

European multicenter survey on the laparoscopic treatment of gastroesophageal reflux in patients aged less than 12 months with supraesophageal symptoms

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Received: 7 December 2004/Accepted: 7 April 2005/Online publication: 11 August 2005

Abstract

Background: This multicenter survey includes neonates and infants who underwent surgery for primary gastroesophageal reflux (GER) who presented with supraesophageal symptoms of unknown origin with a minimum of 12 months postoperative follow-up.

Methods: A total of 726 patients underwent GER surgery in 10 European Centers in the period 1998–2002. Respiratory symptoms were present in 204 patients (28%); 135 patients (17%) had surgery under 1 year of age, and 46 of them (6.3%) because of respiratory symptoms. Surgery was performed without any previous medical treatment in 10 cases (21%). The type of procedure included 37 complete 360° wraps (80%) (Nissen, 12, and Rossetti, 25) and nine partial wraps (20%) (Thal five, Lortat Jacob one, Toupet one, others two). Gastrostomy was associated in 17 cases (37%) (6 PEG and 11 modified Stamm). No gastric emptying procedures were recorded.

Results: No major intraoperative complications were reported. Six patients developed complications (13%) and a redo operation was performed in three (6.5%). Respiratory outcome after antireflux surgery was good in 35 patients (76%) and fair with significantly improved respiratory symptoms in 11 (24%).

Conclusions: This multicenter survey underlines that GER has to be suspected and aggressively treated in infants with difficult-to-treat supraesophageal symptoms, and also in high-risk cases, in order to prevent major complications.

Key words: supraesophageal — reflux — laparoscopic — Nissen — neonates — impedance

Gastroesophageal reflux (GER) with supraesophageal symptoms, particularly respiratory symptoms, has been described. However, the North American guidelines state that in case of supraesophageal symptoms there is insufficient evidence and experience to provide recommendations for uniform approach to diagnosis and treatment [14].

It is still now debated whether reflux can cause supraesophageal symptoms, and some authors consider this correlation as ballyhoo [16].

In contrast, other studies underline the importance of the early diagnosis of GER and of aggressive management, which may decrease neonatal morbidity and result in earlier discharge from the NICU [7].

The peak age of onset of GER during infancy is 1–4 months, and premature infants have a higher incidence. This population is considered to benefit from aggressive treatment [5].

Antireflux surgery in premature infants with bronchopulmonary dysplasia and close association between chronic respiratory distress and GER has facilitated early postoperative weaning from the ventilator and reduced the requirement for supplemental oxygen in premature newborns [4].

Considerable criticism is evident in the literature regarding fundoplication in early infancy, as it proved to be unsuccessful in a high proportion of patients, with the best results achieved in infants emesis [8]. In contrast, many other papers suggest the importance of antireflux surgery to treat respiratory symptoms, and the results emphasize its good outcome [1–3, 6, 13].

With specific regard to the Gaslini Research Institute, surgery was necessary in 8% of cases with GER and supraesophageal respiratory symptoms with a very low recurrence and complication rate. However, it is not always easy to identify a close correlation between reflux and atypical symptoms. Prolonged esophageal pH monitoring, scintigram, and bronchoalveolar lavage (BAL) are the diagnostic tools generally used to suspect and detect aspiration. However, it is very difficult to detect non-acid reflux with supraesophageal symptoms, particularly in neonates and infants, and esophageal impedance technique have been suggested in difficult cases [10, 15, 18].

Chronic respiratory disorders are not contraindications for the laparoscopic approach to the treatment of GER in children, and early surgery is supposed to prevent chronic pulmonary disease such as bronchiectasis or asthma [9, 11]. This multicenter survey collects the experience of 10 European pediatric centers on laparoscopic correction of primary GER, in patients younger than 12 months with supraesophageal, mainly respiratory, symptoms without major anatomical anomalies.

Materials and methods

Fifteen European pediatric surgery units with a large experience in laparoscopic surgery in infants were asked to participate in this survey. Two questionnaires were sent to all the centers in May 2003. The first one was a computerized data sheet collecting detailed data of each treated patient. The second questionnaire included questions on the routine clinical protocols used by each surgeon for the diagnosis and treatment of infants and neonates with suspected reflux and supraesophageal symptoms. Data input was completed in December 2003.

We included in the study patients who underwent surgery for primary GER in the first year of life, during the period 1998–2002. We focused particularly on neonates and infants who presented with supraesophageal symptoms of unknown origin: respiratory distress, aspiration, chronic cough, bronchospasm/asthma, pulmonary infection, laryngitis, laryngospasm, life-threatening events (LTE), apnea events with cyanosis, and bronchopulmonary dysplasia (BPD) with oxygen dependence.

