



A narrative review of gastroesophageal reflux in the pediatric patient

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Abstract: Gastroesophageal reflux (GER) is the retrograde passage of gastric contents into the esophagus. It is a physiologic condition that is common in neonates, typically resolves spontaneously, and does not result in clinically significant complications. When pathologic, gastroesophageal reflux disease (GERD) can cause numerous complications including persistent emesis, failure to thrive, aspiration, and respiratory symptoms. While a diagnosis can often be made from a thorough history and physical, some patients may require further testing. In general, many clinicians will reserve extensive investigation such as multiple intraluminal impedance and pH monitoring for patients with a confounding clinical picture or relative contraindications to medical or surgical management. Whereas most pediatric GER resolves spontaneously, medical management including lifestyle changes, changes to feeds, and the use of H₂-antagonists and/or proton pump inhibitors (PPIs) can be utilized to alleviate symptoms. Surgical treatment is reserved for patients who are refractory to medical management or have suffered significant complications as a consequence of GER. In this article we seek to provide a concise but detailed review of recent updates in the understanding, work up and management of GER in the pediatric patient. A summary of new technologies used in the diagnostic and therapeutic arms of this disease are included.

Keywords: Gastroesophageal reflux (GER); gastroesophageal reflux disease (GERD); antacids; Nissen; fundoplication

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Introduction

The understanding and management of gastroesophageal reflux (GER) have significantly changed and developed over time with advancements in medicine and technology. Technological advances have been widely applied in the adult population, but less so in the neonatal and pediatric populations due to a variety of limitations such as size and physiology. In this article, we aim to provide a detailed review of the current literature pertaining to the understanding, evaluation, and management of GER in children. This includes a review of the latest available technologies with regard to diagnosis and treatment as

well as a detailed analysis of the evolution of the surgical techniques currently used to treat reflux.

We present the following article in accordance with the Narrative Review reporting checklist (available at <http://dx.doi.org/10.21037/tgh-20-245>).

Study methods

A systematic search of PubMed and MEDLINE databases using the terms “gastroesophageal reflux”, “gastroesophageal reflux disease”, “GERD”, “antacids”, “Nissen”, and “fundoplication” from 1980 to the present

was conducted. Both adult and pediatric literature were reviewed. All available, high quality resources written in English or with an available English translation were eligible for inclusion in this review.

Epidemiology, pathogenesis and presentation

GER is the retrograde passage of gastric contents into the esophagus (1-5). This physiologic condition is most common in infants but can be present in older children as well. Current literature suggests GER may have a peak incidence in infants 3–4 months of age (60–70%) with an incidence of 50% in infants less than 2 months and down to 5% of infants by 1 year of age (2,6,7). Gastroesophageal reflux disease (GERD) is a pathologic condition characterized by the reflux of gastric contents into the esophagus and oropharynx, resulting in complications (1-5). These include failure to thrive, recurrent respiratory symptoms or changes in the epithelial lining of the distal esophagus (Barrett's esophagus).

The first report of a reflux associated esophageal ulceration was in the late 19th century by Quincke (8). Several reports followed and the presence of a hiatal hernia (HH) was thought to be the primary cause of GER. The development of continuous measurement of the lower esophageal sphincter (LES) subsequently led to the understanding that GER was secondary to transient lower esophageal sphincter relaxation (TLESR) and not a lower basal LES pressure (9). In an excellent review of the topic, Herregods *et al.* provide a summary of the mechanisms resulting in reflux as well as the factors that affect the perception of symptoms (9). The factors leading to reflux are the presence of a HH, lower basal LES pressure, TLESR, acid pocket (i.e., the physiologic layering of acidic gastric secretions at the stomach fundus or gastroesophageal junction above a food bolus), increased distensibility of the esophagogastric junction (EGJ), esophageal clearance, and delayed gastric emptying (DGE) (9). Essentially the first three result in an incompetent barrier between the esophagus and stomach and the latter four lead to prolonged acid exposure through ineffective clearance (9).

