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Review Article

Current Surgical Role in Pediatric Gastroesophageal Reflux

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Abstract Reflux of gastric content into the esophagus is a physiologic event that mostly disappears with body growth. However, infants and children with gastroesophageal reflux may develop pathologic consequences, from esophagitis, failure to thrive to airway problems. Such gastroesophageal reflux with a pathologic consequence is known as a gastroesophageal reflux disease (GERD). Certain groups of pediatric patients, including children with neurological impairment, congenital esophageal malformation or congenital diaphragmatic hernia, have increased risk of GERD and these groups of patients have poorer response to non-surgical management. Wrapping the gastric fundus around the distal esophagus, fundoplication, is a surgical technique that has long been practiced to treat GERD. Although the procedure has been proven to support the shutter mechanism of the esophagogastric junction, it comes with potential complications such as swallowing difficulty, gas bloating syndrome or dumpling syndrome. Smart patient selection, detailed pre-operative evaluation, precise technical tailoring and post-operative follow-up are key success factors that a care team should develop when considering this procedure. In addition, frontier technologies, such as transoral endoscopic fundoplication, robotic-assisted fundoplication and magnetic bead esophageal supporting device, are on their way to this arena.

Keywords: Gastroesophageal reflux disease, Fundoplication, Esophagus

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Introduction

Regurgitation of gastroesophageal content from the stomach to the esophagus, known as gastroesophageal reflux (GER) can be a physiologic condition occurring normally in neonates and an occasional event in all age groups. In cases in which the GER results in a pathologic condition or a complication such as reflux esophagitis, respiratory tract symptoms or nutritional problems, the condition is termed as gastroesophageal reflux disease (GERD), although demarcation between GER and GERD can be unclear in real clinical practice.[1,2]

It has been estimated that physiologic reflux occurs in about 25-40% of infants 4-6 months of age.[3-6] Spontaneous resolution occurs in a majority of these children, as the anti-reflux mechanisms mature, usually by 12 months of age.[7] Premature birth, congenital esophageal anomalies (e.g. esophageal atresia), congenital diaphragmatic hernia or neurological impairment increase risk the of developing GERD in childhood.[8,9] According to a primary care data from the UK, the population-based overall incidence of GERD in children aged 1-17 years was estimated at 0.84/1,000 person-years.[10] This finding was consistent with a large population-based cohort study from New Zealand which reported that about 1% of infants aged less than 12 months were admitted to a hospital with a diagnosis of GERD-related complications.[2]

Surgeons are often consulted to participate in the management of pediatric patients with reflux symptoms. Failed medical treatment is a mainstay indication for anti-reflux surgery.[11] In addition, an anti-reflux procedure is considered to be a part of a gastrostomy operation in children with neurological impairment who require a feeding gastrostomy.[12] This paper aimed to review up-to-date data on physiologic fundamentals, surgical indications, surgical technique and expectable outcome that are essential for a surgeon to understand as a team member in pediatric GERD management.

1. Anti-reflux mechanisms and natural history of pediatric GER

Immaturity of anti-reflux mechanisms and a predominantly liquid diet explain the high incidence of GER in the neonatal period. A recent cohort study from France used a parent-reported questionnaire to assess the incidence of GER in 157 full-term neonates and reported that 72% had GER related symptoms at 1 month age and the figures reduced to 56% and 14% at the ages of 6 month and 12 month, respectively.[13] The anatomical components of anti-reflux mechanisms include the lower esophageal sphincter, mucosal folding at the esophagogastric junction, diaphragmatic crura, length of intraabdominal esophagus and angulation between the lower esophagus and the gastric fundus (angle of His). Maturation of these structures together with the esophageal peristalsis and the gastric emptying function explain the decreasing incidence of GER as age increases. The change from liquid food to a semi-solid baby diet also help reduce splashing events. The lower esophageal sphincter and its surrounding organs keep a positive intraesophageal pressure gradient in relation to the intragastric pressure. After one year of age, GERD is an uncommon symptom, and is it occurs, defects in the anti-reflux mechanisms should be sought out through clinical evaluation and investigations.[14]

