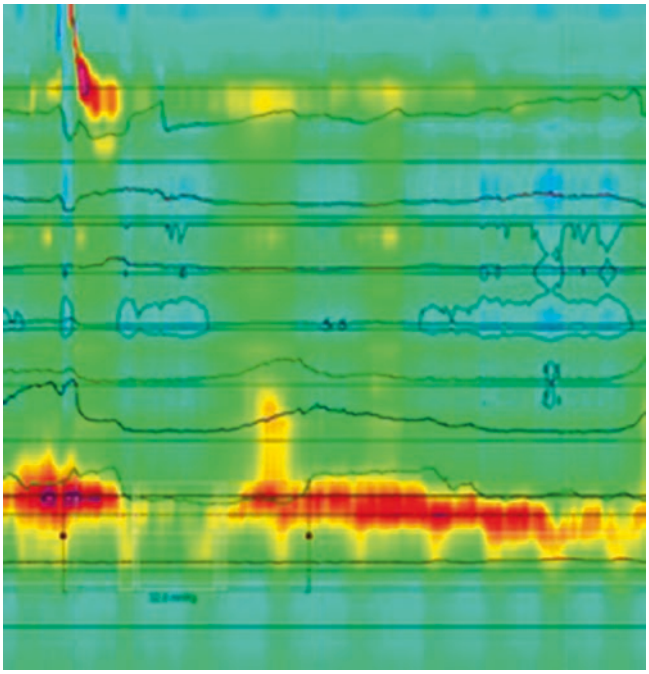

Fig. 50.12 Esophageal high-resolution impedance manometry in a 17-year-old female with previous esophageal atresia repair experiencing severe post-fundoplication dysphagia. Pressure topography shows a iatrogenic achalasia-like pattern characterized by the absence of peristalsis and the presence of outflow obstruction at the level of esophagogastric junction denoted by the elevated integrated relaxation pressure (IRP) and by the elevated intrabolus pressure. Of note, impedance tracing shows impaired bolus clearance

Fundoplication is performed in up to 45% of EA patients and almost all long-gap EA patients even if the indications for fundoplication are not clearly delineated as no controlled trial has been reported regarding the role of surgical management of GERD in patients with EA [110–113]. It is important to emphasize that, since virtually all EA survivors exhibit esophageal dysmotility [114], careful attention must be paid when fundoplication is considered because the outflow obstruction generated by the wrap is more likely to worsen the symptoms of esophageal dysmotility or produce new-onset of symptoms, in particular postoperative dysphagia (Fig. 50.12).

Current recommendations indicate to consider fundoplication in presence of poorly controlled GERD despite maximal PPI therapy, recurrent anastomotic strictures, especially in long-gap EA, long-term dependency on trans-pyloric feeding, acute life-threatening event [73].

It is noteworthy that data on prevalence of GERD demonstrated a high variability, ranging from 20% to 70% [115,

116], and that they are mainly obtained from studies using non-objective measures of GERD, such as the presence of symptoms [73]. However, although clinical suspicion has a main role in diagnosis GERD, it is important to highlight that esophageal symptoms in EA patients may be misinterpreted because of other comorbidities such us dysmotility, eosinophilic inflammation, anastomotic strictures, or other associated malformations [73].

Nevertheless, different studies recently published underestimate the true burden GERD and questioned about the widespread use of PPIs and the extensive indication for fundoplication [117–120]. Indeed, neither PPI treatment nor antireflux surgery have been found able to prevent the occurrence of esophageal histopathological complications that remain highly prevalent despite the extensive use of these treatments [117–119]. On the other hand, pressure-flow analysis on high-resolution impedance manometry revealed that abnormal peristalsis and impaired bolus transport are associated to histological changes [121]. These observations are raising the hypothesis that most EA patients might suffer from "retention esophagitis", which is secondary to the impaired motility, rather than GERD-related esophagitis [120, 122].

GERD is also considered an important risk factor for recurrence of anastomotic strictures. Therefore, although its pathogenesis of is not fully understood [123], the occurrence of refractory anastomotic stricture represents a main indication for systematic PPI treatment and antireflux surgery [73]. However, different studies demonstrated that treatment with PPIs is unable to prevent anastomotic structuring in EA children questioning the real pathophysiological role of GERD in anastomotic stricture formation [124–127].

These findings coupled with the widely reported poor outcomes of fundoplication in EA patients [128, 129] require a necessary reconsideration of the extensive use of antireflux surgery in this specific population. It is established that fundoplication has an unquestioned value in improving quality of life in many EA children, but there must be a clear awareness that a significant portion of patients may experience worsening of their clinical condition. Although we are currently unable to predict which EA patient may benefit from antireflux surgery, a thorough multidisciplinary evaluation of the benefit-risk balance and extensive preoperative workup, incorporating the whole diagnostic armamentarium, should always be done before considering antireflux surgery in EA population.

Pediatric Intestinal Pseudo-Obstruction

Pediatric intestinal pseudo-obstruction (PIPO) is the most severe form of intestinal dysmotility in children.

Surgery and endoscopy are generally involved in outcome of PIPO patients: full thickness biopsy specimen to improve diagnosis, central catheter placement for parenteral nutrition support, decompressive intervention through enterostomies to manage abdominal distension, nutritional enterostomies to allow enteral autonomy, and major surgery for complication and/or for congenital association (malrotation) and intestinal transplantation. Patients often require surgical approach combined to medical and nutritional treatment to reach growth and development, to avoid disease complications and to improve quality of life.

A high complication rate after enterostomy formation and after surgical intervention is often detected; right indications and timing and specific technical expedients may be multidisciplinary decided and planned, individualizing the choices to each patient.

Pediatric Intestinal Pseudo-Obstruction: The Diagnostic and Therapeutic Role of Surgery

Pediatric intestinal pseudo-obstruction (PIPO) is the most severe form of intestinal dysmotility disorders in children, difficult to diagnose and treat. Most cases occur during neonatal period [130].

PIPO is characterized by an impairment of coordinated propulsive activity of the gastrointestinal tract, resulting in recurrent obstructive symptoms, without mechanical reasons.

PIPO diagnosis is a multistep path that relies on clinical picture and radiology (abdominal radiology, contrast study of small intestine, etc.), together with specialised tests (e.g., intestinal manometry) and surgery to obtain histopathology, in order to rule out the secondary causes of obstruction [131–133].

Therapeutic approaches are variable with high morbidity and mortality rate. Medical and surgical treatments are used to support the nutritional status, to prevent sepsis, and to restore the intestinal motility.

Despite the well-known certitude stating that in PIPO patient the surgical approach should be limited to biopsies (not systematically needed according to the ESPGHAN recommendations [131]) and eventually stoma creation, patients with PIPO frequently undergo repetitive and useless surgical procedures, often performed during newborn period also in non-specialized centre [130, 134, 135].

Unnecessary surgery exposes these patients to potential severe complications such increased risk of prolonged ileus, adhesions, leading to a possible progressive reduction of intestinal function up to the irreversible intestinal failure.

In all patients with suspect of PIPO, even if surgery represents one of the diagnostic and therapeutic tools, a dedicated

trained medico-surgical multidisciplinary team should always discuss the indication.

Patients with evidence of PIPO from clinical and radiologic presentation should not be operated for diagnosis [135].

Surgical approach may be performed by laparotomy or laparoscopy depending on surgical expertise; laparoscopy may be challenging in newborn because of small operative space and dilation of the small bowel. Laparoscopy can be performed in children who had undergone previous laparotomy.

The indication for surgery allows two crucial points in the management of this complex disease:

1. Diagnostic to exclude specific anatomical obstruction or congenital diseases (i.e., Hirschsprung's disease);
2. Therapeutic: enterostomy formation, treatment of associated malformations and resective surgery; intestinal transplantation.

Diagnostic Surgery

In newborns or children with persistent bowel obstruction without clear clinical, radiologic and/or manometric etiologic evidence, a diagnostic exploratory laparotomy or laparoscopy should be performed looking at the following steps.