Physiologic GER, characterized by mild or intermittent regurgitation, may be seen between 1 week and 6 months of age (10). These episodes become less frequent with age and the associated transition from supine to more upright posture, as well as with the transition to solid food (1,3). Despite these episodes, children with GER continue to feed well and thrive in the absence of other symptoms (2).

They may often be referred to as “the happy spitter” by pediatricians. This is in stark contrast to children with GERD who may have failure to thrive or chronic respiratory illnesses.

The presentation of GERD in pediatric patients varies by age. Infants and young children may present with: failure to thrive, irritability, excessive crying, poor food intake and tolerance, sleep disturbances, coughing, wheezing, stridor, recurrent aspiration and pneumonia, recurrent otitis media, grimacing, opisthotonos, or torticollis (2,3,11-13). Older children and adolescents may present with symptoms more similar to that of adults. These include: regurgitation and emesis, nausea, dysphagia, retrosternal or epigastric pain, nausea, chronic cough, wheezing, hoarseness, halitosis, and/or dental erosions (2-4). As gastric contents may or may not reach the oropharynx to induce nausea or vomiting, postprandial emesis itself is not pathognomic and may be frequently ignored due to its ubiquitous nature in infants (1).

It is reasonable to counsel families that symptoms typically improve after 1 year of age in the overwhelming majority of healthy infants. GERD does, however, demonstrate an increased prevalence in children affected by: prematurity, obesity, neurological impairment, congenital heart disease, congenital diaphragmatic hernia, gastrointestinal (GI) tract abnormalities, and chromosomal abnormalities (2,14-21). Refractory GERD refers to GERD symptoms that do not respond to medical treatment after 8 weeks (10).

Diagnostic methods

The diagnosis of GER is primarily clinical. It is important to discern the age of onset of symptoms, feeding/dietary history, pattern of regurgitation including timing and relation to meals, any prior pharmacologic or dietary interventions, patient's growth trajectory, assessment of possible environmental triggers, and family history. Signs and symptoms that suggest a diagnosis of GERD include: postprandial emesis or discomfort as demonstrated by significant arching of the back and even spasmodic torticollis and dystonia, as are seen in Sandifer syndrome (2,10).

Whereas diagnostic testing and treatment are not typically indicated for GER, further investigation may be warranted in those with severe symptoms or GERD (10). Diagnostic tools for the evaluation of GERD symptoms include: upper GI series, 24-hour pH monitoring, impedance testing, manometry, and endoscopy.

Esophageal pH monitoring

Esophageal pH monitoring involves the use of intraluminal probes passed through the nares to evaluate the pH proximal to the LES, and ideally, the upper esophagus, as well as the stomach (1,2). Alternatively, a wireless esophageal pH capsule can be used (2). The normal pH of the esophageal lumen ranges from four to seven (2). The purpose of monitoring is to detect all pH drops below four lasting for at least 15 seconds (i.e., the number of refluxes), the time required to correct this drop in pH (i.e., reflux clearance), the number of reflux episodes with clearance requiring more than 5 minutes, and the longest reflux episode. These values are used to calculate a reflux index, which reflects the percentage of time over a 24-hour period in which esophageal pH is less than four (1,2). A reflux index greater than 11% in infants or 7% in older children typically qualifies as abnormal (2,22,23). Esophageal pH monitoring has a relatively high sensitivity and specificity for GERD in comparison to other testing modalities, making it a long-standing key diagnostic technique (1,2).

Combined multichannel intraluminal impedance and pH monitoring

Combined multichannel intraluminal impedance and pH monitoring allow for the analysis of all refluxes and their pH, as well as the direction of food boluses over 24 hours (1,3). It is estimated that approximately 45% of infants with GERD demonstrate normal pH monitoring, as their GER episodes are more likely to be weakly acidic, normal, or even alkaline (3,24). Combined testing therefore allows for the evaluation of microaspiration of nonacid refluxes, which contribute to recurrent respiratory tract infections in young pediatric patients (1). Despite the increased cost of this combined modality, the significantly increased yield makes combined multichannel impedance and pH monitoring a frequent test of choice in the evaluation of pediatric GERD (3).