Certain pediatric surgical diseases are associated with an increased risk of GERD. In an infant with a congenital esophageal anomaly, a surgery itself may cause upward migration of the intra-abdominal esophagus to the chest, hence losing the pressure tone positivity at the lower esophageal sphincter mechanism. GER following an esophagoesophagostomy was reported in 15-50% of infants with esophageal atresia, depending on the method of evaluation; the same study hypothesized that acid reflux may have been related to anastomotic stricture.[15] Using pH monitoring, Vergouwe and colleagues reported 17.5% of 57 children previously treated with esophageal atresia had abnormal gastroesophageal reflux index.[16] Patients with spastic cerebral palsy often have a higher risk of GER due to increased intraabdominal pressure. In addition, patients forced to maintain a long-term supine position and chronic use of anticonvulsants may contribute to GERD.[17] Children with morbid obesity also have a higher risk of GERD.[18]

2. Clinical manifestation and diagnostic approach

GERD is literally defined as 'troublesome GER' but drawing a clear line between such pathologic conditions and physiologic variations is difficult. Regurgitation and vomiting are the most common problems that bring a child to medical attention. In general, regurgitation of not more than 6 times a day in an infant who accepts feeding and thrives well can be regarded as within normal limits and does not require intervention beyond observation to ensure the condition does not worsen.[19]

Chronic vomiting might lead to esophagitis, pain and food aversion. Failure-to-thrive can be a consequence of GERD. Apart from the gastrointestinal symptoms, a child with GERD may present with extraesophageal manifestations, from respiratory wheezing, intractable asthma or recurrent pneumonia to apparent life-threatening events such as food aspiration. Sinusitis, sleep disturbance, otitis media and dental erosion can be related to GERD. In neurologically impaired children, a typical form of posturing called the Sandifer syndrome including arching of the back, torsion of the neck and left-up chin is highly specific to GERD.[19]

Differential diagnosis of GER/GERD is broad and consists of a variety of disease entities, ranging from allergy, infection/inflammation, inborn errors of metabolism, cyclic vomiting, and increased intracranial pressure to anatomical obstruction of the upper gastrointestinal tract (Table 1). Red-flag symptoms that are indications for investigations in a vomiting child include late onset of persistent vomiting (> 6 months age) and prolonged symptoms of longer than 12-18 months, weight loss/failure-to-thrive, abnormal head circumference, seizure and long-term constipation. In a child with non-alarming vomiting symptoms, time is allowed for therapeutic trials which should focus on diet modification and a cow's milk withholding trial in infants and gastric acid suppression in older children. Diet modification in infants includes such things as division of feeding into smaller volume meals and addition of thicker food such as congee (rice porridge) or cereal. Obesity management is advisable in older obese children with reflux symptoms.

On surgical consultation, before planning for a surgery, a surgical team should play an active role in excluding other anatomical obstructions of the gastrointestinal tract. A thorough clinical evaluation focusing on feeding history, bowel habits and growth usually provide clues to select appropriate investigations. In young infants, intractable vomiting can be caused by pyloric stenosis or duodenal web or midgut malrotation/volvulus. Chronic constipation and abdominal distension may indicate low gut obstruction as in Hirschsprung disease. The choice of investigative approach depends on the relevant clinical information.