Firstly, all gastrointestinal tracts should be carefully evaluated, from stomach to rectum to exclude causes of mechanical obstruction such as congenital stenosis or atresia/diaphragm, meconium ileus, duplication, abnormalities of intestinal rotation and fixation, the latter may be associated in 30% of cases of PIPO [131].

Secondly, in these patients without specific mechanical causes, serial full thickness biopsies from proximal jejunum to rectum should be performed for histopatologic analysis to assess nerve, muscle, Interstitial Cells of Cajal [136]. During surgery, extemporary frozen sections of rectal biopsies are mandatory to assess the presence of ganglion cells to exclude Hirschsprung's disease.

Finally, as reported above, avoiding multiple surgeries is the goal of our practice; therefore, if patient is candidate to therapeutic surgery, (enterostomies) simultaneous biopsies should be considered as evidence and consensus statement recommendation of ESPGHAN proposed in 2018 [131].

Therapeutic Surgery

Therapeutic aims of surgery involve avoiding useless surgery and specific indications to required surgery:

(A) Nutritional (enterostomy); decompressive (enterostomy).
(B) Treatment of associated anomalies (malrotation); treatment of complications (stoma prolapse, post-surgical mechanical occlusion, colonic or small bowel volvulus).
(C) Replacement (transplantation).

Enterostomies

Enterostomy is often performed as one of the first therapeutic measures. Bypassing the functional obstruction and obtaining digestive decompression, it may offer the chance to restore an intestinal transit allowing feeding and reducing parenteral nutrition (PN). The location of enterostomy is a matter of debate [135].

In 1985, Pitt et al. already stated that patients with chronic Intestinal pseudo-obstruction who receive total parenteral nutrition (TPN) at home and have a venting enterostomy could be safely managed for prolonged periods and require fewer hospitalizations for obstruction [137, 138].

Furthermore, Goulet et al. confirm that decompression ileostomy and colostomy represent one of the most useful tools to allow survival to adult life, together with careful treatment of urinary tract infections and bacterial overgrowth, and judicious use of PN [135].

Nutritional strategies tailored to the single patient enable one to reach enteral autonomy in several cases. As most of the patients requires PN to maintain normal growth and development, it is important to allow partial or total intestinal autonomy through gastrostomy and jejunostomy also like feeding routes with specialised feeds (e.g., hydrolysed protein feeds, amino acid formula, etc.). When PIPO is suspected, during explorative laparotomy, actual recommendations suggest gastrostomy insertion and ileostomy formation at the same time of full-thickness biopsies with the aim to minimize the number of procedures [131].

Gastrostomy and Proximal Jejunostomy

PIPO patients, because of severe pan-enteric motility troubles, experienced recurrent acute episodes of gastric outlet or duodenal functional obstruction, gastrectasis, preventing feeding and requiring decompression. Creating a gastrostomy, sometimes associated to a proximal jejunostomy (Fig. 50.13), is of great benefit because it avoids the recurrent placement of nasogastric tubes, allows the venting of the gastric content, decompresses the stomach, duodenum, and first jejunal loops, promoting a restoration of some degree of bowel movement with consequent enteral feeding tolerance.

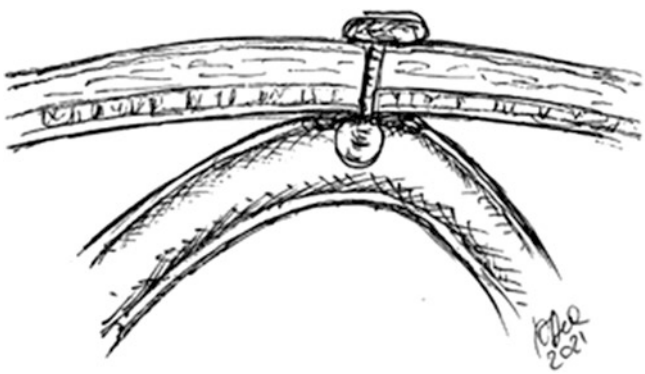

Fig. 50.13 Jejunostomy: low profile device

In these patients that experience prolonged PN, enteral feeding, also if minimal and for short periods, should be considered an indispensable therapeutic weapon because of its protective effect from TPN associated complications particularly on liver function (intestinal failure associated liver disease IFALD), avoiding or retarding liver deterioration with consequent possible indication for intestinal transplantation. Since enteral feeding should always be preferred than using PN, intragastric administration of feeding may be achieved by the gastric or jejunal tube as continuous or bolus enteral feeding. Percutaneous endoscopic gastrostomy (PEG) or gastro-jejunostomy (PEG-J) tube placement is easily achieved in these children and should be preferred as first choice because it avoid laparotomy and intestinal manipulation with increased risk of prolonged intestinal postoperative obstruction, adhesion formation, and surgical complications. Pull or push technique, according to centre expertise and patient's characteristic and requiring, is recommended for endoscopic placement of gastrostomy or gastro-jejunostomy [139, 140].

When surgery is required, surgical gastrostomy should be considered during the same procedure.

Distal Ileostomy or Colostomy

ESPGHAN expert group recommends considering the formation of a decompressive enterostomy in all patients with PIPO on parenteral nutrition [131].

Furthermore, other authors underline as the enterostomies, such as ileostomies and/or colostomies, as distal as possible, represent the most logical approach to enable transit and to resume the obstructive episodes, obtaining some degree of intestinal autonomy with variable dependence from artificial nutrition [135].

However, despite stoma surgery is quite easy, in PIPO patients, it represents a challenge for several reasons.

Firstly, in most cases, the motor function is impaired throughout the intestine then, the choice of bowel segment for diversion is tricky, particularly in newborn and small children. A more proximal stoma such as a more distal stoma can have a worse effect on intestinal function related to high output fluid and electrolytes loss or persistence of obstruction, respectively. Even if ESPGHAN expert group does not recommend the use of scintigraphy for the measurement of small bowel and colon transit given that it has not been validated in the paediatric age, this investigation can add more information on the right and best site for enterostomy.

Second, the present knowledge in PIPO physiology highlights as the motor function of the bowel often is variable during the time alternating periods of occlusion to periods of restored transit therefore, a terminal enterostomy could be inaccurate as choice because it excludes a variable length of bowel which could retain some degree of active absorptive role during the periods of restored motor activity.

Finally, children with gastrointestinal motility disorders had high complication rate after enterostomy formation more as compared to children without motility disorders. Stoma prolapse, diversion colitis and electrolyte and fluid imbalance are the most common complications reported in these patients [141].

According to all reported above, a side-to-side Mikulicz or side-to-end Santulli enterostomy might be the choice better than terminal enterostomy (Figs. 50.14 and 50.15). Their advantages are represented by the restoration of intestinal transit, recruitment of the distal efferent bowel during the possible transient period of restored motility with increase of absorptive intestinal surface, and consequent possible reduction of the parenteral nutrition dependence.

Ideally, enterostomy formation should be done at the same time of intestinal biopsies.

Enterostomy represents a milestone in the management of PIPO patients so that about more or less of 50% of patients

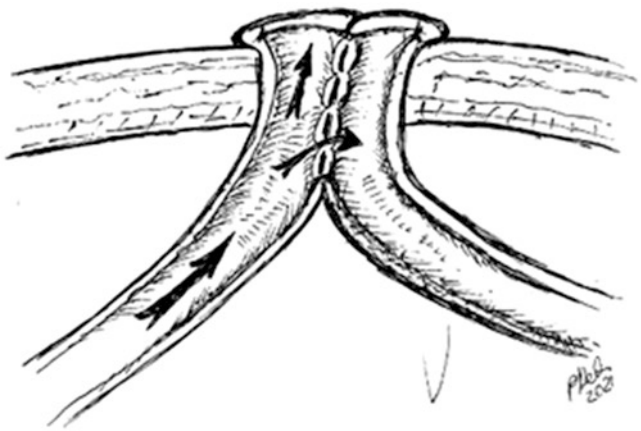

Fig. 50.14 Side-to-side Mikulicz enterostomy

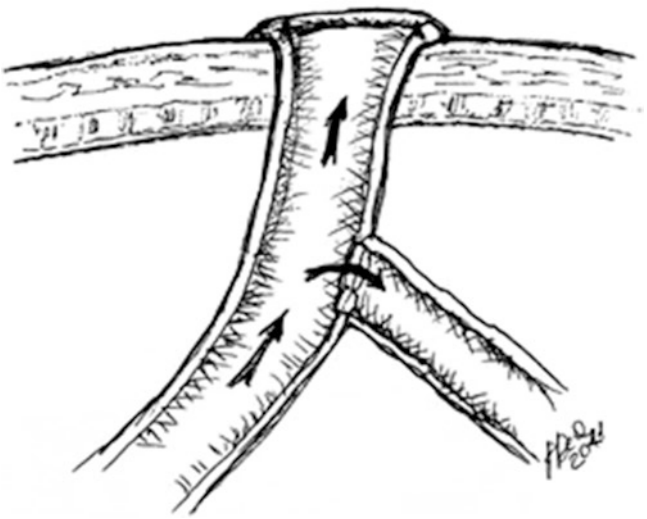

Fig. 50.15 Side-to-end Santulli enterostomy

improve after enterostomy as to be weaned from PN; in patients in which clear improvement from ileostomy is observed, with PN weaning and at least 2 years follow up on enteral/oral feeding without exacerbations, total colectomy and ileorectal anastomosis with the Duhamel procedure could be considered [135].