Manometry ± pH monitoring

In contrast to adults, manometry is not currently recommended in the evaluation of GERD in children. It can, however, be used to evaluate and exclude esophageal motility disorders such as achalasia that may resemble GERD. In pediatric patients, it typically requires the use of sedation and/or general anesthesia, limiting its routine use (3). When combined with pH monitoring, it allows

for the evaluation of pH in pathologic reflux with stepwise normalization by swallowing saliva. It can also be used to analyze acidic, neutral, and alkaline refluxes, allowing for similar conclusions as those derived from impedance testing (1).

Upper GI

Upper GI series is not currently recommended in the evaluation and diagnosis of GERD (1,3,10). It does, however, have utility in select patients to exclude conditions that mimic GERD, such as achalasia, malrotation, and pyloric stenosis (1,3,10). Upper GI allows for visualization of the gastroesophageal junction and the angle of His, demonstration of HHs, as well as esophageal peristalsis. Most importantly, it allows for the evaluation of the location of the duodenojejunal junction and can therefore detect malrotation. Due to short radiologic exposure times, however, the degree of reflux may be under- or overestimated on upper GI (24). Brief radiologic exposure contributes to false negative results and non-pathologic reflux contributes to false positive results (24). Upper GI has poor sensitivity, specificity, and positive predictive value ranging from 29–86%, 21–83%, and 80–82% respectively relative to esophageal pH monitoring (24–31). Indirect signs of pathologic reflux include air reflux and/or a positive water siphon test (1,32).

Endoscopy and histology

The role and timing of endoscopy is controversial. Endoscopy is a more invasive modality that can be used to evaluate for eosinophilic or candida esophagitis, HHs, and/or to relieve esophageal outlet obstruction resulting in stasis, cough, and aspiration (1,10). It also allows for tissue biopsy. Further research is needed to evaluate whether endoscopy is more valuable before or after the initiation of acid suppression therapy. Endoscopy performed prior to initiation of therapy allows for definitive diagnosis at first endoscopy; however, patients typically require repeat endoscopy to evaluate for healing after starting therapy (10).

Medical management

Treatment is not indicated in the majority of cases of pediatric GER (2). Esophageal dysfunction and GER resolve spontaneously in 90% of affected infants (1). In patients who do warrant therapy, the approach is to start

with simple modifications and then escalate to medical and finally surgical therapy.

Lifestyle changes

Initial measures for the treatment of GERD include changing the type, volume or frequency of feeds, thickening feeds, and postural therapy. Breastfed infants demonstrate lower rates of GERD than formula-fed infants (2,33,34). Furthermore, the elimination of cow milk protein and other potential allergens from a patient's diet can reduce GERD (2).

Thickening feeds can increase weight gain per day and reduce the frequency of visible regurgitation episodes in infants, although the patient's reflux index may remain unchanged (35,36).

The administration of frequent small meals, followed by maintaining an infant in an upright position for 20–30 minutes after feeds can mitigate regurgitation episodes (2). The supine position with the trunk elevated can also be utilized (1). Supervised positioning in the left lateral position is conditionally recommended in awake infants (1,3). The use of prone positioning in infants, however, is always recommended against due to the increased risk of sudden infant death syndrome (SIDS). Emesis that occurs in prone positioning can obstruct the oropharynx and induce apneic spells and apparent life-threatening events (ALTEs) (1-3).

Medical therapy

H₂-receptor antagonists

Pharmacotherapy should be considered and reserved for patients whose GERD symptoms do not respond to conservative measures. H₂-receptor antagonists and proton pump inhibitors (PPIs) have been proven safe and effective in reducing gastric acid output in pediatric patients (37). Treatment times vary from weeks to months (2).