There is no gold standard investigation in a pediatric case who is suspected to have GERD.[9] Barium swallowing (upper gastrointestinal tract study, UGIS) is the most widely used radiologic study to look for refluxing events. A UGIS is useful to study the anatomy of the esophagus and the stomach in relation to the diaphragm and other mediastinal structures. Anatomical obstructions at the pylorus and/or duodenum can be excluded by this type of study. When performed under real-time video fluoroscopy, the swallowing mechanism can also be evaluated, especially in a child with neurological impairment. The main limitation of UGIS is that it is performed over a very short time, hence it may miss refluxing events occurring during the rest of the day. Also, although UGIS can demonstrate a reflux event, it cannot tell the acidity of the refluxed content.[20]

Table 1 Differential diagnosis of gastroesophageal reflux disease in pediatric age group

Physiologic change	- Physiologic reflux in infants - Overfeeding
Neurological problems	- Increased intracranial pressure caused by intracranial hemorrhage or a mass - Hydrocephalus
Metabolic disorders	- Inborn errors of metabolism e.g., galactosemia, urea cycle defects, organic acidemia, adrenal crisis - Toxic substance, e.g., lead poisoning
Gastrointestinal tract disorders	- Gastrointestinal obstruction e.g., pyloric stenosis, malrotation, duodenal web, superior mesenteric artery syndrome, foreign body ingestion - Motility disorders, e.g., achalasia cardia, gastroparesis - Inflammation, e.g., eosinophilic esophagitis, food allergy
Others	- Cyclic vomiting - Psychological, e.g., self-induced vomiting

Direct monitoring of esophageal pH is an investigation that provides an advantage in fulfilling some limitation gaps of UGIS. This instrument monitors pH at the lower esophagus over a long enough duration to detect acid regurgitation, usually a 24-hour period. The percentage of the time that the pH falls lower than 4, calculated as reflux index (RI), is the most reliable measurement of esophageal exposure to acid. An RI of less than 3% is within normal limits, while 3% - 7% is equivocal and > 7% can be regarded as abnormal. Although 24-hour pH monitoring provides high sensitivity to detect GER, the tool detects only acid reflux and may not correlate well with the reflux-related pathology. A more advanced investigative tool for GER is a multiple intraluminal impedance with pH monitoring (MII-pHM), which detects all refluxing events and can distinguish between solid, liquid and gas refluxes. A study that used nuclear scintigraphy as a reference reported sensitivity of 24-hour MII-pHM at 87.2%, which was much higher than that of 24-hour pH monitoring alone (53.2%).[21] In cases with significant GER, esophageal and gastric mucosa can be further studied through esophagogastroduodenoscopy (EGD). EGD may also detect associated anatomical anomalies such as an esophageal, hiatal hernia.

3. Management of pediatric GERD

One of the common indications for anti-reflux surgery in children with GERD is GERD in children with cerebral palsy. Typical clinical features in these children are a swallowing handicap, generalized motor spasms, and/or recurrent pulmonary infection. Some authors suggest adding a fundoplication as a part of a feeding gastrostomy operation, if indicated following pre-operative evaluation of the reflux using UGIS and 24-hour pH monitoring.[22,23] In children without neurological impairment, there are 2 categories of surgical indication for GERD: failed non-operative treatment and severe reflux consequences.

Most GERD cases in children can be successfully managed with lifestyle modifications and acid-suppressing medications. In the infant age group, feeding volume splitting, formula thickening and feeding in a semi-erect posture are recommended when body weight control and avoiding caffeine or spicy food are advisable in older age group. GERD associated with severe pulmonary consequences, apparent life-threatening events or failure-to-thrive are common indications for anti-reflux surgery in infants while esophageal stricture and Barrett's esophagus are more common in teenage children.[24,25] The main objectives of anti-reflux surgery are to correct any anatomical risks of GER and to re-create a high pressure zone at the lower esophagus.[11]

