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Pediatric surgeons and gastroesophageal reflux

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Abstract

Background/Aims: Better antacid medications and the introduction of laparoscopy destabilize the indications for fundoplication. This study aims at raising a discussion among pediatric surgeons on these indications, modalities, and the results of this operation.

Materials and Methods: A total of 252 refluxing children operated between 1992 and 2006 were divided into groups according to predominant symptoms (93 digestive, 47 respiratory, and 68 neurologic) or to comorbidities (27 esophageal atresia, 10 diaphragmatic hernia, 5 abdominal wall defects, and 2 caustic stricture), and the indications, complications, mortality, and long-term results were reviewed. Features of open (n = 135) and laparoscopic (n = 117) approaches were compared, and long-term integrity of the wrap was analyzed using the Kaplan-Meier method.

Results: Digestive, respiratory, and neurologic patients had more often laparoscopic plications, whereas all others rather had an open approach. The rate of complications was 22%, and they were more frequent in children operated by laparotomy ($P < .05$). Median follow up was 51.3 months (range, 6-160). Overall wrap integrity was maintained in 89% of the children, and the proportions for digestive, respiratory, and neurologic groups were 95%, 95%, and 87%, respectively. For esophageal atresia, congenital diaphragmatic hernia, abdominal wall defects, and caustic stricture, they were 72%, 77%, 100%, and 0%, respectively. The functional results were fully satisfactory in 83% of patients. There were 17 deaths (6.7%), but only 3 in the first postoperative month and only 1 related to the operation (0.4%).

Conclusions: Fundoplication is a powerful method of reflux control. It is indicated after failure of medical treatment in gastroesophageal reflux disease and in symptomatic refluxers with some particular comorbidities. Surgery should be offered only after diagnosis has been firmly established, and the indications must remain identical for open and laparoscopic procedures. High technical standards and rigorous report of the results are required for keeping a relevant place of pediatric surgery in the treatment of this disease.

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Gastroesophageal reflux (GER) is a frequent phenomenon in infancy with a so marked tendency to improve spontaneously, that only a fraction of these children end up suffering real GER disease (GERD). Posture and diet without any

sophisticated diagnostic procedures help outgrow reflux in most cases before the age of 12 to 18 months. Antacid and prokinetic medications are indicated as the first-line therapy for cases with GERD [1,2], and only a minority of them require ultimately surgical treatment [3], which consists generally of one of the varieties of fundoplication.

The experience gained in adults and children [4,5] with proton pump inhibitors (PPI) as a powerful long-term medication for GERD and some critical judgements on

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antireflux surgery by influential pediatric gastroenterologists [6-10] have thrown doubts in the pediatric arena about its indications. These authors claim that long-term PPI treatment may be less dangerous than operations in which high rates of complications, wrap malfunction, and even mortality are to be expected. Furthermore, they warn pediatricians about the risks of loosening the indications after the introduction of more palatable alternatives like laparoscopic fundoplication and on the alleged weakness of the assessment of results of such operations by surgeons.

These appreciations might be slightly hypercritical, but they, nevertheless, contain the core of a pertinent discussion on the state of the art of surgical treatment of GERD in children. The well-known tendency of surgeons to be satisfied with what they do, together with the widespread use of the minimally invasive approach as particularly suitable for fundoplication, has probably loosened the indications for this operation, which is performed increasingly often in vomiting infants, in neurologically impaired children, and eventually as an adjunct to feeding gastrostomies indicated for malnutrition in renal failure or other diseases. The variability with which this is indicated in different countries and even in different departments in the same city prompts rethinking of what we, pediatric surgeons, are doing with this powerful tool.

The present work does not aim only at analyzing retrospectively yet another series of funduplications to add to the several large ones already published [11-14] but rather at finding in our own recent experience arguments for a critical discussion on the indications of these procedures, the potential problems created by them, the implantation of the laparoscopic approach in pediatric surgical departments, and the long-term results.

1. Material and methods

We reviewed patients treated surgically for GERD between 1992 and 2006. The nature of our institution's referral involved, in most cases, pediatric gastroenterologic filters that put refined diagnostic procedures and optimal nonoperative therapy before the surgical consultation. Gastroesophageal reflux was therefore diagnosed on the basis of clinical history and invariably documented by barium meal, extended pH metering, endoscopy, and mucosal biopsy. In addition, many patients had stationary and/or 24-hour ambulatory esophageal manometry as well. Gastroesophageal scintigraphy was only performed in a few children in whom delayed gastric emptying was suspected on the basis of clinical symptoms, radiologically enlarged stomach with slow emptying, or long periods of neutralization or alkalization after meals upon double gastroesophageal prolonged pH monitoring.