H₂-receptor antagonists reduce gastric acid secretion by competitively inhibiting the interaction between histamine and the H₂-receptor on gastric parietal cells (2,22). They also reduce pepsin and the volume of gastric acid (2,22). They have a rapid onset of action. Commonly used H₂-receptor antagonists include: cimetidine, ranitidine, famotidine, nizatidine.

In their meta-analysis of eight studies including 276 children, van der Pol *et al.* found that H₂-receptor antagonists were more effective than placebo in promoting

histologic healing, increasing gastric pH, and with regard to overall treatment effective in children 0–15 years of age (38).

The use of H₂-receptor antagonists is limited by several factors. First, decreased gastric acid and hypochlorhydria can allow for gastric bacterial colonization. This can lead to an increased risk of certain infections, such as community-acquired pneumonia, enteric infections, and *Clostridium difficile* (1,2). Second, H₂-receptor antagonists have side effects that include abdominal pain, diarrhea, headache, somnolence, and dizziness (2). Third, patients will develop a tolerance to H₂-receptor antagonists with time (2,3).

In April 2020, the U.S. Food and Drug Administration (FDA) requested the immediate withdrawal of ranitidine from the market in light of ongoing investigations of contaminants in the medication. N-Nitrosodimethylamine (NDMA) is a probable human carcinogen that has been found in ranitidine. Concentrations appear to increase over time when stored above room temperature and could therefore result in dangerous levels of ingestion (39).

Proton pump inhibitors

PPIs inhibit gastric acid secretion by selectively blocking the hydrogen-potassium-adenosine triphosphatase (H⁺-K⁺-ATPase) pumps found on the gastric parietal cell membrane (2,22). They effectively ameliorate dyspepsia, and both prevent and accelerate the healing of esophagitis and esophageal injury (2,3). They are well tolerated and more effective than H₂-receptor antagonists, making them the drug of choice for the treatment of pediatric GERD (2). Furthermore, patients are less likely to develop a tolerance compared to H₂-receptor antagonists (3). Common agents include: omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole (2).

In their study of 30 infants aged 3–12 months, Moore *et al.* concluded that omeprazole was more effective than placebo in reducing esophageal acid exposure. Irritability improved with time in both groups (40). The International Pediatric Omeprazole Study Group concluded that omeprazole is effective for the treatment of erosive esophagitis and GERD symptoms at dosages of 0.7–3.5 mg/kg/day. In this study, 54 of 57 patients demonstrated healing of their erosive esophagitis, defined as macroscopically normal esophageal mucosa on endoscopy performed 3 months after initiation of treatment. Ninety-three percent of patients reported absent or mild GERD symptoms after treatment (41).

However in another systematic review of 12 studies, van der Pol *et al.* concluded that although well tolerated,

PPIs are not effective in reducing GERD symptoms in infants and that additional placebo-controlled trials in older children are needed (42).

Side effects of PPIs include: abdominal pain, diarrhea, nausea, somnolence, dizziness, headaches. Similar to H₂-receptor antagonists, patients are at increased risk of hypochlorhydria contributing to gastric bacterial colonization, community acquired pneumonia, and enteric infections including *Clostridium difficile* (1-3).

In a study of 1,815 individuals, Imhann *et al.* demonstrated significant changes to the gut microbiome with PPI use. This included a significant decrease in Shannon's diversity, changes in 20% of the bacterial taxa, and over-representation of oral bacteria in the fecal microbiome (43). There are currently ongoing observational studies in the adult population examining whether these changes to the gut microbiome may increase the risk of gastric or colon cancer with prolonged PPI use. Although PPIs have been shown to increase serum gastrin concentration, they have not yet been shown to increase the risk of gastric or esophageal cancer, enterochromaffin-like cell hyperplasia, or carcinoid tumors (44).