Surgical Techniques

Fundoplication has long been a standard anti-reflux procedure. The technique was developed by Rudolph Nissen (1896-1981), a German-trained surgeon who was working in the University of Basel, Switzerland, when he published the very first report on 'A simple operation for control of reflux esophagitis' in 1956,[26] and now laparoscopic Nissen fundoplication is the most common anti-reflux operation in both adults and children. The most important step in Nissen fundoplication is using the gastric fundus to wrap around the lower esophagus in its total circumference (360 degree), with a wrap length of around 2 centimeters. Before undertaking this procedure, the intraabdominal esophagus must be mobilized from its diaphragmatic attachment by means of dividing the phrenoesophageal membrane. Care should be taken at this step to keep the vagus nerves on the surface of the esophagus intact. Such mobilization not only helps increase the length of the intraabdominal esophagus and correct a hiatal hernia, division of the phrenoesophageal membrane makes the diaphragmatic crura become clear enough for approximation. On gastric fundus mobilization, the short gastric vessels do not always need to be sacrificed. Laparoscopy provides a magnificent view for fundoplication and has become a surgical standard for Nissen fundoplication (Figure 1).

Multiple versions of fundoplication have been developed with an aim to reduce complications of the total wrap, especially swallowing difficulty or dysphagia.[27] Table 2 summarizes the principles of each technique.[28-33] Apart from these methods, novel fundoplication techniques are being developed in adult patients including the transoral rotational esophagogastric fundoplication, which is a total endoscopic approach.[34] In older children, the transoral technique was reported to be feasible although, of unclear efficacy.[35] Currently, although there is no consensus technique for fundoplications, all technical modifications seem to be towards less invasive procedures.