With a few exceptions that will be addressed later, surgery was never indicated as a first-line therapy. All patients were treated with posture, prokinetics (particularly

cisapride until it was withdrawn from the market), and antacid medications that evolved from ranitidine to PPI in more recent times. This treatment was applied during a minimum of 6 to 12 months (often several years), and surgery was only proposed after the persistence of the symptoms under medication was consistently demonstrated.

Our preferred operation was standard floppy Nissen fundoplication over a very large orogastric tube. Since 1993, we favored the laparoscopic approach. Although pyloromyotomy was often performed in the 1990s, this or formal pyloroplasty was progressively restricted since then to cases with demonstrated delayed gastric emptying. Gastrostomy was used in neurologically impaired patients who had swallowing difficulties and in babies with associated conditions in which this addition facilitated management like esophageal atresia with anastomotic stenosis, diaphragmatic hernia, or abdominal wall defects.

Feeding per os was resumed on the second postoperative day, a bland diet was advised for the first 3 weeks, and unrestricted feedings were allowed since then. At 6 months, the position of the wrap was verified by barium meal, and all patients with recurrent symptoms of GER were subjected to pH monitoring and/or endoscopy and biopsy. Whenever the wrap was disrupted or ascended, we advised reoperation except in patients wherein the symptoms were mild. Follow-up included at least one outpatient clinic visit per year, and all patients living in other countries or distant regions were contacted and interviewed by phone between January and March 2006.

Survival analysis (Kaplan-Meier) and log-rank tests were used to examine the persistence of the antireflux function of the wrap and the differences among groups by this respect. Comparison between groups of patients was made with contingency tables, as well as nonparametric or parametric tests as indicated with a level of significance of 5%.

2. Results

Over the study period, our department operated on 72,653 children, and 262 of them had Nissen fundoplication. We had to exclude 10 cases in which the charts were not complete, and we ended up with 252 patients for analysis.

The main indications and the age at operation are shown in Table 1. The 3 main groups of patients had predominantly digestive and respiratory symptoms or neurologic impairment. In these cases, surgical indication was only proposed after failure of optimal medical treatment had been documented. The only exceptions were major hiatal hernia, peptic strictures, and Barrett esophagus among the "digestive" patients, and asphyxia-suffocation-apnea grouped as apparent life-threatening events (ALTE) associated to demonstrated GER during infancy among the "respiratory" ones. In these cases, surgery was indicated primarily. Children previously operated for esophageal atresia, congenital diaphragmatic hernia (CDH), and abdominal wall defects with persistent

Table 1 Main indication for fundoplication, approach, and age at operation in 252 children (1992-2005)

	Open	Laparoscopic	All	Age at operation, median (range), mo
Gastrointestinal symptoms	40	53	93	67.3 (0.5-265)
Neurologic impairment	27	41	68	89.5 (3.8-274)
Respiratory symptoms	29	18	47	22.6 (1.3-298)
Esophageal atresia	23	4	27	22.1 (2.1-259)
CDH	10	0	10	5.1 (1-69)
Abdominal wall defects	5	0	5	13.2 (4.4-214)
Caustic structure	2	0	2	60.6 (55-66)
Total	135	117	252	50.2 (0.4-274)

symptoms of documented GER had operations without prolonged courses of medical therapy. A total of 59 babies had fundoplication below the age of 12 months, and most belonged to such categories.

As an indication of the severity of reflux and its concurrent conditions in our material, it should be pointed out that of 252 patients, 117 (46%) were below percentile 3 for weight, 19 had esophageal stenoses (10 of which were anastomotic after esophageal atresia repair), 9 had Sandifer syndromes, 8 had bronchopulmonary dysplasia, 8 had Barrett esophagus, 4 had mucoviscidosis, 4 had intrathoracic stomach, 4 had intestinal atresia, 3 had extreme short bowel syndrome (2 had an ultimately successful hepatointestinal transplantation), and a baby operated for esophageal atresia and for biliary atresia had her fundoplication during the anhepatic phase of liver transplantation. Five patients had been previously operated elsewhere for GER (one 3 times), and 5 had been previously treated for pyloric stenosis.