The hypochlorhydria thought to contribute to increased risk of enteric infections has also been hypothesized to limit calcium and magnesium absorption. In a meta-analysis of 18 studies, Zhou *et al.* demonstrated that PPI use increased the risk of hip, spine, and any-site fractures in both short-term use (i.e., less than 1 year) and longer use (i.e., greater than 1 year) groups (45).

Antacids

Antacids neutralize gastric acid, minimizing exposure of the esophageal mucosa to gastric acid (2). They are not effective in the treatment of GERD in infants, but may be used for short-term symptomatic use in older children and young adults (2). This drug class includes: aluminum hydroxide, calcium carbonate, and magnesium hydroxide (2).

Prokinetics

Prokinetic agents improve esophageal contractility, increase LES pressure, and promote gastric emptying (4). These drugs, which include metoclopramide, cisapride, domperidone, and baclofen, have not however been proven to be effective in the treatment of pediatric GERD (24,46). Furthermore, they have a significant side effect profile that includes: extrapyramidal effects, prolactinemia, galactorrhea, ventricular arrhythmias, QT prolongation,

drowsiness, and restlessness (1-3).

Endoscopic management of GERD

New endoscopic techniques are emerging for the treatment of pediatric GERD. The benefit of these techniques is that they would be able to be performed in an outpatient setting. Endoscopic fundoplication includes three techniques: endoscopic suturing devices, endoscopic radiofrequency, and endoscopic implantation of inert material (1). Endoscopic suturing devices function by constructing mucosal valves to prevent reflux (47,48). Gerson *et al.*'s meta-analysis of 233 patients over three randomized controlled trials demonstrated that transoral incisionless fundoplication (TIF) improves esophageal pH, decreases PPI utilization, and improves quality of life at 3-year follow-up (49). In one of these trials, the TEMPO trial, which consisted of 63 patients, troublesome regurgitation was eliminated in 88% of patients at 1-year follow-up, 90% at 3-year follow-up, and 86% at 5-year follow-up after TIF (50). Endoscopic radiofrequency techniques use metallic prongs and radiofrequency energy to create thermal lesions in the muscle wall of the LES (47,51). Fass *et al.*'s meta-analysis of 28 studies and 2,468 patients evaluated the effectiveness of endoscopic radiofrequency procedures (Stretta). Stretta improved patients' health-related quality of life score by -14.6 (-16.48, 12.73) (P<0.001) and improved pooled heartburn standardized score by -1.53 (-1.97, -1.09) (P<0.001). Stretta reduced the incidence of erosive esophagitis by 24% and reduced PPI use from 100% of patients at baseline to 49% at follow-up (52). Endoscopic implantation of inert material decreases reflux events by reducing the distensibility of the LES (53,54). Johnson *et al.* and Cohen *et al.*'s sequential studies evaluated the effectiveness of Enteryx implantation at 12 and 24 months, respectively. Johnson *et al.* demonstrated a 50% or greater reduction in PPI use in 84% of their 144 patients at 12-month follow-up (53). At 24 months, Cohen *et al.* (n=64 patients) demonstrated a 50% or greater reduction in PPI use in 72% of patients and PPI cessation in 67% of patients (54). Esophageal acid exposure (i.e., total time pH was less than 4) was reduced by 31% at 12 months (53,54). These techniques are still being developed and tested.