In order to reduce bias we excluded patients with neurological impairment, diaphragmatic hernia, and esophageal atresia because these congenital problems can cause pulmonary symptoms due not only to reflux but also to primary pulmonary and airway pathology. Another exclusion criterion was typical evidence of GER as vomiting more than once a day.

Diagnostic tools were 24-h esophageal pH monitoring, x-ray contrast study, ultrasound of the upper digestive tract, manometry, and endoscopy with histologic and cytologic examination of the upper digestive tract and airways.

Continuous enteral feeding (CEF) through a nasogastric tube (NG-tube) or a gastrostomy tube was used in case of suspected aspiration in order to reduce the risk of aspiration or in case of dysphagia. Medical treatment included proton pump inhibitors (omeprazole), histamine-2 receptor blockers (ranitidine), and prokinetics (domperidone or cisapride).

Surgery was indicated in cases with correlation between respiratory symptoms and reflux events, when there was failure or only partial response to medical therapy, and in case of recurrence of symptoms after cessation of medication. Surgery was especially indicated in cases of high risk of complications due to reflux, such as aspiration and pneumonia or prolonged apnea and life-threatening events (LTEs).

Surgical steps included hiatoplasty, fundoplication and/or gastroptexy. Additional procedures included gastrostomy (PEG or modified Stamm procedure) and operations to increase gastric outflow.

All cases were reviewed to detect complications intra- and post-operatively, and the treatment undertaken was analyzed. A minimum of 12 months' postoperative follow-up was mandatory.

Outcome evaluation (symptoms, stricture, recurrence, and need of redo surgery) included clinical status (Visick, [17]), upper GI radiological contrast study, and prolonged esophageal pH monitoring.

The following queries were made to each surgeon:

1. What is the best age, in your opinion, for the treatment of this population? As soon as you have the diagnosis, is conservative treatment always mandatory?
2. Who are the physicians who refer these patients for surgery?
3. Which is the best method to obtain an early diagnosis?
4. Define pH monitoring results: which are your parameters to define the examination as pathological and/or positive for reflux.
5. What do you think about nonacid refluxers, with negative esophageal pH analysis?
6. In case of negative esophageal pH analysis, what are the main diagnostic factors that lead you to operate on the patient (including symptoms response to conservative treatment)?
7. What is the best diagnostic tool in case of negative pH-metry?
8. Do you think intraluminal impedance technique is mandatory in case of nonacid refluxers?
9. In case of poor outcome after surgery, persistence of symptoms, and negative exams for recurrence of reflux, do you think surgery should not have been done (failure in indication) or should there have been better diagnosis and treatment of the primary respiratory problem?

Data for each patient were collected using Access software (Microsoft Corp.). Data are expressed as sum, average, range, and percentage. Student *t*-test and chi-square were used to analyze the results. Results were considered statistically significant for a *p*-value < 0.05.

Informed consent was obtained from the relatives and guardians of the patients before every procedure.

Results

Ten centers completely collected and sent back all the data sheets and the answers to the queries.

In the period 1998–2002, 726 patients underwent GER surgery. Respiratory symptoms were present in 204 patients (28%); 135 patients (17%) had surgery under 1 year of age, and 46 of them (6.3%) because of respiratory symptoms.

If we consider only the patients operated on under 1 year of age, the percentage of cases with respiratory symptoms was 34% (46 of 135) (Table 1). Details on the data of each center are shown in Table 2. The cases who met the inclusion criteria for the survey were 46 (Table 3).

There were 28 boys (61%) and 18 girls (39%) (sex ratio males to females: 1.5). The mean age at surgery was 7.38 months (range 1–2) and the mean weight, 6.64 kg (range 2.9–14).

