

## Is there a changing trend in surgical management of gastroesophageal reflux disease in children?

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### Abstract

Gastroesophageal reflux disease (GORD) is a pathological process in infants manifesting as poor weight gain, signs of esophagitis, persistent respiratory symptoms and changes in neurobehaviour. It is currently estimated that approximately one in every 350 children will experience severe symptomatic gastroesophageal reflux necessitating surgical treatment. Surgery for GORD is currently one of the common major operations performed in infants and children. Most of the studies found favour laparoscopic approach which has surpassed open antireflux surgery as the gold standard of surgical management for GORD. However, it must be interpreted with caution due to the limitation of the studies, especially the small number of subject included in these studies. This review reports the changing trends in the surgical treatment of GORD in children.

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**Key words:** Children; Gastroesophageal reflux; Antireflux surgery; Laparoscopic fundoplication

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### INTRODUCTION

Symptomatic gastroesophageal reflux (GOR) has been identified in children with increasing frequency over the

last two decades<sup>[1]</sup>. The perceived increase in incidence since the late 1970s is due to an improved awareness of the condition, and to increasingly sophisticated diagnostic techniques for identifying the disorder<sup>[2]</sup>. The term GOR implies a functional or physiological process in a healthy infant with no underlying systemic abnormalities<sup>[3]</sup>. It is a self-limiting process in infants that usually resolves by 6 to 12 mo of age<sup>[4]</sup>. Gastroesophageal reflux disease (GORD) is a pathological process in infants manifesting as poor weight gain, signs of esophagitis, persistent respiratory symptoms and changes in neurobehaviour<sup>[3]</sup>.

Conservative first line management involves thickened feeds, positioning of the infant and parental reassurance. Second line management is through medication and includes the use of antacids, H<sub>2</sub> antagonists, proton pump inhibitors (PPIs) and pro-kinetic agents. Surgical intervention should be considered after the patient has failed conservative and medical interventions. It is currently estimated that approximately one in every 350 children will experience severe symptomatic GOR necessitating surgical treatment<sup>[2]</sup>.

Surgery for GORD is currently one of the common major operations performed in infants and children by paediatric surgeons in the United States<sup>[5]</sup>. Prior to 1991, the open Nissen fundoplication was the standard surgical procedure for severe GORD in adults<sup>[6]</sup>. The first laparoscopic Nissen fundoplication was performed by Dallemagne and colleagues in Belgium in April 1991<sup>[6]</sup>. It has been shown that the principles learned through open antireflux surgery can be applied to the laparoscopic approach, and this breakthrough has since been translated to pediatric surgery.

This study reviews the aetiology, risk factors, signs, clinical symptoms, diagnosis, and management of GORD in children. A Pubmed database search was performed. All abstracts were reviewed and all articles and prospective randomized clinical trials of GORD in children were further scrutinized. Further references were extracted by cross-referencing.

### PATHOGENESIS AND RISK FACTORS

The pathogenesis of reflux is not completely understood. A combination of factors appears to contribute to the development of GORD in infants and children. It appears that a decrease of lower esophageal sphincter tone plays a role in contributing to reflux. Transient lower esophageal sphincter relaxation not associated with swallowing has been implicated as the major mechanism allowing the

Table 1 Clinical manifestations of GORD<sup>[11]</sup>

	GOR	GORD
Symptoms	'Happy sitter'	Regurgitation/persistent vomiting/feeding refusal/hypersalivation Arching/irritability/persistent crying
	Regurgitation	Abdominal pain/heart burn/hematemesis/chest pain
	Vomiting but thriving	Sleep disturbance Silent reflux- stridor, wheezing, cough Sandifer's syndrome - head turning episodes to lengthen the oesophagus and LES pressure; repetitive stretching and arching, which gives the appearance of seizure/dystonia
Complications	GORD	Esophagitis/failure to thrive
	Esophagitis	Reactive airway disease/recurrent pneumonia Apnoea/bradycardia/acute life threatening events Barrett's esophagus/esophageal ulceration and perforation/stricture formation Anaemia/seizure

gastric contents to return into the esophagus<sup>[7]</sup>.