Surgical management

Absolute indications for surgical intervention in the treatment of GERD include apnea or near-SIDS secondary to GERD, pneumonitis with lung changes, and esophagitis

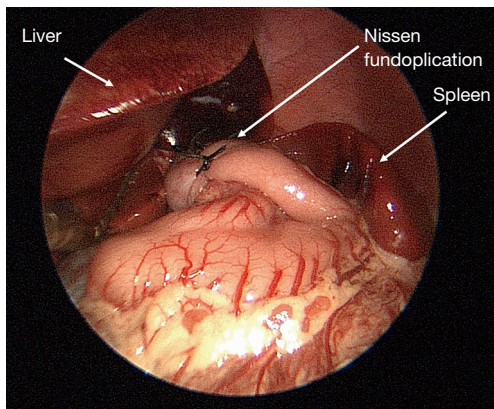


Figure 1 Intraoperative photograph of a laparoscopic Nissen fundoplication.

with ulceration or stricture. Relative indications include failure of symptoms to resolve with medical management, failure to thrive, recurrent pneumonia, asthma and/or chronic cough secondary to GERD, and chronic emesis (4).

Surgical principles

Classically, surgical fundoplication involves mobilization of the gastroesophageal junction, forming approximately 2 to 3 centimeters of intra-abdominal esophagus around which the fundus of the stomach is wrapped. This procedure is performed over an intraesophageal dilator/bougie to prevent narrowing of the GE junction and stomach that would lead to post-operative dysphagia. In patients with a HH, this procedure is accompanied by hiatoplasty: approximation of the crura, and/or anchoring of the wrap to the diaphragm, to prevent herniation into the thorax.

Minimally invasive surgical approaches to GER

Laparoscopic Nissen fundoplication is commonly regarded as the operation of choice for the management of refractory GERD (*Figure 1*) (1,4). The Nissen fundoplication is a 360-degree wrap, relative to the partial dorsal wrap known as the Toupet technique or the partial ventral wrap known as the Thal technique (1). Gastrostomy tube placement can be performed concurrently with fundoplication, as is frequently seen in neurologically impaired children who both suffer from GERD and require long-term feeding access (1,4). The success rate of fundoplication is cited as 60–90% (10). Complications, when they do occur, include: persistent GERD symptoms, surgical site infection,

bleeding, GI perforation, dysphagia, stricture, breakdown of the wrap, pneumothorax, dyspepsia, vagus nerve injury, dumping syndrome, and obstruction (2,4,55,56).

Kubiak *et al.* performed a prospective randomized study comparing long-term outcomes of laparoscopic Nissen *vs.* laparoscopic Thal fundoplication in children from 1998 to 2007. They demonstrated that patients, particularly those with neurological disorders, who undergo laparoscopic Nissen fundoplication have decreased recurrence rates in the long-term relative to those who undergo laparoscopic Thal fundoplication (57).

Ru *et al.* performed a systematic meta-analysis using nine studies to compare open versus laparoscopic Nissen fundoplication. Of 916 patients, 557 underwent laparoscopic Nissen fundoplication and 359 patients underwent open Nissen fundoplication. Although the laparoscopic group demonstrated longer operative times, there were less total post-operative complications compared to the open group (58). Patients in the laparoscopic group demonstrated less retching postoperatively (58). This was thought to be due to reduced trauma to the stomach when using a minimally invasive approach, causing less impairment to the autonomic pathways to the stomach (58). Thatch *et al.*, whose study was included in Ru *et al.*'s meta-analysis, further demonstrated that patients in the laparoscopic group had decreased post-operative opiate requirements (59). Ru *et al.* also concluded that there were no significant differences with regard to time to full feed, surgical site infections, or need for redo fundoplication between the two groups (58). Laparoscopic Nissen fundoplication is a safe and feasible surgical treatment of GERD in children (58).

Techniques for performing pediatric laparoscopic Nissen fundoplication have been modified throughout the last 20 years. The initial approach involved an extensive hiatal dissection with complete division of the phrenoesophageal attachments and skeletonization of the crura before performing a hiatoplasty as described above.