Table 1. Cumulative results from the multicenter survey

	Total	%	Resp	%	< 12mo	%	< 12mo Resp	%1	%2	< 12mo noResp	%1	%2
Total	726	100	204	28	135	17	46	6.3	34	89	12.3	66
Average	72.6		20.4	28	13.5	18.5	4.6	6.3	34	8.9	12	66
Median	70.5		16	22	11.5	16	3	4.2	26	7	9.9	61
Range	46–92	7–14.1	3–51	3.7–58.7	3–27	6.5–35.4	1–11	1.5–17.7	7.4–100	0–25	0–32.3	0–92.6

A total of 726 children were operated in the period 1998–2002. In order to better understand the incidence in the different group we performed the percentage using different parameters: column %1 refers to the general population of operated patients and column %2 to the cases operated under 1 year of age. Respiratory symptoms were present in 204 patients (28%). Patients operated before 1 year of age were 135 (17%). Patients operated before 1 year of age because of respiratory symptoms were 46, accounting for 6.3% of the whole population (726) and 34% of the 135 cases operated before age 12 months. Patients operated before 1 year of age who did not complain of respiratory symptoms were 89, accounting for 12.3% of the whole population and 66% of the 135 cases operated before age 12 months. Mean operated cases for each center were 72.6 (46–92), mean respiratory cases were 20.4 (3–51), mean cases aged less than 12 months were 13.5 (3–27), mean cases aged less than 12 months with respiratory symptoms were 4.6 (1–11) and without respiratory symptoms were 8.9 (0–25)

Table 2. Indication to laparoscopic fundoplication in the different centers in the period 1998–2002

Institution ^a	Total ^b	%	Resp ^c	%	< 12mo	%	12mo Resp	%1	%2	< 12mo noResp	%1	%2
1	92	14.1	51	55.4	12	13.0	11	12.0	91.7	1	1.1	8.3
2	58	8.9	5	8.6	16	27.6	3	5.2	18.8	13	22.4	81.3
3	62	9.5	11	17.7	11	17.7	11	17.7	100.0	0	0.0	0.0
4	91	13.9	16	17.6	10	11.0	6	6.6	60.0	4	4.4	40.0
5	68	10.4	36	52.9	10	14.7	1	1.5	10.0	9	13.2	90.0
6	82	12.6	3	3.7	8	9.8	3	3.7	37.5	5	6.1	62.5
7	73	10.0	30	41.1	15	20.5	4	5.5	26.6	11	15.1	73.4
8	65	10.0	9	13.8	23	35.4	2	3.1	8.7	21	32.3	91.3
9	89	13.6	16	18.0	27	30.3	2	2.2	7.4	25	28.1	92.6
10	46	7.0	27	58.7	3	6.5	3	6.5	100.0	0	0.0	0.0

^a The number of the surgical unit as printed in the list of authors in alphabetical order

^b Cases operated under 14 years of age for GER in the same period

^c Patients operated on for supraesophageal symptoms

Percentages are expressed in relation to the total numbers. Column %1 refers the general population of operated patients and %2 to the cases operated under 1 year of age

There was a statistically significant difference between centers 1, 5, and 10 and the others because of a greater percentage of GER patients with respiratory symptoms (55.4, 52.9, 58.7). The same difference was found for centers 2, 8, and 9, which had a higher percentage of cases operated in the first year of life (27.6, 35.4, 30.3)

The supraesophageal symptoms that indicated the procedure were aspiration in 30 cases (65.5%), apnea and life-threatening events (LTE) in six (13%), bronchopulmonary dysplasia and oxygen dependence in eight (17.5%), recurrent bronchospasm in one (2%), and laryngitis/laringospasm in one (2%). Esophageal pH monitoring was performed in 32 cases (69%), upper-GI series in 45 (97%), digestive endoscopy in 18 (39%), bronchoscopy and bronchoalveolar lavage (BAL) in nine (19.5%), ultrasound of the cardias in four (8.6%), and esophageal manometry in 13 (28.2%). Scintigraphic examinations were not recorded.

Conservative treatment before surgery included continuous enteral feeding via nasogastric tube in 18 cases (39%), administration of antisecretive drugs in 26 (56.5%) (PPI in 17 and H2-blockers in nine) and of prokinetics in 12 (26%) (cisapride in 5 and domperidone in 7).

Surgery was performed without any previous medical treatment in 10 cases (21%). The type of procedure included 37 complete 360° wraps (80%) (Nissen 12 and Rossetti 25) and nine partial wraps (20%) (Thal five, Lortat Jacob one, Toupet one, others two). Gastrosto-

my was associated in 17 cases (37%) six PEG and 11 modified Stamm).

No gastric emptying procedures were recorded. No major intraoperative complications were reported. The procedures were laparoscopically completed in 45 cases (97%).

Six patients developed complications (13%): pneumonia one, stricture two (one reoperation), pneumothorax one, disruption of the wrap one (reoperation), dislocation one (reoperation). A redo operation was performed in three of these six complicated cases (6.5%). The other three cases were conservatively treated.

Respiratory outcome after antireflux surgery was good in 35 patients (76%) and fair with significantly improved respiratory symptoms in 11 (24%). Three cases (6.5%) suffered temporary dysphagia.