Delayed gastric emptying has also been implicated as another mechanism in GORD in children<sup>[8]</sup>. It predisposes to gastric distension, increased acid secretion and esophagitis. Other factors associated with the mechanism of reflux include positional factors, neurological disease, stress manoeuvres and hiatus hernia<sup>[9]</sup>.

While many factors contribute to reflux mechanism, the composition of the refluxate and the time spent with an acidic refluxate (pH < 4) are related to the development of GORD<sup>[10]</sup>.

## CLINICAL SYMPTOMS AND DIAGNOSIS

### Clinical manifestations

Clinical manifestations of GORD cover a wide spectrum with truly physiological reflux at one end to complicated esophagitis at the other (Table 1)<sup>[11]</sup>. Complications such as respiratory symptoms and neurobehaviour may be present. In older children the most common symptoms are recurrent emesis, esophagitis, chronic respiratory infections or asthma caused by repeated aspiration, which seldom represent an immediately life-threatening condition<sup>[12]</sup>. However, in infants, GORD often occurs in association with other congenital anomalies, indicating that certain anatomical factors might influence the development of reflux<sup>[12]</sup>. There is recognition that severe GORD can cause life-threatening bradycardic and apnoeic spells and even sudden death in infants<sup>[13]</sup>. A number of disorders have been associated with symptomatic GOR<sup>[14]</sup>. A higher prevalence of GORD is present in children who have a history of esophageal atresia with repair<sup>[15]</sup>. Neurologically impaired children have an increased incidence of GORD and comprise the majority of pediatric patients

Table 2 Disorders that have been associated with symptomatic GORD<sup>[21]</sup>

Neurological	Mental retardation from any cause Brain injury from any cause Cerebral palsy Down's syndrome Microcephaly Seizure disorders Mobius syndrome Cornelia-de lange syndrome Hydrocephalus
Gastrointestinal	Gastric outlet obstruction from any cause Esophageal atresia Pharyngeal swallowing uncoordination Congenital duodenal obstruction (Ladd's band, diaphragm) Congenital abdominal defects (omphalocele, gastroschisis) Short bowel syndrome Hirschsprung's disease Portal hypertension Ascites
Cardiac	Anomalies causing left heart failure
Respiratory	Congenital diaphragmatic hernia Tracheal or subglottic stenosis Cleft palate Pierre Robin syndrome Phrenic nerve palsy Bronchopulmonary dysplasia
Prematurity	
Multiple anomalies	

who undergo antireflux surgery<sup>[16,17]</sup>. Hiatus hernia and respiratory diseases have also been associated with the occurrence of GORD in children<sup>[18,19]</sup>. Table 2 shows the disorders that have been associated with symptomatic GORD.

A complete history and clinical examination are still the mainstays in diagnosing GORD. Evaluation should pay particular attention to the occurrence and frequency of symptoms and associated complications. If the initial evaluation points toward GOR, a period of lifestyle modification and empirical pharmacotherapy may be used to confirm the diagnosis. At this stage, parental reassurance, education and anticipation are important<sup>[20]</sup>. If the history and clinical examination point towards symptomatic GOR or GORD, a variety of diagnostic studies are available to assess the extent of the reflux, severity of the complications and contributing factors.

### Diagnosis

No single definitive investigation can diagnose GORD. Therefore the choice is based on the clinical context. A 24-h pH probe remains the gold standard in diagnosing GORD. This test will determine the extent of esophageal acid exposure by measuring the frequency and duration of acid reflux exposure<sup>[20]</sup>. Radiography and pulmonary scintiscan may be useful in identifying the severity of pulmonary infections due to aspiration. The barium contrast upper gastrointestinal study is also helpful in identifying the presence of hiatus hernia and stricture. It is useful to exclude anatomical abnormalities<sup>[20]</sup>. Gastric

emptying studies are used to assess gastric motility and identify patients who have increased gastric emptying in the absence of mechanical obstruction. Gastroscopy is helpful in detecting reflux esophagitis and biopsy is taken to assess the severity of esophagitis<sup>[20]</sup>. Esophagogastric manometry is an accurate method for quantifying the resistance of the lower esophageal sphincter to reflux of gastric juice. The esophageal motility study is used to evaluate peristaltic contractions in the esophageal body. The benefits and limitations of commonly used diagnostic tests are described in Table 3.