Surgery of Associated Malformations or Complications

PIPO patients are exposed to variable risk of mechanical occlusion or postsurgical complications related to associated intestinal anomalies, chronic segmental bowel dilation, postoperative adhesions, and stoma prolapse.

During radiologic assessment in patients with suspected PIPO, upper gastrointestinal contrast study is mandatory to evaluate the configuration of the duodenal C- loop, the duodenojejunal flexure position and the position of the small bowel loops. If small bowel malrotation is confirmed, Ladd procedure should be performed at the same time of intestinal biopsies and enterostomies formation. In fact, conditions such as anomalies of intestinal fixation and rotation, observed in about 30% of PIPO, or segmental chronic colonic dilation and elongation related to prolonged stasis associated to motility troubles, may expose these patients to acute life-threatening complications such as midgut or segmental colonic volvulus, respectively.

Mechanical intestinal occlusion related to acute midgut or segmental colonic volvulus or postoperative adhesions may present as an acute episode of obstruction; in PIPO patients, this diagnosis may be challenging and delayed, because of misunderstanding with functional acute pseudo-obstructive episode. Mechanical occlusion may be suspected when occlusive symptoms and signs persist associated to clinical deterioration, despite correct conservative management by fluid and electrolytes balance and infusion, bowel venting manoeuvres (nasogastric tube, open gastrostomy and jejunostomy tubes, fasting, enterostomy tube placement), and intravenous antibiotic administration. Moreover, caution should be exercised during the occlusive episode, when abdominal distension and bowel loop dilation are overcoming the habitual dimension for the patient, on physical and plain radiographic examination [142]. In this situation, an abdominal CT scan coupled with contrast enema is helpful and recommended before surgery. In case of confirmed colonic volvulus, colonoscopy may be attempted before surgery (Fig. 50.16). If strongly suspected small bowel mechanical obstruction (i.e., volvulus, strangulation, kinking) or failed colonoscopy, an emergency laparotomy is mandatory.

Stoma prolapse is frequently observed in PIPO. While its pathogenesis is multifactorial, the variability and anarchy of the bowel movements probably play the main role.

The length of prolapsed bowel may be different even in a few hours observing few tens of centimetres into the ostomy bag. Signs and symptoms are not related to the length of the prolapsed intestine. Manual reduction or surgical correction of the prolapse can be frustrating with high recurrence rate so, the treatment should be carefully evaluated on a case-by-case basis, to avoid unnecessary surgery. If required, because of symptoms such as bleeding, obstruction, intestinal impairment, re-do stoma formation represent the best choice, avoiding, if possible, resection of the prolapsed bowel.

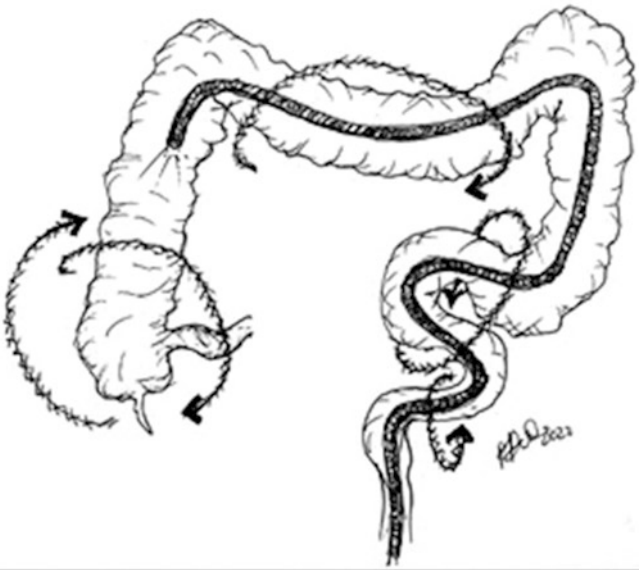

Fig. 50.16 Site of colonic volvulus in PIPO and colonoscopy treatment

Transplantation

Intestinal transplantation, either isolated small bowel or multi-visceral, should be considered in patients presenting with life threatening TPN related complications such as intestinal failure associated liver disease (IFALD), or in patients whose intravenous access has become unreliable and precarious because of repeated sepsis and extensive thrombosis and finally, in patients with poor quality of life with high risk of morbidity and mortality related to frequent pseudo-obstructive episodes with difficult fluid electrolyte imbalance due to excessive fluid shifts necessitating repeated hospitalizations [131]. Transplant procedure varies according to the need of replacing liver and to the experience of the transplant surgical team.

Conclusions

Digestive Endoscopy and surgery represent challenging diagnostic and therapeutic tools in the armamentarium of the multidisciplinary dedicated medico-surgical team in PIPO patients. Surgical interventions should be minimised to avoid potential related complications (adhesions, prolonged paralytic ileus, etc.), which could worsen the outcome of these patients. Resective surgery (gastrectomy,

colectomy, and small bowel resection) is often affected by failures, complications, and inadequate responses, compared to expectations [143]. An enterostomy is often performed as one of the first endoscopic or surgical therapeutic measures. Full thickness biopsies are mandatories to classify PIPO and they must be carried out at the same time of surgery for enterostomy creation. Enterostomies are very commonly used to decompress and reduce pseudo-obstructive events, to allow nutritional feeding through gastrostomy and jejunostomy reducing PN during the life of patients. Emergency laparotomy should be reserved only when a mechanical obstruction is assessed. Intestinal transplantation should be reserved only in selected cases with life threatening PN related complications or loss and unreliability of intravenous access.

When possible, endoscopy and surgery in children with suspected or known diagnosis of PIPO should be restricted to centres and practitioners with great experience in managing such patients with the aim to propose a structured approach.

Hirschsprung Disease

Hirschsprung's Disease (HD), also known as "congenital aganglionic megacolon", is a rare motor disorder of the gut, which is caused by a failure in the cranio-caudal migration of the neural crest cells during the 5–12 weeks of gestation, resulting in an aganglionic intestinal segment.

The incidence of HD is reported in about 1:5000 live births; the male to female ratio in recto-sigmoid disease is 4:1, but in longer segment disease is 1:1–2:1 [144, 145].

Intestinal aganglionosis extends proximally from the rectum for a variable length, with a recto-sigmoid involvement in about 80% of patients; a long-segment type in 15–20% of cases and a total colonic aganglionosis (TCA) in approximately 5% of subjects. In rare cases, a total intestinal aganglionosis with absent ganglion cells from the rectum to the duodenum is described. In ultra-short HD type, the aganglionic tract is limited to the distal 2–3 cm of the rectum [146, 147].

Antenatal suspicion and/or diagnosis of HD is rare. Most patients are diagnosed in neonatal period or even later, due to the variability in clinical presentation, which is dependent on the length of the aganglionosis.

Genetics

HD occurs as an isolated condition in 70% of the cases, associated with additional congenital anomalies in 18% of patients (cardiac defects 8%, genitourinary 6%, gastrointestinal abnormalities 4%), and as a part of a genetic syndrome in up to 12% of cases (i.e., Down Syndrome, Waardenburg syndrome, Mowat-Wilson syndrome, MEN type 2A) [146].