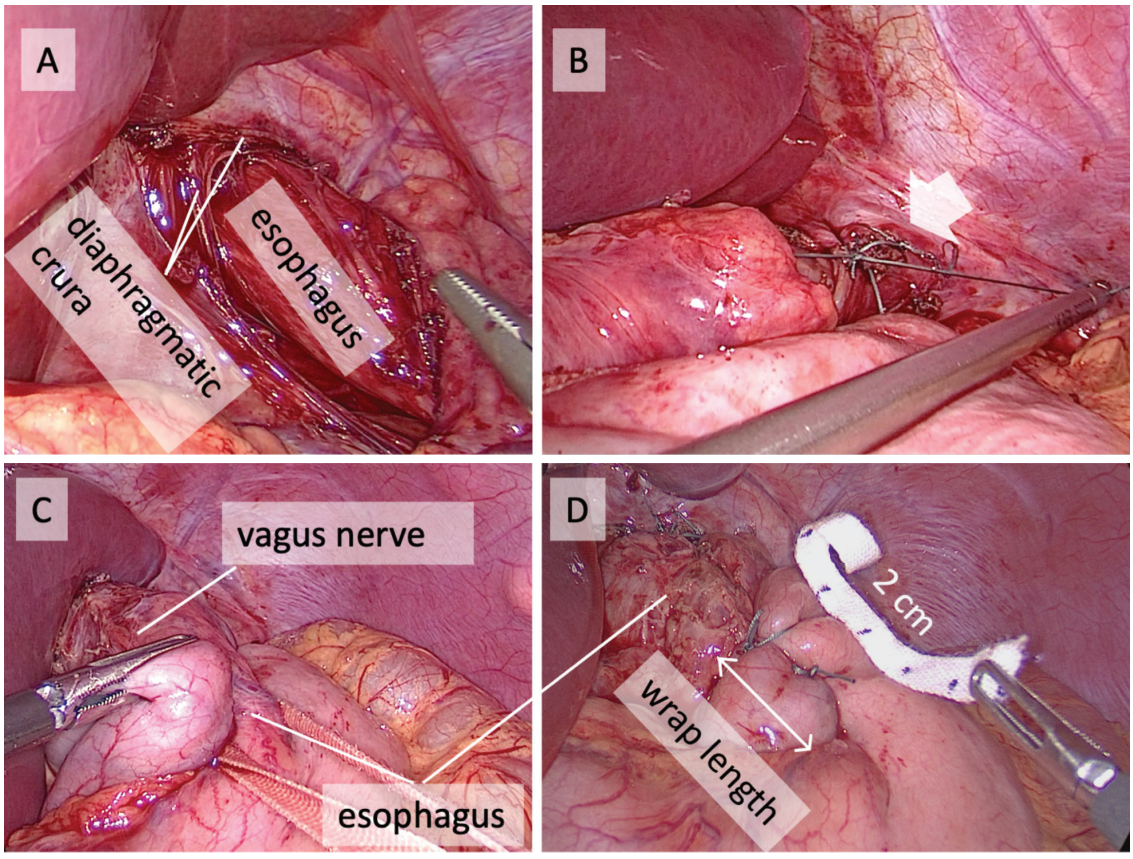

Figure 1 Laparoscopic view of a Nissen fundoplication in a child. A) Mobilization of the distal esophagus by dissecting into the phrenoesophageal membranes, B) Closure of the diaphragmatic crura with anchoring stitches to hold the esophagus, C) Mobilizing the gastric fundus to the left of the distal esophagus, D) Completion of the fundoplication, which was a 360-degree (complete) wrap of 2 cm length in this case

In children with recurrent respiratory tract infection, pre-operative preparation is important as an existing infection can increase the risk of post-operative complications. However, it might not possible to wait until a patient is absolutely clear of respiratory symptoms. Cooperation among pediatricians, anesthesiologists and the surgical team is one of the keys to operative success. An intensive care facility should be prepared for the post-operative period. Usually, enteral feeding can be resumed as soon as hemodynamic stability is restored. Feeding volume titration may be necessary at the early post-operative period.

Complications

A fundoplication in children, especially in neurologically impaired children, is not a low-risk procedure. One study reported that up to 50% of children undergoing a fundoplication experienced one or more early post-operative complications[36] (Table 3). While pulmonary complications were prevalent in patients with neurological impairment, feeding problems were more common among those without a neuronal condition. Serious complications at the early post-operative period include wrap disruption, gastrostomy leakage, and gastric necrosis. On Nissen fundoplication, excessively tight wrapping can be very problematic as it will lead to dysphagia and aspiration. A large bore nasogastric tube should be in place during the wrap. Unintended suturing of the nasogastric tube to the wrap is possible and it should be checked by the anesthesiologist before commencement of the operation. Also, the condition of 'gastric inlet obstruction' caused by and overly tight wrapping may cause a gas-bloat syndrome which is defined as the inability to burp gas out of the stomach when there is acute gastric distension. When a fundoplication is performed without a gastrostomy, this condition can even be so serious that gastric overdistension leads to stimulation of the vagovagal reflex.

Table 2 Technical variants in fundoplication used in the pediatric age group

Technique	Technical principles	Remarks
Nissen[28]	Abdominal approach, complete (360° wrap) with a bougie in place, diaphragmatic crura approximation	Current standard
Toupet[29]	Abdominal approach, posterior partial wrap (270°)	Less dysphagia[27]
Thal[30]	Abdominal approach, Anterior partial wrap (270°), Angle of His reconstruction[32]	
Dor	Abdominal approach, Anterior partial wrap (180°, fundus laid-over)	Optimum choice following Heller myotomy for achalasia cardia[33]
Boix-Ochoa[31]	Abdominal approach, Restoration of the normal anti-reflux anatomy and fundus unfolding	

Recurrence of GERD has been reported in around 7-15% of neurologically impaired patients following an anti-reflux procedure and 2-10% of neurologically normal patients.[36-38] Transthoracic migration of the wrap is among the most common anatomical reasons for recurrence. Therefore, a contrast study is recommended in cases with recurring reflux symptoms. In a systematic review of laparoscopic fundoplication in children, pooled mortality in neurologically impaired cases was at 18% and most of the mortalities were associated with progression of the underlying condition(s).[39,40]

Associated esophageal atresia or diaphragmatic hernia are predictors of failed anti-reflux surgery.[41] One study reported that redo-operations were required in 13% and 8% of patients following primary fundoplication in patients with and without esophageal atresia, respectively.[42] Poorer esophageal motility and a short esophagus explain the risk in this group of patients. Partial fundoplication or loose Nissen fundoplication are recommended for correcting intractable GERD in patients with esophageal malformation.[43-46]