## TREATMENT

The objectives of therapy include decreasing the symptoms, frequency and duration of reflux episodes, healing the injured mucosa and preventing complications<sup>[21]</sup>. The approach to the treatment of GORD is age-dependent<sup>[22]</sup>. The management of symptomatic disease often follows the line of conservative therapy which includes posture and feeding techniques, medication and antireflux surgery.

### Conservative treatment

Frequent small feeds of thickened formula or food minimise gastric distension and reduce GOR. Elevation of the upper body at 60 degrees, maintained for 24 h a day, favours esophageal clearance and effectively reduces symptoms of reflux in two-thirds of infants while awake and during sleep<sup>[2]</sup>. Positional therapy is based on the gravitational phenomenon and when discontinued the reflux may reappear.

### Medical treatment

If conservative measures do not improve symptoms, medical therapy is recommended. Pharmacological therapies are aimed at the various steps in the pathophysiology of GORD. These include the use of antacids, hydrogen ion-blocking drugs, PPIs and prokinetic agents. Antacids work by neutralising gastric acid. H<sub>2</sub>-blockers and proton pump inhibitors work by decreasing the secretion of gastric acid. Prokinetic agents work by increasing esophageal peristalsis, increasing the lower esophageal sphincter pressure and enhancing gastric emptying.

### Surgical treatment

Until the early 1990s, antireflux surgery was the main stay treatment for severe GORD, until the emergence of PPIs<sup>[23]</sup>. Surgical treatment of GORD has considerable appeal as it offers potential cure and avoids the need for long-term medication use. The primary indication for performing an antireflux operation is the control of intractable and symptomatic GOR which has been clearly demonstrated by 24-h pH probe and a barium study of the esophagus<sup>[2]</sup>. Operative treatment is usually undertaken after an unsuccessful trial of a few weeks of medical therapy; for patients with severe complications of reflux, such as aspiration, failure to thrive or esophagitis with stricture. Antireflux surgery may be performed shortly after diagnosis is established<sup>[2]</sup>. However, the majority of children appear to present for surgery after only a barium

**Table 3** Benefits and limitations of commonly used diagnostic tests

Study	Advantages	Disadvantages
Barium esophagram	Readily available Evaluates upper GI structure	Inadequate screen for GORD Results are operator dependent
24-h pH probe	Quantification of reflux Evaluates atypical symptoms Monitors medical treatment	Requires hospitalization Requires special equipment and trained personnel
Endoscopy with biopsy	Evaluates persistent GORD, PUD, <i>H Pylori</i> infection, allergic enteropathy and Barrett's oesophagus	Invasive and requires sedation/general anaesthesia

study; less than 25% undergo basic objective testing such as endoscopy and fewer have pH or gastric emptying studies<sup>[1]</sup>.

The major objectives of operative repair are to increase the high pressure zone in the lower esophagus by accentuating the angle of His and increasing the length of the abdominal esophagus<sup>[2]</sup>. Surgical therapy is effective because it improves sphincter function, which is one of the main contributing factors in most cases of GORD<sup>[6]</sup>. The most widely used fundoplication procedure was originally described by Nissen and Rosette in 1959. Nissen fundoplication is still a commonly used technique, with intra-abdominal positioning of the distal esophagus, hiatus hernia repair, and a 360° fundal wrap<sup>[24]</sup>. The term 360° fundoplication refers to total fundoplication. The technique has been developed and we now have the option of a partial fundoplication wrapping technique which refers to any wrap less than 360°. For example, Thal fundoplication requires only a partial wrap (210°-270°) of the fundus around the anterior side of the oesophagus<sup>[24]</sup>, Toupet fundoplication a 270° posterior partial fundoplication<sup>[25]</sup> and Watson fundoplication a 120° anterior partial fundoplication<sup>[26]</sup>.