Several genes have been found to be involved in HD (i.e., GDNF, NRTN, SOX10, EDNRB, EDN3 ECE1, ZFHX1B, PHOX2B, KIAA1279, TCF4, L1CAM, and IKBKAP) [148, 149].

The major susceptibility gene is proto-oncogene RET, which is implicated in about 50% of family forms, in 40–45% of sporadic cases, and in a higher percentage of long than of short type HD (76% vs. 32%) [150–154].

More than 100 different mutations have been described in the RET gene [150], some of which are also associated with the development of Multiple Endocrine Neoplasia type 2A (MEN 2A), a cancer syndrome characterized by medullary thyroid carcinoma, phaeochromocytoma of the adrenal glands, and hyperplasia of the parathyroid glands [155].

Therefore, ERNICA guidelines for HD suggest, in non-syndromic cases, to offer referral to parents or patients who wish to have a genetic screening and recommend genetic consultation for subjects with a family history of HD, where the incidence of RET mutations is even higher. In syndromic types, the genetic screening must be associated with the specific gene of the syndromic phenotype [156].

Clinical Presentation

HD should be suspected in any newborn with intestinal obstruction, in any infant and child with refractory severe constipation, chronic abdominal distention and history of delayed or failed passage of meconium within the first 24–48 h of life. This latter is the cardinal clinical feature in about 80–90% of infants with HD but also in 30–40% of healthy children and in 30–35% of preemies [144].

Intestinal obstruction symptoms (bilious vomiting, abdominal distension, and constipation), spontaneous intestinal perforation or episodes of acute "toxic" enterocolitis are typical findings during the neonatal period in the recto-sigmoid or in longer types of HD [150, 157–159].

Explosive bowel movements caused by functional colonic obstruction and enterocolitis-related diarrhoea rather than constipation are possible symptoms in infants with HD [160].

Refractory constipation, frequently associated with abdominal distension and failure to thrive, seems to be the only symptom in the ultra-short form and in older children. Rectal examination usually reveals a tight anal sphincter and explosive discharge of stool and gas.

Diagnosis

Tests available for diagnosing HD include manometric, radiological, and histological studies.

Anorectal manometry assesses the correct innervation of the internal anal sphincter (IAS) eliciting the recto-anal

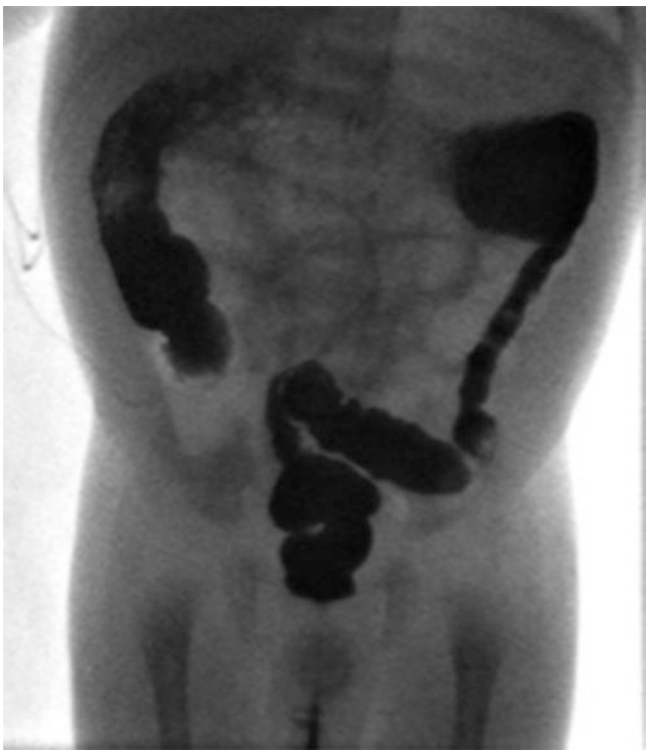

Fig. 50.17 Contrast enema shows a transition zone at the splenic flexure. At the operation, the transition zone correlated with the histological findings

inhibitory reflex (RAIR) via the myenteric plexus. RAIR is a relaxation response in the IAS, namely a pressure drop of at least 25% in the anal canal following rectal distension. The absence of RAIR is indicative of HD [161].

Contrast enema is a useful screening test for a pre-operative morphological evaluation of the colon. The finding of the pathognomonic sign of "transition zone" (Fig. 50.17), a funnel-shaped segment between the narrowed aganglionic rectum and the proximal normally innervated segment, may aid in surgical procedure planning since the location of the radiographic transition zone correlates with the level of aganglionosis in 63% to 90% of cases [162–164].

Unfortunately, the transition zone may not be detected in neonates, because of insufficient time to develop the dilation, or in infant treated by frequent saline rectal irrigations.

Rectal suction or full-thickness biopsy remains the gold standard test in the diagnostic workup of HD. The tissue samples should be taken a minimum of 2 cm above the dentate line to avoid the physiologic aganglionic/hypoganglionic zone of the distal rectum [165], specimens should be at least 3 mm diameter and one-third of them should comprise submucosa [166, 167].

The absence of ganglion cells confirms the clinical and radiological suspicion of HD.

Differential diagnosis may consider meconium ileus secondary to cystic fibrosis, gastrointestinal malformations (intestinal atresia, malrotation, duplication cysts), multiple endocrine neoplasia type 2A (MEN 2A), intestinal neuronal dysplasia, meconium plug syndrome, small left colon syndrome, chronic intestinal pseudo-obstruction, and hypothyroidism [146].

Surgical Techniques

The aim of treatment in HD is the resection of the aganglionic segment, the anastomosis to the anus of the normally innervated bowel, and the preservation of the anal sphincter function.

Historically, colostomy was performed at diagnosis of HD and colonic pull-through was scheduled 6–12 months later. Thanks to the improvement of diagnostic and surgical techniques, surgery shifted from multistage to single stage.

Temporary stoma is indicated in presence of intestinal perforation or acute enterocolitis unresponsive to non-operative treatment and when rectal washouts are not effective to decompress the bowel [168].

In emergency settings, the level of the stoma should be proximal to the site of perforation or empirical in the distal ileum. In elective conditions, the stoma may be performed above the transitional zone (also known as "leveling stoma"), in a normal neuronal pattern bowel segment, detected by peri-operative biopsies [169].

According to ERNICA HD guidelines, the pre-operative management includes: 1–3 times per day saline rectal irrigations to decompress the bowel until the definitive pull-through operation; contrast enema, that may help to define the level of aganglionosis with possible identification of the transition zone, although it does not replace the need for histological assessment; pre-operative one dose of broad-spectrum intravenous antibiotics, which should be continued for 24–48 h post-operatively [156].

Different surgical options are available using an abdominal and/or trans-anal approach and the choice of procedure is usually based on the training and experience of the surgeon.

Full-thickness biopsies should be performed intra-operatively to define the correct level of aganglionosis and identify the normally innervated colon to bring down to the anal canal for anastomosis [156, 170].