The technique has since evolved and Holcomb & St Peter published a series of technical considerations for performing a laparoscopic Nissen fundoplication. The authors provide a list of “error traps” to mitigate the impact of lack of surgeon experience and hazard unawareness that may lead to human error. The first error trap described is failure to ligate and divide the short gastric vessels (60). They elaborate that failure to do so creates excessive tension on the wrap, contributing to post-operative dysphagia. They state that this departure from the previously described Rosetti modification typically takes less than five minutes

and does not devascularize the greater curvature of the stomach (61-65). Furthermore, it improves visualization of the esophageal dissection and mobility of the wrap (60). The second error trap is failure to correctly identify the retroesophageal space and instead bringing the fundus up the free space inferior to the left gastric artery (60). The correct space is inferior to and abutting the crus, and cephalad to the left gastric artery (60). The third error trap described is division of the phrenoesophageal membrane and extensive esophageal mobilization (60). Minimal esophageal mobilization decreases the risk of transmigration of the wrap into the lower mediastinum (60,66,67). The fourth error trap is failure to use a bougie when performing the fundoplication, increasing the risk of dysphagia and/or need for dilation. The authors recommend a 2 centimeter wrap for infants and a 2.5 to 3 centimeter wrap for older children (60). The fifth and final error trap described is bringing too much fundus under the esophagus, contributing to dysphagia (60). The suture line should be placed at approximately 11 o'clock to allow for an even distribution of the wrap anterior and posterior to the esophagus and to reduce the risk of dysphagia post-operatively (60).

St Peter *et al.*'s two-center, prospective, randomized trial utilized 177 patients to compare transmigration rates after laparoscopic Nissen fundoplication in patients who underwent circumferential division of phrenoesophageal attachments [i.e., extensive esophageal mobilization (MAX group)] versus no violation of the phrenoesophageal membrane [i.e., minimal esophageal mobilization (MIN group)]. Patients in the MAX group demonstrated increased transmigration rates at 30% *vs.* 7.8% in the MIN group ($P=0.002$) (66). Furthermore, patients who underwent extensive esophageal mobilization had higher rates of reoperation at 18.4% *vs.* 3.3% in the MIN group (66).

St Peter's research group later examined long-term outcomes of minimal *vs.* extensive esophageal mobilization during laparoscopic Nissen fundoplication. In this study by Desai *et al.*, at 6.5-year median follow-up, re-herniation was noted in 22.7–36.5% of patients in the MAX group *vs.* 2.8–12.2% in the MIN group (67). Time to diagnosis of herniation was 14.7 ± 9.5 months in the MAX group compared to the more prolonged time to diagnosis of 30.2 ± 23.6 months in the MIN group (67). There was no significant difference between the two groups with regard to reflux symptoms or PPI use (67).

Muensterer *et al.* has described success with single incision pediatric endosurgery that leaves patients without

any appreciable scar (68). While this is a novel technique, it is technically quite challenging and therefore has not been widely adopted. Furthermore, in Gasior *et al.*'s study evaluating patient and parent satisfaction after single incision versus multi-port appendectomy, there was no significant difference between the two groups regarding scar assessment at long-term 25-month follow-up (69).

There is currently minimal data available in the pediatric population evaluating the role of robotic Nissen fundoplication. In the adult population, Markar *et al.*'s meta-analysis comparing robotic *vs.* laparoscopic Nissen fundoplication demonstrated similar results between the two groups. There was no significant difference in need for re-operation or post-operative dysphagia between the robotic and laparoscopic groups (70). There was also no significant difference with regard to hospital stay or operative complications (70). There were, however, increased operative times and procedure costs in the robotic group (70).

There is also currently limited data regarding the potential role for magnetic sphincter augmentation (MSA) in pediatric patients with GERD. Clinical trials evaluating the efficacy of MSA in the adult population, however, have demonstrated improvement of GERD symptoms, as well as decreased rates of gas-bloat, esophageal acid exposure, and PPI use after intervention (71,72). Ganz *et al.*'s prospective clinical trial, which included 85 patients at 14 centers in the United States and the Netherlands, evaluated the efficacy and safety profile of MSA over a 5-year follow-up period. In their patient population, PPI use decreased from 100% to 15.3%, moderate or severe regurgitation rates decreased from 57% to 1.2%, and gas-bloat decreased from 52% to 8.3% at 5 years. There were no reported device erosions, migrations, or malfunctions (71). Rona *et al.* demonstrated that MSA remains efficacious even in the presence of a large HH (73).