Pediatric surgeons have documented high rates of failure and morbidity for antireflux surgery<sup>[27]</sup>. The problems with antireflux surgery occur especially in children with neurological impairment, repaired esophageal atresia or chronic lung disease<sup>[28]</sup>. The combination of antro-duodenal dysmotility and a wrap at the proximal stomach often cause difficulty eructating or vomiting and raised intragastric pressure with discomfort ("gas bloat syndrome"), resulting in forceful vomiting or retching<sup>[23]</sup>. This can cause wrap disruption or slippage of the wrap into the chest, the main causes of operative failure. Martinez *et al*<sup>[16]</sup> reported that more than 30% of children with neurological impairment had major complications or died within 30 d of surgery. Within a mean follow up period of 3.5 years, 25% had documented operative failure and overall, 71% had recurrent symptoms of GOR.

In children, the level of experience of the surgeon and surgical centre and appropriate case selection are key factors for determining the surgical outcome. Hassall<sup>[28]</sup> suggested that children who are the best candidates for

fundoplication have no neurological impairment, have endoscopically-established GORD and have exhibited an improvement in symptoms with PPIs therapy.

Most fundoplication surgery in the pediatric population is done through an open abdominal approach. In recent years, many reports have been published on the advantages and effectiveness of the laparoscopic approach for the management of patients with GORD<sup>[27]</sup>.

## CONCLUSION

Globally, the surgical management of GORD in children has changed dramatically with the refinement and clinical acceptance of the laparoscopic approach for fundoplication. Retrospective studies have established the benefits of the laparoscopic approach including more rapid recovery, faster return to unrestricted activity and decreased hospital stay while maintaining low complication and recurrence rates<sup>[29,30]</sup>. A clear increase in the number of publications related to laparoscopic fundoplication was noted supporting the global emergence and place of this technique in the management of GORD in pediatric surgery. Therefore, it shows there has been a change in the way children with GORD are managed surgically.

Collins *et al*<sup>[31]</sup> reported studies involving 120 patients that showed laparoscopic fundoplication complication rates for children were similar to those reported for open fundoplication. Blucher *et al*<sup>[32]</sup> reported that hospital stays after laparoscopic fundoplication were considerably shorter and patients returned to school and regular activities sooner. Somme<sup>[30]</sup> showed, in studies of 55 infants less than one year old, that in the laparoscopic Nissen fundoplication group, the time to initiation of feeding was significantly shorter than in the open Nissen fundoplication group. Rothenberg's<sup>[33]</sup> single large prospective study of laparoscopic fundoplication in 220 infants and children further supported the benefits of laparoscopic fundoplication. It showed that although the learning curve for laparoscopic fundoplication may be steep, the procedure is safe and effective in the pediatric population. The clinical results were comparable to the traditional open fundoplication but with a significant decrease in morbidity and hospitalization. A more recent prospective comparative study by Mattioli *et al*<sup>[34]</sup> confirmed that a minimally invasive approach was safe and effective for the treatment of primary GORD in children. Several studies reported that laparoscopic fundoplication has good long term outcomes<sup>[28,35]</sup> irrespective of neurological impairment associated with GORD<sup>[36]</sup>.

Four failure patterns after open fundoplication have been described: the slipped or misplaced fundoplication, the disrupted fundoplication, the herniated fundoplication and the fundoplication that is too tight or too long<sup>[37]</sup>. Since the introduction of laparoscopic fundoplication, two additional failure patterns have emerged: the twisted fundoplication and the two-compartment stomach<sup>[37]</sup>. Some reports have emphasized the high incidence of early post-laparoscopic complications and re-operation<sup>[38-40]</sup>. The long learning curve for all-laparoscopic technique has been identified as a confounding factor<sup>[38-40]</sup>. However, most of these studies are based on laparoscopic fundoplication in

adults, and whether the results will translate to children remains to be seen.