Swenson Procedure

The Swenson procedure, first performed in 1948, was the original pull-through procedure used to treat HD. The technique consists of a deep pelvic dissection with mobilization of rectum and left colon to bring normal bowel down the perineum. The rectum is intussuscepted through the anus and an incision is made 1.5 cm above the dentate line of the anal

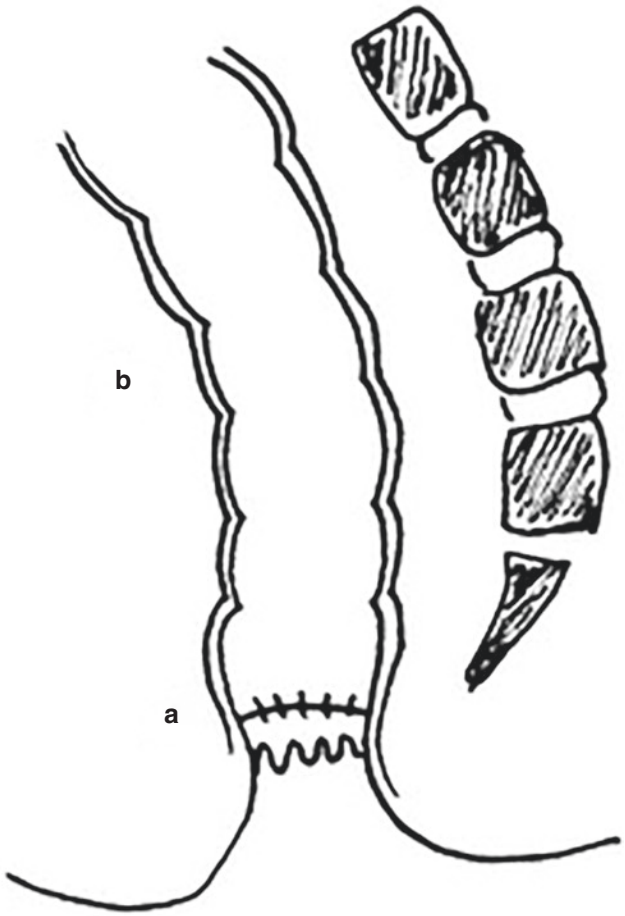

Fig. 50.18 Swenson procedure: the aganglionic bowel is resected and an end-to-end anastomosis (**a**) of the normal colon (**b**) to the low rectum is performed. This operation is done through a laparotomic, or laparoscopic approach and the anastomosis is performed from a perineal approach after eversion of the aganglionic rectum

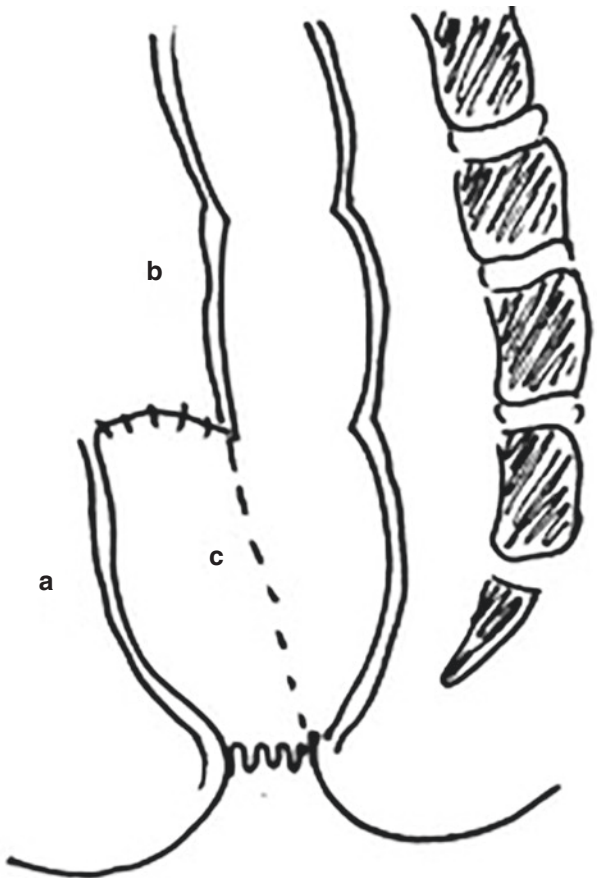

Fig. 50.19 Duhamel procedure: The aganglionic colon is resected to the rectum; a residual pouch of aganglionic rectum is left intact (**a**) and the normally innervated bowel (**b**) is attached behind the rectum with an end-to-side anastomosis (**c**). By joining the two walls, a new lumen is created which is aganglionic anteriorly and normally innervated posteriorly

canal, in the anterior zone of the circumference, in order to preserve faecal continence and facilitate voluntary bowel movements. The intussuscepted colon is pulled through until the correct level is visualized. An anastomosis between pulled-through ganglionic colon and anal canal is performed obliquely outside the anus as the bowel is divided and removed (Fig. 50.18). Finally, the anastomosis is returned to the pelvis [171, 172].

Duhamel Procedure

The Duhamel procedure, described in 1956, requires much less pelvic dissection than the Swenson procedure with a lower risk of incontinence. The aganglionic bowel is resected down the rectum that is maintained in situ. The ganglionic bowel is brought down to the level of anal canal through a bloodless retro-rectal space between rectum and sacrum. A side-to-side anastomosis between the anterior aganglionic rectal stump and the posterior pulled-through ganglionic bowel is performed using a linear stapler which simultaneously joins the two segments and divides the common wall between them to create a single lumen (Fig. 50.19) [173].

Soave Procedure

The endorectal pull-through operation was first described by Soave in 1964 and later modified by Boley. An accurate trans-abdominal submucosal dissection of the aganglionic segment of the colon is extended down to the anal canal, leaving the muscular coat of the rectum intact, avoiding lesions of pelvic innervation. The ganglionic bowel is pulled through the muscular cuff and anastomosed to the anal canal about 1 cm above the dentate line. The original procedure left a 5- to 10-cm length of the pull-through colon hanging out through the anus and the final anastomosis had to be created several weeks later [174].

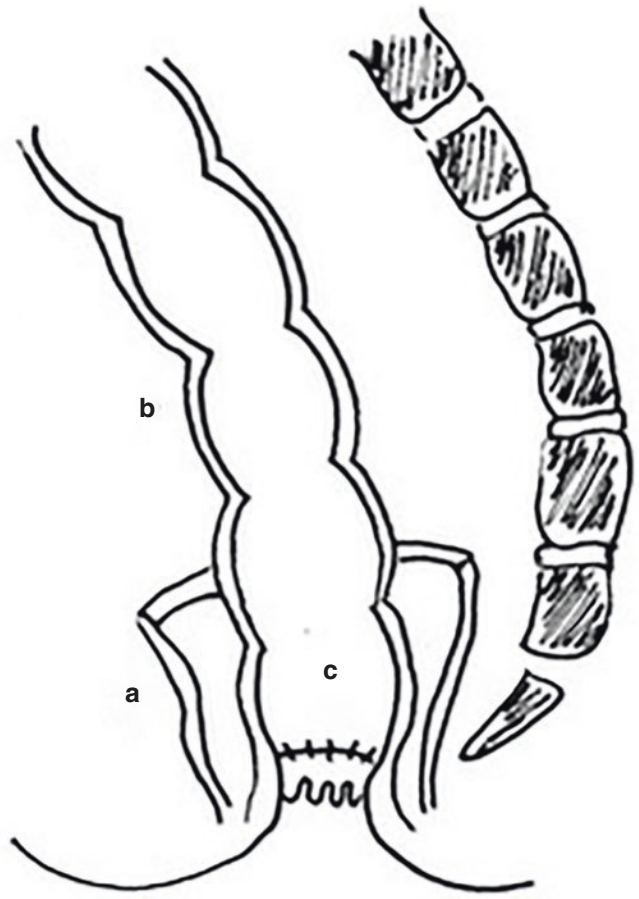

Fig. 50.20 Soave/Boyle procedure: The mucosa and submucosa of the rectum have been removed. The outer layer of the aganglionic rectum (**a**) is left in place and the ganglionic colon (**b**) is pulled through within the muscular cuff with an end to end primary anastomosis (**c**) at the anus

Boley modified this procedure, performing a single stage operation with primary anastomosis at the anus with or without splitting of the aganglionic muscular cuff (Fig. 50.20) [175].

Transanal Endorectal Pull-Through

The transanal endorectal pull-through was introduced by De la Torre-Mondragon and Ortega Salgado in 1998, as a modification of the Soave procedure [176, 177].

This technique consists of a totally transanal endorectal pull-through without any laparotomic or laparoscopic mobilization.

As first step, the rectal mucosal layer is incised 0.5–1 cm above the dentate line and a rectal mucosal cylinder is dissected as far as the peritoneal reflexion. Multiple 5-0 silk traction sutures are placed in the mucosa to facilitate its separation from the muscular wall (Fig. 50.21).