Answers to queries:

1. Surgery should be performed as soon the diagnosis is made (the major complaint was asphyxia/apnea, aspiration, and life-threatening cyanotic spells), as a matter of urgency in patients with acute life-threat-

Table 3. Results of data collection (percentages refer to 46 cases who met the inclusion criteria)

Cases included	46	
Males	28	(61%)
Females	18	(39%)
Ratio	1.5	
Mean age	7.38 months	(range 1–12)
Mean weight	6.64 kg	(range 2.9–14)
Main symptoms		
Aspiration	30	(65.5%)
Apnea and LTE	6	(13%)
BPD and oxygen dependence	8	(17.5%)
Asthma	1	(2%)
Laryngitis	1	(2%)
Diagnostic tools		
Esophageal pH monitoring	32	(69%)
Upper-GI tract series	45	(97%)
Digestive endoscopy	18	(39%)
Bronchoscopy + BAL	9	(19.5%)
Ultrasound of the cardias	4	(8.6%)
Esophageal manometry	13	(28.2%)
Previous treatment		
Continuous enteral feeding	18	(39%)
Antisecretive drug	26	(56.5%)
Prokinetics	12	(26%)
None	10	(21%)
Type of surgery		
Complete 360° wrap	37	(80%)
Partial wrap	9	(20%)
Gastrostomy	17	(37%)
Completed by laparoscopy	45	(97%)
Complications	6	(13%)
Pneumonia	1	
Stricture	2	
Pneumothorax	1	
Disruption of the wrap	1	
Dislocation	1	
Reoperation	3	(6.5%)
Outcome		
Good (Visick 1)	35	(76%)
Amelioration (Visick 2)	11	(24%)
Temporary dysphagia	3	(6.5%)

LTE, Life-threatening event; BPD, broncho pulmonary dysplasia; BAL, broncho alveolar lavage

ening events only. In all other patients first-line treatment is conservative. Only one surgeon stated that surgery is immediately needed only in case of large hiatal hernia. The other surgeons consider mandatory medical therapy trials and CEF first.

- The clinicians suggesting surgery for this population are different for each center, but they mainly include pneumologist and neonatologist (NICU). Gastroenterologists generally do not suggest surgery, as this group of infants generally does not complain of major gastrointestinal symptoms.
- Prolonged esophageal pH recording, in this group of patients, was considered the best method to reach the diagnosis by seven centers. Clinical evaluation, including response to conservative treatment, chest x-ray, and upper GI series and bronchoscopy with BAL, were the diagnostic tools used to confirm the correlation between reflux and supraesophageal symptoms.
- Reflux Index and the clinical correlation between reflux event and symptoms were used to define the pH-exam positive for reflux.

- In case of negative pH monitoring all the authors agreed on considering the importance of clinical status and on ruling out other causes of symptoms. Nonacid refluxers, with negative esophageal pH analysis, should be operated on if reflux is proven or if symptoms are strongly correlated with reflux events.
- Symptoms and response to conservative treatment were considered the most important indication for surgery, and also in case of negative pH analysis.
- X-ray, bronchoscopy with BAL, and manometry were considered the best diagnostic tools in case of negative pH-metry.
- No experience in endoluminal impedance studies was reported; however, it was considered interesting by all the authors but one, who preferred manometry, focusing on the typical single-camera aspect of the reflux event.
- In case of poor outcome after surgery, persistence of symptoms, and negative examinations for recurrence of reflux, investigations should be repeated to determine a reason for failure. However, antireflux surgery can be considered successful in avoiding recurrent cyanotic spells. A bad outcome generally results from a bad diagnosis or a too-late operation. Surgery can be considered in very difficult cases the single method to reach a correct diagnosis as it allows better respiratory treatment.

Discussion

This article reports the experience of a group of surgeons from different European countries in the diagnosis and treatment of GER with supraesophageal symptoms in a selected population of infants and neonates. The diagnosis of refractory respiratory symptoms and life-threatening events of unknown origin is not easy, and GER can cause or can be caused by these symptoms and events. Many reasons have to be ruled out. Tracheo-esophageal fistulas, tracheomalacia, aspiration from mouth and pharynx (incoordinate swallowing), and primary pulmonary disorders should be excluded before any surgery; otherwise the outcome could be disastrous.

Moreover, a gastric outlet disorder has to be evaluated as a reason for secondary reflux, particularly in case of nonerosive reflux disease (NERD) and of nonacid reflux with supraesophageal symptoms. In this situation, surgery of the LES alone can cause worsening of the gastric function, requiring major emptying procedures or diversion.