Fundoplication was more often open (n = 135) than laparoscopic (n = 117), although the latter was the procedure

Table 2 Complications observed after fundoplication in 252 children (1992-2005)

	Open (n = 135)	Laparoscopic (n = 117)	All (N = 252)
Wrap disruption	9	9	18
Dumping syndrome	4	3	7
Wound infection	7	0	7
Adhesive obstruction	6	0	6
Gastrostomy problems	2	3	5
Wound disruption	3	0	3
Incisional hernia	2	1	3
Tight wrap	1	2	3
Pneumonia	0	1	1
Pneumothorax	0	1	1
UTI-septic shock	1	0	1
Total	37 (27.4%)	19 (16.2%)*	56 (22.2%)

* P < .05 vs Open, Fisher's Exact test.

of choice during this period. In 6 cases, the laparoscopic procedure was converted to open because of technical difficulties (4 cases) or hemorrhage (2 cases). The open procedure was preferred in infants less than 6 months, in cases with previous operations, and in babies with esophageal atresia, CDH, and abdominal wall defects. Gastrostomy was used as a temporary or permanent adjunct in 53 (39%) of 135 cases operated openly and in 29(25%) of 110 operated laparoscopically (P < .05). The figures for pyloromyotomy were, respectively, 58 (42%) of 135 and 1 (0.8%) of 117, and for pyloroplasty 4 (2.9%) of 135 and 2 (1.7%) of 117.

Median follow up was 51.3 months (range, 6-160). Complications are summarized in Table 2. Wound infections or disruptions and adhesive obstructions were significantly more frequent in patients in whom fundoplication was open than in those in whom it was laparoscopic (37/135 [27.4%] vs 19/117 [16.2%]; P < .05, Fisher's Exact test).

Of 252 children 17 (6.7%) died during follow-up. Eleven were neurologically impaired individuals who ultimately died to their original disease a median of 15.5 months after the operation (range, 3-44). Only 3 babies died during the first postoperative month. One of these deaths was related to the operation (0.4% of total) because of wound disruption, reoperation, and infection, and this child had Di George syndrome and cyanotic congenital heart disease. The other 2 early deaths were because of persistent pulmonary hypertension in a patient with CDH who was never off the respirator and because of postoperative complications of a switch procedure for transposition in the other one. The remaining 3 deaths occurred at least 1 year after the Nissen fundoplication (1 child with a giant omphalocele and pulmonary hypoplasia, 1 with cardiomyopathy, and 1 with extreme short bowel who was on the waiting list for small bowel transplantation).

Excluding the deceased patients and taking demonstrated wrap failure as the end point, the function of the wrap remained intact in 89% of patients overall at a maximum

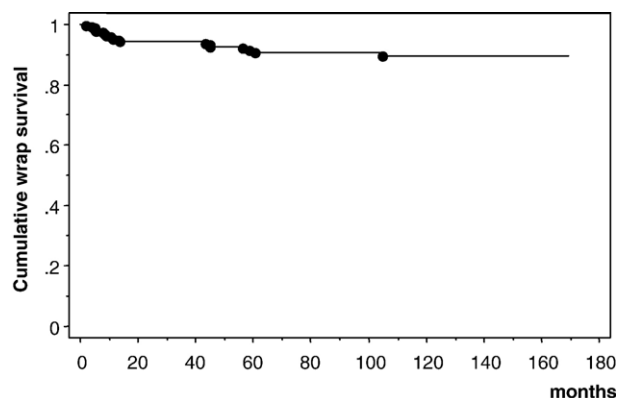


Fig. 1 Kaplan-Meier analysis of the integrity of wrap function over the 160 months of follow-up. This figure corresponds to the 235 survivors. It can be seen that most wrap disruptions occurred in the first 12 months after the operation, and that some became evident much later.

follow-up of 160 months (Fig. 1). Those with predominant gastrointestinal and respiratory symptoms had the best results by this respect (95% of functioning wraps each). Neurologically impaired patients had less good results in the long-term (87% of functioning wraps), although upon comparison with the other 2 groups, the differences were not significant (Fig. 2A). The highest percentages of wrap failure were observed in patients with esophageal atresia and CDH (72% and 77% of functioning wraps, respectively). The 4 surviving patients with abdominal wall defects had intact wraps, and in the 2 with caustic esophageal stenosis and secondary GER, they failed and the esophagus was replaced (Fig. 2B). Wrap failure rate was identical (8%) for open and laparoscopic funduplications. Of the 18 patients in whom the wrap ultimately failed, 12 were reoperated successfully (all but one by laparotomy).