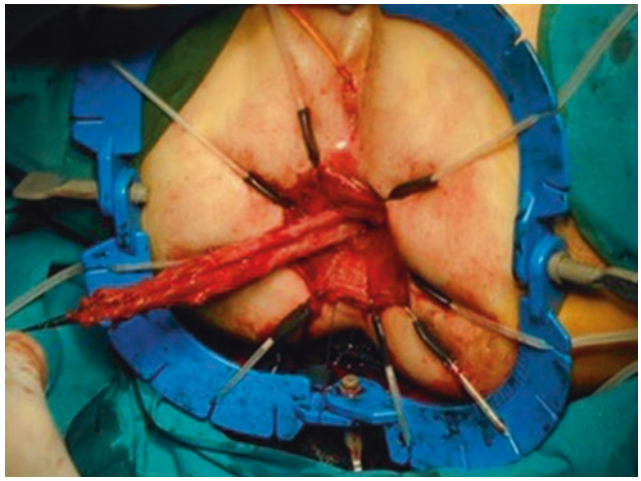

Fig. 50.21 Trans-anal endorectal pull-through procedure, first step. The rectal mucosal layer is incised 0.5–1 cm above the dentate line and a rectal mucosal cylinder is dissected as far as the peritoneal reflexion

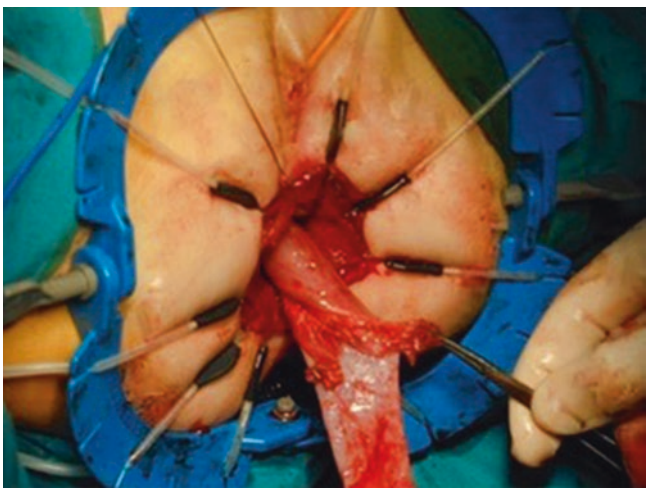

Fig. 50.22 Trans-anal endorectal pull-through procedure, second step. The division of the muscular rectal wall is continued circumferentially, freeing the intra-abdominal colon from the muscular sleeve

The division of the muscular rectal wall is continued circumferentially, freeing the intra-abdominal colon from the muscular sleeve (Fig. 50.22). A posterior myotomy of the muscular sleeve is made above the place where the anastomotic line should be created (Fig. 50.23).

Once the muscular sleeve is prepared and liberated, the rectum is pulled down and perirectal tissues are easily exposed and the mesenteric vessels are dissected, tied, and divided. Thus, the colon is pulled through the rectal muscular sleeve onto the anus (Fig. 50.24).

During this step, full-thickness biopsy specimens of the colon are examined through frozen sections to assure normoganglionic level. The aganglionic colon is resected, and a primary anastomosis is made between the normally ganglionic colon and the rectal mucosa.

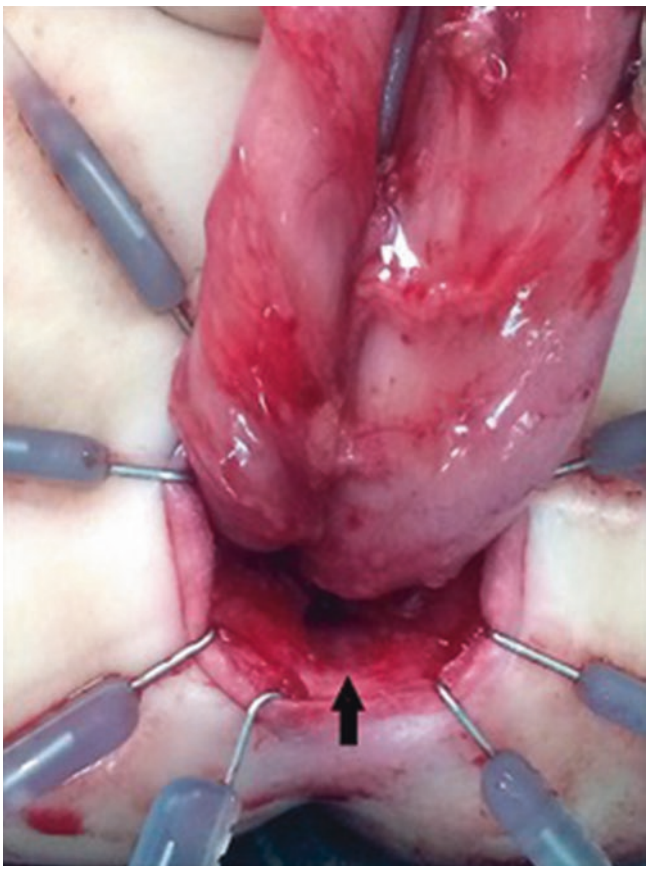

Fig. 50.23 Trans-anal endorectal pull-through procedure. The rectal muscular cuff is incised posteriorly

Laparoscopic- and Robotic-Assisted Colon Pull-Through

Laparoscopic-assisted colon pull-through procedure exploits the well-known advantages of laparoscopy, such as less postoperative pain, quicker recovery, less adhesive bowel obstruction and wound complications, better cosmetic results and, furthermore, gives the opportunity to perform intraoperative multiple biopsies, visualizes the pulled through colon, and prevents twisting of the bowel.

The sigmoid colon and the rectum can be mobilized laparoscopically; a submucosal sleeve is crafted trans-anally to meet the dissection from above. The ganglionic colon is then pulled down in continuity, divided above the transition zone and anastomosed to the anal mucosa 5 to 10 mm above the dentate line [178].

During the last decade, the robotic assisted pull-through procedure has been used to treat infants, even younger than 12 months of life, and children suffering from recto-sigmoid HD, long segment HD and TCA [179–181].

Some potential advantages of robotic surgery include greater surgical precision, increased range of motion, improved dexterity, enhanced visualization, and better access to hard-to-reach areas.

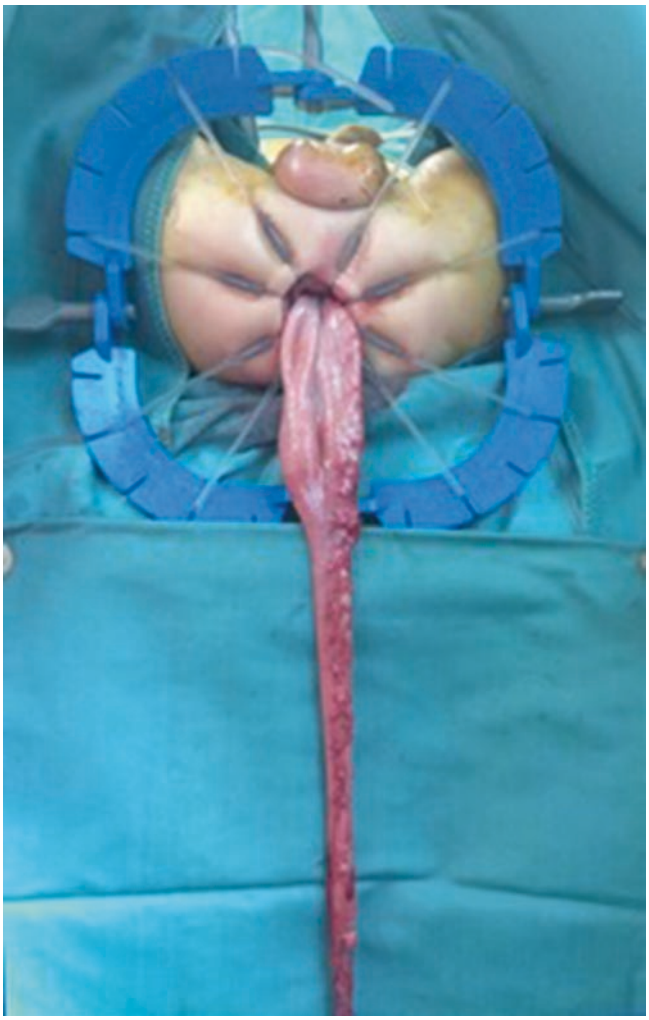

Fig. 50.24 Trans-anal endorectal pull-through procedure, final step. The aganglionic segment (narrow colon), the transition zone and the normal ganglionic bowel (dilated bowel) are pulled through transanally

Four trocars are needed to perform the intraoperative seromuscular levelling biopsies and to mobilize the rectum down to the anal canal with an intracorporeal endorectal cranial dissection; the rectal cuff is divided posteriorly, the previously isolated colon is then pulled-through and a colo-anal anastomosis is achieved at the pectinate line by an endoanal approach.