Injury to the vagal trunks may lead to decreased gastric emptying time, thus more rapid passage of food from the stomach into the small intestine. High osmolarity chyme absorbs fluid into the intestinal lumen and stimulate secretion of various gut hormones including serotonin, bradykinin, enteroglucagon, cholecystokinin and vasoactive intestinal peptide.[47] In addition, a rapid surge of insulin may result in hypoglycemia. Dumping syndrome following a fundoplication is usually transient and can be managed by adjusting the formula and rate of feeding.

4. Surgical outcomes

Surgical outcome measures of anti-reflux surgery in children usually focus on improvement of reflux associated consequences, including episodes of pneumonia that requires hospitalization, feeding tolerance, physical growth and quality of life. Significant weight gain following fundoplication has been reported and this effect is even clearer in neurologically impaired children[48]. Contrarily, evidence did not support an impact of fundoplication on reducing reflux-related admissions due to respiratory problems in neurologically impaired children.[49] However, a large study in 182 neurologically intact children showed that partial (Thal) fundoplication significantly improved airway symptoms and reduced the need for medications.[50] In general, recurrence rates have been reported at around 2% - 12%[51-53] and redo-operations around 15%.[54] Neurologically impaired children had higher rate of recurrence when compared to their counterparts.

5. New technologies

Robotic assisted fundoplication in children

Case series reporting technical success in robotic assisted fundoplication in children began to appear in the medical literature at the beginning of the 2000s[55-60] and there was a meta-analysis in 2014.[61] According to the meta-analysis, the overall conversion rate was 3% and operative times ranged from 127-186 minutes.

Table 3 Potential complications of fundoplication

Intraoperative complications
- Hypercapnia and respiratory acidosis
- Iatrogenic adjacent organs injury (left lobe of liver, spleen, diaphragm, vagal trunks, pneumothorax, hemothorax)
Immediate post-operative complications
- Respiratory complications (pneumonia, atelectasis)
- Gastrostomy related complications (intraperitoneal leak, bleeding, dislodgement)
- Fundoplication related complications (sewn gastric tube, gastric necrosis, wrap disruption)
Medium and long-term complications
- Recurrent gastroesophageal reflux symptoms
- Transthoracic migration of the wrap
- Gas bloat syndrome
- Dumping syndrome

Although the data have proven technical feasibility and shown a trend toward shorter operative times, there was no significant difference in short term outcomes when comparing robotic assisted surgery and conventional laparoscopic fundoplication.[61]

Magnetic bead esophageal sphincter augmentation device

An esophageal sphincter augmentation device is an alternative treatment for patients who respond only partially to the acid-reducing medications and whose parents are still reluctant for their child to undergo a fundoplication.[62] A prototype of this instrument is the LINX (Ethicon, Johnson & Johnson, Inc.). This device is composed of a string of magnetic beads held together in a ring shape. When surgically applied to the lowermost part of the intraabdominal esophagus, the ring enhances the tone of the lower esophageal sphincter which opens when there is a passage of esophageal content from the upper esophagus but remains closed in prevention of gastric content splashing. Studies in adult patients have shown the safety and efficacy of the device and have suggested it as a first-line surgical anti-reflux procedure.[63-66] Up to the time of this review, there has been no reports of its use in the pediatric age group.

Conclusion

Reflux of gastric content into the esophagus can be pathogenic when it occurs long and frequently enough. Although most pediatric patients with GER can be managed conservatively, surgical therapy has a role in specific groups of patients including children with neurological impairment and infants born with esophageal atresia. Although the current surgical standard is laparoscopic Nissen fundoplication, there are trends toward minimal dissection and avoiding a tight wrap. Surgeons should be aware of post-procedure complications as they are not uncommon. Long term care by multi-disciplinary team is essential.

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