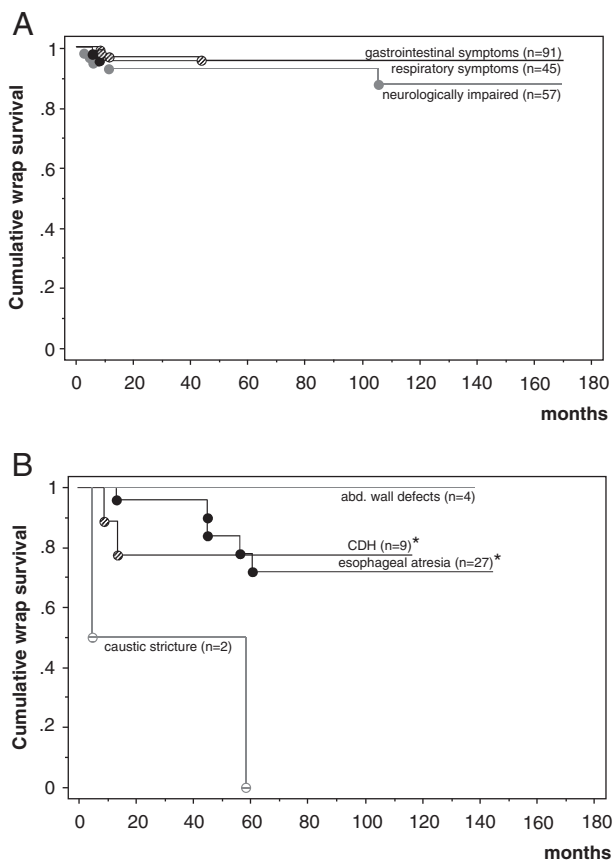


Fig. 2 Kaplan-Meier analysis of the integrity of wrap function in the different groups of surviving children. Those with gastrointestinal and respiratory symptoms had very good functional results and the proportion of failures in neurologically impaired children was surprisingly low. There were no differences among the three groups by log rank analysis (A). In (B) the integrity of the wrap over time in children with esophageal atresia, CDH, abdominal wall defects and caustic strictures is depicted. A substantial number of plications failed in the first 2 groups over the first 5 years after operation but close to 75% remain functional. In the other 2 groups the figures were too small for analysis. * $P < .05$ vs gastrointestinal or respiratory patients by log rank tests.

Upon personal interview or telephone questioning, 193 of the 235 survivors, including those who had early bothersome complications, and their families (83%) were fully satisfied with the long-term results of the operation.

3. Discussion

The following aspects should be discussed: the functional basis of fundoplication and its unavoidable side-effects, indications, laparoscopic approach, complications, and mortality; long-term integrity of the wrap; and expected changes in the treatment of GERD.

3.1. How fundoplication changes physiology

Fundoplication increases the length of the intraabdominal esophagus, recreates an angle of His, and acts as a pneumo-hydraulic valve that blocks retrograde passage of the bolus. On top of this, it decreases the amount and duration of the transient nondeglutitory relaxations of the lower esophageal sphincter that constitute the main mechanism of GER [15,16]. This is achieved by decreasing the compliance of the fundus, whose distension unchains the relaxations [17]. On the other hand, the wrap decreases the compliance of the stomach, within which smaller volumes create higher pressures. Early satiety and some degree of gas bloat are unavoidable early consequences of the operation that, although generally transient, are considerably bothersome for patients and their respective families [18]. In addition, the smaller gastric volume, together with the reduced compliance, accelerates temporarily gastric emptying even if drainage procedures are not used [19], and dumping may ensue as another serious inconvenience of the surgical treatment [20]. These potential problems should be taken into account when indicating the operation. Supporters of other forms of fundoplication claim that these might have less impact on gastric volume or compliance or be more appropriate for patients with esophageal dysmotility, like those previously operated for esophageal atresia, but our results show that when the Nissen is carefully performed, the incidences of gas bloat and/or dumping are not worse than theirs, that they could be controlled with diet alone over a period of months, and that the wraps were not obstructive in patients with motor dysfunction.