The first results are encouraging in terms of intra−/post-surgical complications and continence outcomes.

Future studies are needed to compare the long-term data of this approach with the open and laparoscopic techniques [179].

Total Colonic Aganglionosis (TCA)

Surgical treatment for TCA is a challenge for surgeons (Fig. 50.25). To this aim, various techniques have been per-

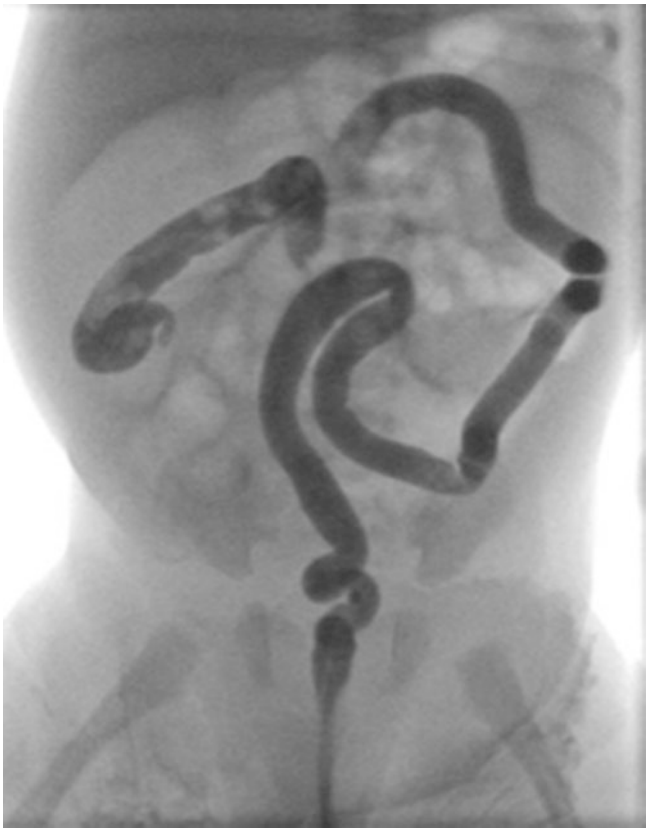

Fig. 50.25 Total colonic aganglionosis. 1-day-old-term male baby with obstructive symptoms and family history of HD. The contrast enema detects a microcolon. Histology confirmed aganglionosis involving colon and terminal ileum (approximately 30 cm)

formed, including a long longitudinal side to side anastomosis between the aganglionic bowel and the pulled-through ganglionic healthy bowel (Lester Martin procedure) [182]; a longitudinal side-to-side ileocolostomy between the normal ileum and the aganglionic ascending colon forming a colonic patch graft (Kimura procedure) [183] and proctocolectomy with J pouch-ileoanal anastomosis [184–186].

Ultra-Short HD

The ultra-short form of HD is an aganglionic segment of less than 2 to 3 cm histologically characterized by the absence of both hypertrophic nerves and abnormal cholinesterase staining [187].

The treatment of ultrashort-segment HD is controversial, so that different therapies, such as intrasphincteric botulinum toxin injections, simple anal sphincter myectomy and excision of the aganglionic segment with bowel pull-through, are taken into consideration [188, 189].

Early Postoperative Management

ERNICA guidelines recommend to adopt the Enhanced Recovery After Surgery (ERAS) protocols in paediatric colorectal surgery to improve surgical outcomes and efficiency of care [156].

Items of ERAS include use of minimally invasive surgical techniques, opioid-sparing analgesia, early post-surgical re-feeding, and judicious use of drains and catheters. ERAS pathways have demonstrated to reduce length of stay and complication rates, with an increment of patient satisfaction [190].

Early Post-Surgical Complications

Anastomotic leak and cuff abscess are rare early post-surgical complications, reported in 1–10% and in 5% of cases, respectively [191–194].

The risk is increased in presence of tension or ischemia of the anastomosis, poor nutritional status, steroid usage, and residual aganglionosis. A water-soluble contrast enema may be useful to make a diagnosis. Treatment may include surgical exploration, diverting colostomy, and revision of anastomosis [146].

Anastomotic strictures are a potential complication after pull-through surgery with an incidence up to 10.6% (range: 0–18.9%) [195].

Predisposing factors include ischemia, anastomotic leakage, and anastomotic tension. The risk is lower after Duhamel procedure since the colo-rectal anastomosis is wider. Calibration of the coloanal anastomosis is advisable at around 2–3 weeks after pull-through surgery, while daily anal dilatations are suitable in case of stricture [146].

Long-Term Post-Surgical Complications

Despite surgical techniques and medical care have improved over recent years, severe constipation (9–40%), faecal incontinence (FI; >8–74%) or Hirschsprung-Associated Enterocolitis (HAEC) (25–37%) can persist after pull through surgery in a long-term outcome [169, 196–203]. According to ERNICA guidelines for HD, a careful re-evaluation of these patients is mandatory to ensure a functional improvement and to prevent a psychosocial unrest [156].

The first step comprises clinical and nutritional check with full survey of the stooling pattern, dietary history, and development.

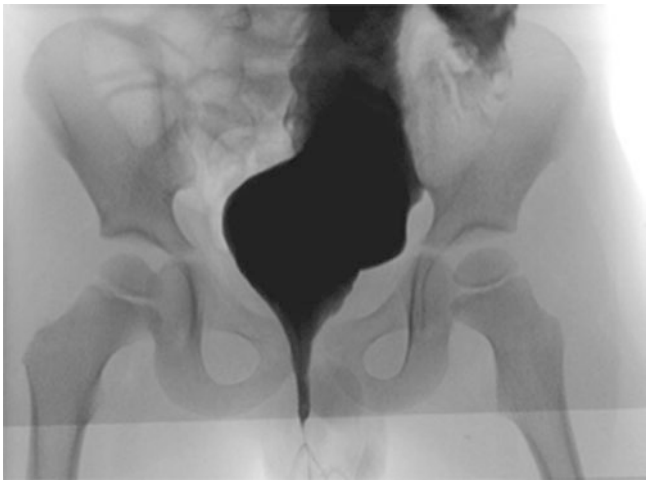

Fig. 50.26 Four-year-old male patient underwent trans-anal endorectal pull-through for diagnosis of recto-sigmoid HD at the age of 14 months. Persistent constipation after surgery. Contrast enema identifies a narrowing (stenosis of rectal cuff) of the distal portion of the pulled colon and a proximally dilated colon. Intraoperative biopsies confirmed a normal ganglionic pattern; a redo myotomy of the rectal cuff has been performed

In persistent post-operative **constipation** or in case of **obstructive symptoms**, anatomical (mechanical or histological) and functional aetiologies should be considered [169].

Rectal examination and contrast enema are required in Soave and in De la Torre-Mondragon procedures to rule out mechanical causes, such as anastomotic stricture, rolled or stenotic muscle cuff (Fig. 50.26) and twisted pull-through; in Duhamel technique occurrence of rectal spur.

Histological review of the proximal margins of the originally resected bowel and/or repetition of rectal biopsies are necessary to exclude an aganglionic residual segment or a pulled-through transition zone.

In accordance with the findings, anal dilations for anastomotic stricture or redo surgery (section of rectal spur; surgical revision of cuff stenosis or bowel torsion; redo pull through in twisted colon and in residual aganglionosis or in incomplete resection of transition zone) should be considered [203, 204]. If no mechanical or histological complications are documented, botulinum toxin can be administered to relax the internal anal sphincter and facilitate the passage of stool [205, 206].