Continuous enteral feeding (CEF) through a nasogastric tube or gastrostomy can help in the diagnosis before surgery. Discontinuance of oral feeds can determine temporary resolution of symptoms and improvement of respiratory conditions and can suggest aspiration due to reflux. However, aspiration from the upper digestive tract has to be demonstrated by different examinations such as videofluoroscopy and UES

manometry. In neurologically impaired children, this study is very difficult and fundoplication is suggested in all cases where reflux reduces quality of life.

We decided to rule out patients who underwent surgery because of esophageal atresia and diaphragmatic hernia that can mimic or can be associated with GER.

Esophageal pH monitoring is the gold standard to detect reflux. However, in patients with supraesophageal symptoms, a single episode of aspiration can lead to lung damage.

In the case of a negative pH examination, the clinical symptoms and signs, response to antireflux therapy, and BAL are considered the gold standard for diagnosis and can advise the surgeon to perform reflux surgery to prevent lung damage and LTE.

Bronchoscopy with BAL was considered useful to perform a correct diagnosis of aspiration, but it was performed in few cases because of the need for general anesthesia and airway manipulation, which can be highly risky in infants with chronic lung disorders.

Esophageal 24-h pH monitoring can be negative because of the type of food intake, which is normally milk formula in infants and neonates, and continuous enteral feeding can increase confusion because of high gastric pH levels. In this age group a negative pH exam is not significant and x-ray and endoscopy (airways and digestive tract) with pathologic examination can improve the diagnosis because it can detect single episodes of aspiration, which can cause bronchospasm and oxygen need, particularly in patients with bronchopulmonary dysplasia.

Scintiscan of the lung can be useful, but it is time dependent, with a large number of false negatives, and it is not always easily performed in patients with respiratory distress.

Esophageal manometry is performed in few centers and interpretation of the results is not well established in nonacid refluxers.

All the authors agree on the importance of a meticulous evaluation of patient history, daily clinical picture, and response to conservative medical treatment and enteral feeding to reach a correct diagnosis and to decide the indication for surgery.

This survey demonstrates the low incidence of the need for surgery in infants and neonates in case of supraesophageal symptoms but, also, the good results of surgery when performed. There was complete resolution of symptoms in 76% of cases, which is not good if compared with the results of the same procedure in case of typical GER symptoms. However, it is generally considered by all the authors that in these cases a complete eradication of reflux events helps clinicians and pulmonologists to better evaluate symptoms and contributes to clinical status improvement.

This experience was also characterized by a very low complication rate, and although 6.5% of patients needed reoperation, there was no major morbidity or mortality.

Gastrostomy was performed, through an open or endoscopic approach, in a small percentage of cases where difficulties in swallowing and suspicion of aspi-

ration not only from the stomach but also from the mouth was high. In these patients, fundoplication and gastric diversion can help to improve lung function. As already underlined by the NASPGAN guidelines [7, 14], early aggressive treatment should be recommended when reflux is confirmed in order to prevent life-threatening events and lung damage that can lead to asthma or pulmonary destruction due to infection and bronchiectasis development.

The surgeons who contributed to this survey consider the laparoscopic approach the gold standard for the treatment of GER because of the evidence of good results from patients, anesthesiologists, and surgeons.

According to our data, the most suitable types of antireflux surgery could not be identified, as a complete or partial wrap with hiatoplasty seemed to give the same results with the same risk of complications. In addition, this survey is not based on sufficient data to state which is the best procedure.

Precise delineation of what is meant by supraesophageal symptoms related to reflux is difficult, and GER can coexist as cause or effect. In order to understand whether symptoms come from a primary respiratory disorder and to properly treat this latter, reflux has to be cured. Antireflux surgery can improve and cure the symptoms if they are due to reflux, but can also help the clinician to better treat pulmonary disorders in difficult cases where reflux, if present, can impair the effectiveness of medical treatment [12].

Diagnosis is difficult but, when reflux is suspected to cause the symptoms, early aggressive treatment is required to prevent lung damage and life-threatening events.

Surgery, in the general opinion, should be done only if conservative treatment is useless, but in selected patients with pneumonia due to aspiration and in case of life-threatening events, early aggressive treatment can be required.

To conclude, this multicenter survey underscores that GER has to be suspected and aggressively treated in infants with difficult-to-treat supraesophageal symptoms, and also in high-risk cases, in order to prevent major complications.

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