3.2. Indications of surgical treatment

We followed the main pediatric gastroenterological guidelines [1-3,21] because we used extensively sophisticated tests to ensure diagnosis and, except in a few cases, we only advised surgery as a second-line therapy after the failure of optimal medical measures. The mean age at operation in the digestive, respiratory, and neurologically impaired groups indirectly reflects the often long duration of medical treatment. The introduction of laparoscopic approach had no measurable impact on the number of

funduplications performed each year, attesting that indications remained unchanged.

Our results were rewarding in children with predominantly digestive symptoms, including stenoses, hemorrhage, and malnutrition. Reflux disappeared in children with Barrett esophagus, who might require endoscopic follow-up for life. All patients with Sandifer syndrome were cured weeks to months after the operation. In general, we also concur with the indications proposed for “asthmatic” and other respiratory children with GER, but we point out the pertinence of promptly addressing surgically the problem of GER in infants with ALTE and documented GER particularly in those who were prematures and had bronchopulmonary dysplasia. Our experience was particularly rewarding in this group of patients.

Antireflux surgery was in general very beneficial for neurologically impaired children. Some of them changed drastically after the operation because nutrition and respiratory problems improved, whereas pain and hemorrhage disappeared. It is true that morbidity in this particular group of patients is higher and that mortality was high, but death caused by the original disease intervened in some of these children months or years after their existence had been transformed by the operation.

When reviewing our experience, we had the impression that pediatric gastroenterological guidelines do not address specifically a considerable number of surgical conditions in which GERD is superimposed. Reflux is another component of esophageal atresia in which both the gastroesophageal barrier and peristalsis are damaged. More than 10% of our funduplications were performed in this group, often for recurrent anastomotic stricture that could be managed only after the operation. It is obvious that pediatricians are less involved than pediatric surgeons in the treatment of these patients. The impact of GER on the quality of life of survivors of neonatal operations for CDH and abdominal wall defects is often disregarded, but these babies bear several esophageal dysfunctions that make spontaneous regression of reflux unlikely. We were disappointed with fundoplication in children with caustic strictures in whom reflux might have contributed to the maintenance of the lesion.

Overall, retrospectively, we found that our indications for fundoplication were markedly conservative except in a relatively large group of infants with concurrent conditions that are in general out of the scope of the pediatricians and pediatric gastroenterologists.

3.3. Laparoscopic approach

Our preference nowadays is laparoscopic fundoplication, but this series shows that open fundoplication was still largely done during the period studied. This may be explained because not all of the 6 consultants involved offered laparoscopic repair and also because patient features discouraged such approach in a considerable proportion of cases. Only 6 of the 59 infants operated in the first year

underwent laparoscopic repair. Open Nissen was preferred at this age because of size and/or associated conditions like esophageal atresia, diaphragmatic hernia, and abdominal wall defects, as well as ALTE. In fact, the indications and the steps of the operation were identical.

In regard to the results of both approaches, they were similar in the long run. Patients operated by laparotomy had more wound complications and adhesive obstructions. Gastrostomy was performed more often in children who had open Nissen fundoplication, but this was probably because of the nature of the indications. Long-term results were identical with both approaches in contradiction with other reports that suggest higher failure rates for the laparoscopic one [14].

Our numbers illustrate how difficult it is for pediatric surgical departments to minimize the risks of several simultaneous learning curves. If a minimum number of operations is required to acquire expertise, it should be acknowledged that either laparoscopic fundoplication is restricted to some surgeons (and this is not realistic), or most operations will be performed by relatively inexperienced surgeons (and this might be dangerous). Looser indications produce indeed larger series (and more opportunities for training), but it should be pointed out that minimally invasive operations are maximally invasive when the indications are poor or weak. We still hesitate to bestow the rank of “gold standard” to laparoscopic fundoplication. This corresponds to a well-performed, loose, and long-lasting fundoplication, and, if this is not achieved laparoscopically, the open approach remains a decent “gold standard.” One should not forget that a dominant proportion of the pediatric population worldwide will not have access to the equipment and the expertise necessary for laparoscopic fundoplication for many years to come, and that it is dangerous to stigmatize the open approach as inadequate or outdated.

3.4. Complications and mortality

The proportion of complications in our series is within the range of what is acceptable. The rate of dumping syndrome, gas bloat, tight wrap, wound complications, or adhesive obstruction was minimal, but an overall risk of 1 in 5 is a reasonable estimate that must be provided to the patients’ relatives before the operation. The need for the family (and their pediatrician) to understand how fundoplication changes gastroesophageal physiology for the first few months is obvious. Mortality is rare, but it happens, particularly in some of the complex patients included in this series. The rates mentioned in some reports that are critical about the surgical treatment of GERD tend to include all neurological deaths, but we believe that this is unfair because most of the deaths are related to the underlying condition rather than the operation.