Bowel management programme is recommended to non-responders after repeated (>3) botulinum toxin injections. There are various management options available (retrograde enemas or antegrade continence colonic irrigations through appendicostomy or cecostomy) which can be suggested by the patient.

Faecal incontinence (FI) is another problem after pull-through surgery, that implies evaluation of the anorectum and colon to distinguish between overflow or retentive and non-retentive type.

Overflow or retentive FI may depend on mechanical obstruction with faecal impaction and overflow of liquid stool; in other cases, hyperperistalsis of the pulled-through bowel determines recurrent soiling, despite normal sphincter function.

Non-retentive or true FI is secondary to anal sphincter injuries or abnormal rectal sensation.

A careful clinical inspection of the anal canal under anaesthesia is mandatory to exclude anatomical causes of retention and to document the site of the anastomosis in relation to the dentate line and its circumferential integrity, necessary to distinguish between gas, liquid, or solid stool [207].

A complete assessment of anal sphincters includes endoanal ultrasonography, which aids in the diagnosis of anal sphincter injuries, and anorectal manometry, which offers useful data about rectal sensation, pelvic floor dyssynergia, and anal pressures [208, 209].

Intestinal peristalsis (hypo- or hypermotility) and dilatation of pulled colon should be evaluated by motility tests (colonic manometry, colonic scintigraphy, and radiopaque markers) and a morphological study (contrast enema), respectively.

Successful management of FI depends on a clear understanding of the underlying problem. Thus, laxatives should be administered in case of intact anal canal, dilated colon and constipation (hypomotility colon); constipating diet, loperamide and bulking agents (pectin, psyllium) are useful for patients without colonic dilatation and a tendency to lose stools (hypermotility colon); a bowel management programme should be proposed in non-retentive FI to completely empty the colon; biofeedback training may be effective in pelvic dyssynergia [156].

Enterostomy remains a rescue option if the other treatments fail to control symptoms.

Hirschsprung-associated enterocolitis (HAEC) is a common and sometimes life-threatening complication of HD. Long-segment disease, older age at radical surgery, Down's syndromee and previous episodes of HAEC are recognised predisposing factors for recurrent HAEC [210].

The aetiology is probably multifactorial; alterations in the intestinal barrier, dysbiosis of the intestinal microbiota, bacterial translocation and impaired gastrointestinal mucosal immunity can contribute to the development of this severe condition [211].

Clinical presentation can include fever, abdominal distension, explosive foul-smelling bloody diarrhoea, lethargy; on this occurrence the abdominal X-rays usually show multiple air–fluid levels, dilated loops of bowel, and pneumatosis (Fig. 50.27a–c).

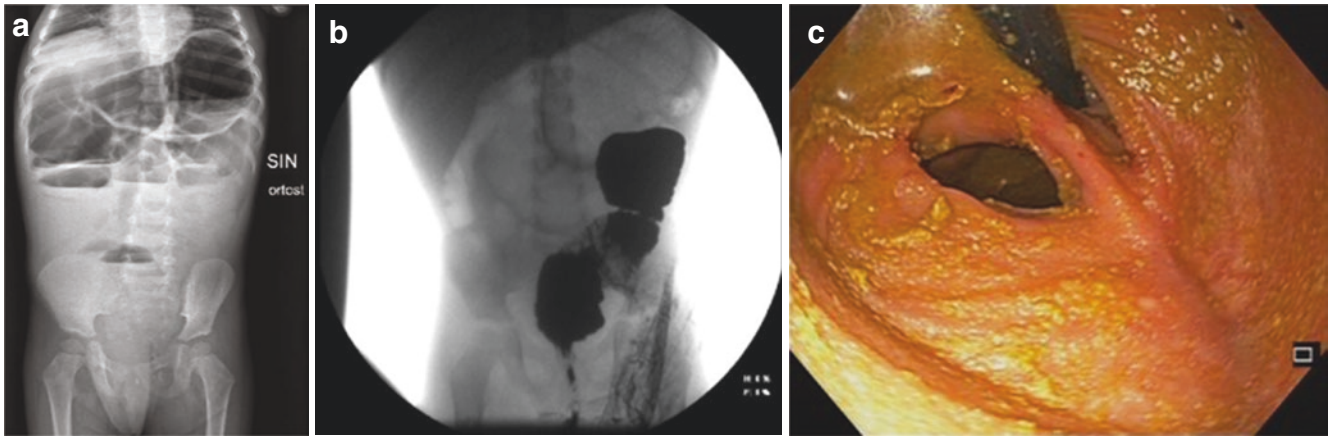

Fig. 50.27 Three-year-old female patient operated on long segment HD at birth (Duhamel procedure). Episodes of HAEC with fever, vomiting, dehydration, abdominal distension, pain, foul smell stools. (**a**) Plain abdominal X-ray: multiple air–fluid levels and dilated loops of ileum. (**b**) Contrast enema: suspect of intestinal stenosis. (**c**) Ano-ileoscopy: no anastomotic stricture, no rectal spur; mucosal bridge and dilation of the ileum

In acute forms, intravenous fluid resuscitation, broad-spectrum antibiotics, and saline rectal washouts to decompress the bowel are recommended [212].

The risk of HAEC may be decreased by using preventive measures such as routine irrigations or/and chronic administration of metronidazole; intra-sphincteric botulinum toxin injection is a valid and minimally invasive therapeutic option, that reduces the incidence of HAEC in 62–89% of HD patients [205, 213–218].

Redo surgery (i.e., posterior myotomy or redo pull-through according to the underlying causes) is indicated in case of mechanical obstruction.

Surgical Procedures and Outcome

In literature, no agreement has been reached about the optimal surgical approach to treat HD. Heterogeneity in the results depends on various parameters such as type of HD, presence of a colostomy, operation timing, complexity of the operation and experience of the surgeon.

Trans-abdominal endorectal pull through techniques spare the perirectal innervation, with a low rate of incontinence and sexual problems. Trans-anal endorectal pull through adds the typical advantages of minimally invasive procedures even if the anal sphincter may be overstretched during anal traction, leading to permanent incontinence/soiling. However, manometric comparison between perineal and abdominal approach shows that the postoperative sphincter function does not decrease in patients undergoing trans-anal endorectal pull through [219, 220].

Likewise, the occurrence of incontinence after the Duhamel operation is like that after the trans-anal endorectal pull through intervention, probably due to minimal pelvic dissection that avoids autonomic nerve damage [221].

As regards constipation, there is no significant difference between the Soave group and the trans-anal endorectal pull through population [222] and between Soave and Swenson operation, notwithstanding the incomplete excision of the aganglionic rectal wall in the first of the two [223, 224].

Chatoorgoon et al. reported a high risk of constipation in patients with a mega Duhamel pouch [225], while Widyasari et al. documented a higher constipation rate in the Soave respect to the Duhamel group, as the latter offers the advantage of a wide anastomosis [226].

A systematic meta-analysis comparing Duhamel with transanal endorectal pull-through procedures in infants and children testified similar results regarding rate of postoperative fecal incontinence and operation time; anyway, Duhamel procedure seems to be associated with longer hospital stay and lower rate of enterocolitis [221].

All the techniques can be performed via laparoscopic surgery, which results in minor trauma, smaller amounts of blood loss, lower intraperitoneal contamination, and less intestinal adhesions [221].

In any case, in a long-term follow up, more than 90% of HD affected individuals relate satisfactory outcomes and approximately only 1% suffers from debilitating incontinence requiring a permanent colostomy [227].

Subjects with chromosomal abnormalities and syndromes or with TCA, have a worse prognosis [228].

Conclusions

HD is a rare, congenital, and complex motility disorder caused by a lack of ganglion cells in the enteric neural plexuses of the intestine. The treatment is primarily surgical and aims at the resection of the aganglionic segment and at a re-anastomosis with ganglionated bowel. Different surgical

options are available and ensure good clinical results in most patients. In any case, a follow up to adulthood, within the context of an interdisciplinary care team, is recommended because of the risk of recurrent enterocolitis, persistent constipation, or faecal incontinence.

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