The minimal trauma to the upper abdominal wall in the laparoscopic approach results in less impairment of respiration and minimizes the need for narcotics and sedatives postoperatively<sup>[41]</sup>. A prospective comparative study of the fundoplication approach on analgesia requirement by Dick *et al*<sup>[42]</sup> showed the benefit of laparoscopic approach over open approach in decreased duration of pain as indicated by the decreased duration of analgesia following surgery. Thanks to the reduction of trauma-related problems, the laparoscopic approach has improved cosmetic results<sup>[30]</sup>.

Laparoscopic surgery has been perceived as having higher procedure costs but lower total costs, primarily because of reduced duration of hospital stay<sup>[43]</sup>. However, a more recent retrospective study on cost effectiveness by Blewett *et al*<sup>[44]</sup> reported that although laparoscopic surgery was associated with a shorter hospital stay, no effect on total hospital costs was seen. They concluded that laparoscopic procedures were comparable with open operations in terms of operative costs<sup>[44,45]</sup>. Therefore, from an economic point of view, the perception that laparoscopic procedures are more cost effective is still inconclusive and subject to further study.

In conclusion, laparoscopic antireflux surgery has surpassed open antireflux surgery as the gold standard in the surgical management of GORD in children. The next question to be addressed should be which operative technique can complement the laparoscopic approach to produce the best operative results. Longer term outcome studies also need to be done to confirm the status of laparoscopic antireflux surgery as the gold standard of surgical treatment for GORD in children.

## COMMENTS

### Background

Gastroesophageal reflux disease (GORD) is a pathological process in infants manifesting as poor weight gain, signs of esophagitis, persistent respiratory symptoms and changes in neurobehaviour. Surgery for GORD is currently one of the common major operations performed in infants and children by paediatric surgeons.

### Research frontiers

This study reviews the aetiology, risk factors, signs, clinical symptoms, diagnosis, and management of GORD in children. A Pubmed database search of GORD in children was performed.

### Related publications

Pubmed database search must be performed for finding related articles.

### Innovations and breakthroughs

Most fundoplication surgery in the pediatric population is done through an open abdominal approach. In recent years, many reports have been published on the advantages and effectiveness of the laparoscopic approach for the management of patients with GORD. Retrospective studies have established the benefits of the laparoscopic approach including more rapid recovery, faster return to unrestricted activity and decreased hospital stay while maintaining low complication and recurrence rates. Laparoscopic antireflux surgery has surpassed open antireflux surgery as the gold standard of surgical management for GORD in children. The next question to be addressed should be which operative technique can complement the laparoscopic approach to produce the best operative results and more long term outcome studies need to be done to confirm the status of

laparoscopic antireflux surgery as the gold standard of surgical treatment for this disease.

### Applications

The study results suggest that surgery for GORD is currently one of the common major operations performed in infants and children while the principles learned through open antireflux surgery can be applied to the laparoscopic approach, and this breakthrough has since been translated to pediatric surgery.

### Terminology

GOR: implies a functional or physiological process in a healthy infant with no underlying systemic abnormalities. It is a self-limiting process in infants that usually resolves by six to 12 mo of age. Nissen fundoplication: is a commonly used technique, with intra-abdominal positioning of the distal esophagus, hiatus hernia repair, and a 360° fundal wrap. 360° fundoplication refers to total fundoplication. Thal fundoplication: requires only a partial wrap (210°-270°) of the fundus around the anterior side of the oesophagus. Toupet fundoplication: a 270° posterior partial fundoplication. Watson fundoplication: a 120° anterior partial fundoplication.

### Peer review

This is a decent review on surgical options for pediatric reflux disease. It's well organized with a very good presentation and readability.

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