3.5. Long-term function of the wrap

The wrap remained functional in close to 90% of our patients with an overall follow-up of more than 10 years,

which is considered satisfactory. Practically all wrap disruptions occurred during the first 5 years, and most failures were noted in the first 12 months. Patients with predominant gastroenterologic or respiratory symptoms did very well. Those with neurologic impairment did slightly less well, and it is important to notice that invasive diagnostic tests tend to be used less frequently in them because of the difficulties involved in performing the tests. A sizeable proportion of patients with esophageal atresia had wrap failures, but we have the impression that in most of them, the absence of reflux was very beneficial and helped them to outgrow serious problems during infancy. Some of these children had successful reoperations. Children with CDH and reflux usually have many more problems, and the rate of success after plication was overall satisfactory. In some cases in which prosthetic patches were used, it was particularly difficult to fashion an appropriate and lasting wrap. Our short experience with plication in children with abdominal wall defects was rewarding. Finally, we discourage fundoplication in patients in whom reflux is supposed to maintain caustic esophageal stricture.

This study is not exempt from the main criticisms directed to surgical series of patients with GERD because, like several others, it is retrospective, did not involve routine use of invasive or expensive diagnostic tests in patients with good clinical postoperative results, and the quality of life or the degree of satisfaction over time were judged subjectively. We accept the possible criticisms but point out that, at issue with other surgical series, the diagnosis of GERD in our study was clearly documented, the operative indications were strict, and the long-term follow-up was available. Prospective randomized studies are probably unrealistic in a disease with so many different symptoms manifested over a wide range of ages. We have been unable to find studies on the effects of PPI and other medications in children with GERD extended as long as that of ours.

3.6. Expected changes in the treatment of GERD

The introduction of esophageal impedance studies in children [22,23] will certainly contribute in the near future to address more adequately the phenomenon of nonacid or biliary reflux. In spite of its well-known role in adult GERD, little is known about this in children mainly because of technical difficulties.

The development of new prokinetics and new refinements of PPIs or other antacid drugs may change pediatric attitudes toward reflux, but it seems hard to accept that chronic use of these medications could be transposed from the adult practice to children with much longer life expectancies. The problems of cost, compliance, and long-term side effects may redirect a number of these patients toward surgery.

Laparoscopic fundoplication became the favorite approach worldwide. We hope that pediatric surgeons will be wise enough to resist the temptation of widening the indications at the expense of the necessary sequence of diagnostic tests to obtain a solid diagnosis. Too many operations

performed by too many surgeons based on too weak indications will do no good to our patients while discrediting our specialty.

Other less-invasive procedures, like endoscopic endoluminal fundoplication [24] or radiofrequency ablation [25], have been seldom used in children to this date mainly because of equipment size. For this reason, these procedures have been restricted to adolescents, and it is doubtful that the current therapeutic trends might be modified in the short-term.

Finally, the place of total esophagogastric dissociation as a valid alternative in cases in which fundoplication is demonstrated or likely ineffective is still debated. When more long-term studies will be available, it is tempting to think that this may have a role for those patients in whom several funduplications have been ineffective or in some selected cases as a first option [26-28].

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References

- [1] Vandenplas Y, Ashkenazi A, Belli D, et al. A proposition for the diagnosis and treatment of gastro-oesophageal reflux disease in children: a report from a working group on gastro-oesophageal reflux disease. Working Group of the European Society of Paediatric Gastro-entology and Nutrition (ESPGAN). *Eur J Pediatr* 1993;152:704-11.
- [2] Rudolph CD, Mazur LJ, Liptak GS, et al. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 2001;32(Suppl 2):S1-S31.
- [3] Vandenplas Y. Reflux esophagitis in infants and children: a report from the Working Group on Gastro-Oesophageal Reflux Disease of the European Society of Paediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1994;18:413-22.
- [4] Gibbons TE, Gold BD. The use of proton pump inhibitors in children: a comprehensive review. *Paediatr Drugs* 2003;5:25-40.
- [5] Hassall E, Israel D, Shepherd R, et al. Omeprazole for treatment of chronic erosive esophagitis in children: a multicenter study of efficacy, safety, tolerability and dose requirements. International Pediatric Omeprazole Study Group. *J Pediatr* 2000;137:800-7.
- [6] Hassall E. Wrap session: is the Nissen slipping? Can medical treatment replace surgery for severe gastroesophageal reflux disease in children? *Am J Gastroenterol* 1995;90:1212-20.
- [7] Hassall E. Antireflux surgery in children: time for a harder look. *Pediatrics* 1998;101:467-8.
- [8] Di Lorenzo C, Orenstein S. Fundoplication: friend or foe? *J Pediatr Gastroenterol Nutr* 2002;34:117-24.
- [9] Hassall E. Outcomes of fundoplication: causes for concern, newer options. *Arch Dis Child* 2005;90:1047-52.
- [10] Hassall E. Decisions in diagnosing and managing chronic gastroesophageal reflux disease in children. *J Pediatr* 2005;146:S3-S12.
- [11] Fonkalsrud EW, Ashcraft KW, Coran AG, et al. Surgical treatment of gastroesophageal reflux in children: a combined hospital study of 7467 patients. *Pediatrics* 1998;101:419-22.