Complications of surgical management

Surgical antireflux procedures are relatively safe when performed by experienced providers (74). In one of the largest published series regarding laparoscopic Nissen fundoplication, with 2008 operations performed over 20 years, Rothenberg reported an intraoperative complication rate of 0.13% in the primary group and 2.2% in the redo fundoplication group. Intraoperative complications include bleeding, gastric or esophageal perforation, pneumothorax, or vagal nerve injury (75).

Dysphagia & gas-bloat syndrome

Modifications to the original Nissen fundoplication have been made over time to address the unique complications of dysphagia and gas-bloat syndrome (76). “Gas-bloat syndrome” refers to bloating with inability to belch seen in some patients after Nissen fundoplication (76). Post-operative dysphagia rates are known to be higher in patients who undergo 360-degree wraps (57,76). The use of a 270-degree wrap, however, was not successful in reducing rates of gas-bloat. Rates of post-operative dysphagia and gas-bloat, however, both decreased with the advent of the “floppy Nissen”, the creation of a loose 360-degree wrap around a bougie (60,76,77). The floppy Nissen prevented pathologic reflux and decreased the rates of post-operative dysphagia and gas-bloat without prohibiting belching or physiologic vomiting (78). Patients who continue to demonstrate post-operative dysphagia despite the creation of a floppy Nissen typically demonstrate resolution of their symptoms within 2 years of their operation (57,76).

Delayed gastric emptying

DGE has been reported after surgical fundoplication; however, this is more commonly a pre-existing condition, as opposed to a complication, of fundoplication (79). This condition is seen in both neurologically normal and neurologically impaired children, but it is more common in the latter (79). Furthermore, many patients in both the pediatric and adult populations demonstrate improvement of DGE after fundoplication, as demonstrated by multiple studies comparing pre- and post-operative gastric emptying scans (57,79). Pyloroplasty has not been shown to have an effect on rates of DGE when performed in conjunction with Nissen fundoplication. In Maxson *et al.*'s study of 40 patients, the Nissen with pyloroplasty group demonstrated an increased rate of post-operative complication rates at 23.8% *vs.* 5% in the Nissen only group (80).

Wrap failure/migration

One of the most common long-term complications of laparoscopic Nissen fundoplication is failure or migration of the wrap. Wrap failure most commonly occurs 16 months after fundoplication and is typically diagnosed due to recurrent GERD symptoms (79). Fundoplication failure can be classified by four types:

Type 1: Complete or nearly complete disruption of the

fundoplication wrap.

Type 2: Malpositioned fundoplication with sliding of the hernia in the setting of an intact wrap.

Type 3: Slipped Nissen fundoplication (slippage of the stomach above the wrap).

Type 4: Transhiatal herniation of the wrap (81,82).

Failure of the wrap occurs in 2% of neurologically normal children and in approximately 12% of neurologically impaired children (83). In Rothenberg's series, he reports 4.6% and 6.8% wrap failure rates for primary and redo fundoplications, respectively. The highest incidence of wrap failure occurred in patients younger than 6 months of age. The most commonly cited causes of wrap failure were HH, followed by slipped Nissen (75).

Conclusions

GER is common in pediatric patients, particularly in neonates and infants. It is characterized by functional disturbances of the esophagus with prolonged transient LES relaxations. It resolves spontaneously in approximately 90% of affected infants (1). Conservative management is typically sufficient in managing symptoms. When reflux persists or causes life-threatening conditions or consequences despite lifestyle changes and optimal medical therapy, surgical fundoplication is indicated. Further studies are required to determine the role of novel endoscopic approaches to reflux in the pediatric patient.

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