- [12] Gilger MA, Yeh C, Chiang J, et al. Outcomes of surgical fundoplication in children. *Clin Gastroenterol Hepatol* 2004;2:978-84.
- [13] Rothenberg SS. The first decade's experience with laparoscopic Nissen fundoplication in infants and children. *J Pediatr Surg* 2005;40:142-6.
- [14] Diaz DM, Gibbons TE, Heiss K, et al. Antireflux surgery outcomes in pediatric gastroesophageal reflux disease. *Am J Gastroenterol* 2005;100:1844-52.
- [15] Werlin SL, Dodds WJ, Hogan WJ, et al. Mechanisms of gastroesophageal reflux in children. *J Pediatr* 1980;97:244-9.
- [16] Kawahara H, Dent J, Davidson G. Mechanisms responsible for gastroesophageal reflux in children. *Gastroenterology* 1997;113:399-408.
- [17] Kawahara H, Imura K, Yagi M, et al. Mechanisms underlying the antireflux effect of Nissen fundoplication in children. *J Pediatr Surg* 1998;33:1618-22.
- [18] Hogan WJ, Shaker R. Life after antireflux surgery. *Am J Med* 2000;108(Suppl 4A):181S-91S.
- [19] Bustorff-Silva J, Fonkalsrud EW, Perez CA, et al. Pyloroplasty improves long-term gastric emptying in rats undergoing fundoplication. *J Pediatr Surg* 2000;35:1087-90.
- [20] Samuk I, Afriat R, Horne T, et al. Dumping syndrome following Nissen fundoplication, diagnosis, and treatment. *J Pediatr Gastroenterol Nutr* 1996;23:235-40.
- [21] Vandenplas Y, Belli D, Benhamou PH, et al. Current concepts and issues in the management of regurgitation of infants: a reappraisal. Management guidelines from a working party. *Acta Paediatr* 1996;85:531-4.
- [22] Condino AA, Sondheimer J, Pan Z, et al. Evaluation of infantile acid and nonacid gastroesophageal reflux using combined pH monitoring and impedance measurement. *J Pediatr Gastroenterol Nutr* 2006;42:16-21.
- [23] Rosen R, Lord C, Nurko S. The sensitivity of multichannel intraluminal impedance and the pH probe in the evaluation of gastroesophageal reflux in children. *Clin Gastroenterol Hepatol* 2006;4:167-72.
- [24] Thomson M, Fritscher-Ravens A, Hall S, et al. Endoluminal gastroplasty in children with significant gastro-oesophageal reflux disease. *Gut* 2004;53:1745-50.
- [25] Islam S, Geiger JD, Coran AG, et al. Use of radiofrequency ablation of the lower esophageal sphincter to treat recurrent gastroesophageal reflux disease. *J Pediatr Surg* 2004;39:282-6.
- [26] Bianchi A. Total esophagogastric dissociation: an alternative approach. *J Pediatr Surg* 1997;32:1291-4.
- [27] de Lagausie P, Bonnard A, Schultz A, et al. Reflux in esophageal atresia, tracheoesophageal cleft, and esophagocoloplasty: Bianchi's procedure as an alternative approach. *J Pediatr Surg* 2005;40:666-9.
- [28] Lall A, Morabito A, Dall'Oglio L, et al. Total oesophagogastric dissociation: experience in 2 centres. *J Pediatr Surg* 2006;41:342-6.