Fundoplication in neurologically impaired children: Nissen or Thal?

Kamal Abel-Elah Aly[a], Ahmed Megahed[b] and Mohammed Khalifa[c]

Background/purpose **Gastroesophageal reflex disease (GERD) is a highly prevalent problem in infants and children with severe neurological impairment (33–75%). It occurs in 44–67% of children undergoing antireflux surgery. This study is conducted to compare the results of fundoplication, according to the Nissen and Thal procedure for management of GERD in neurologically impaired children.**

Materials and methods **Between May 2007 and January 2011, 69 neurologically impaired children with severe GERD underwent fundoplication (Nissen = 32, Thal = 37) with construction of a Stamm gastrostomy tube in 58 patients. The male-to-female ratio was 1.6 : 1; the mean age was 1.8 years. Preoperative workup of the patients included upper gastrointestinal tract contrast series, upper gastrointestinal tract endoscopy, and a 24-h pH study.**

Results **Perinatal asphyxia was the most common cause of neurological impairment (30.4%). Feeding dysfunction represented the most common indication for surgery (52.2%). Recurrence of symptoms was found in 14 patients (20.3%); 10 patients (14.5%) died because of respiratory failure. Acid pH-metry showed a statistically significant difference between preoperative and postoperative data; however, this difference was insignificant on comparing the postoperative parameters of the Nissen fundoplication group with the Thal fundoplication group.**

Conclusion **GERD in neurologically impaired children is a very common problem associated with a high failure rate after properly performed fundoplication. In our series, the outcome of Thal fundoplication showed an insignificant difference when compared with that of Nissen fundoplication with less dissection and less dysphagia or gas bloat. Long-term evaluation is needed as incidence of recurrence increases with time secondary to the persistent comorbidities. Further refinement of management strategies is required to decrease incidence of recurrence and to improve the overall quality of life.** ***Ann Pediatr Surg*** **8:99–104 © 2012 Annals of Pediatric Surgery.**

Annals of Pediatric Surgery 2012, **8**:99–104

Keywords: fundoplication, gastroesophageal reflux disease, neurological impairment

[a]Department of Surgery, Pediatric Surgery Unit, [b]Department of Pediatrics, Pediatric Gastroenterology, Mansoura University, Mansoura and [c]Pediatric Surgery Unit, Department of Surgery, Menofiya University, Shebein ElKom, Egypt

Correspondence to Kamal Abel-Elah Aly, MD, Department of Surgery, Pediatric Surgery Unit, Faculty of Medicine, Mansoura University, Mansoura, Egypt
Tel: +20 122 447 637; fax: +20 50 9182131; e-mail: kamalaly5@yahoo.com

Received 1 January 2012 **accepted** 15 July 2012

Introduction

Gastroesophageal reflux disease (GERD) is a very common problem in infants and children with severe neurological impairment (NI). The prevalence of GER in this population of patients is reported to be between 33 and 75% [1,2]. This group of patients includes 44–67% of patients undergoing antireflux surgery [3–5].

This high rate of GERD is because of a combination of poor esophageal and gastric motility (due to vagal nerve dysfunction), chronic supine positioning, abdominal spasticity, diaphragmatic flaccidity, scoliosis, retching, and increased use of gastrostomy for feeding [6].

Medical treatment is often ineffective, and surgical fundoplication may be necessary to control symptoms [7]. In addition to GER, many other deleterious mechanisms contribute to the feeding and respiratory problems in these patients like abnormalities in lower esophageal function [8,9]; delayed gastric emptying [10,11]; and antroduodenal dysmotility [12].

The diagnostic tools routinely used for GERD do not identify these abnormalities correctly. Careful observation of clinical symptoms [13] or other investigative methods, such as antroduodenal manometry [14] or transit time measurement, may be necessary to detect these underlying gastrointestinal motor problems in handicapped children.

Morton *et al.* [15] reported that oral and pharyngeal motor problems are the major causes of respiratory tract infection in children with severe neurodisability, leading to direct aspiration.

Excellent results are obtainable with conventional antireflux surgery as long as it effectively eliminates reflux [16]; but postfundoplication failure rate in children with NI reaches up to 71% within 1 year of conventional antireflux surgery [17].

Nissen fundoplication (NF) is the most commonly performed antireflux procedure, and experience with other antireflux procedures is limited in neonates and infants having this problem, although the data available seem to confirm that Thal fundoplication (TF) is as effective as NF and, at the same time, that patients can burp and vomit if necessary and have less dysphagia or 'gas bloat', which may otherwise be present after NF [18,19].

Recurrent GERD after fundoplication in children with NI could be treated using gastrojejunal feeding tubes, a Roux-en-Y jejunostomy tube, esophagogastric dissociation, or redo antireflux surgery. However, redo fundoplication

1687-4137 © 2012 Annals of Pediatric Surgery DOI: 10.1097/01.XPS.0000418469.20879.0b

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.

has a higher failure rate with greater risks of redo surgery like excessive bleeding [20].

Aim of the work

This work was conducted to compare the outcome of the 360° NF and the partial 270° TF the in management of GERD in neurologically impaired children at the Mansoura University Children's Hospital.

Patients and methods

Between May 2007 and January 2011, 69 neurologically impaired children with severe GERD underwent fundoplication after failure of medical therapy (NF = 32, TF = 37) with construction of a Stamm gastrostomy tube in patients with difficulty in swallowing. The male-to-female ratio was 1.6 : 1 (43 boys : 26 girls). Medical treatment included fractionation of feeds into small frequent meals, positioning after feeds, and use of thickening meals and pharmacological treatment that was mainly in the form of H_2 blockers or proton pump inhibitors. Four patients presented with nasogastric feeding because of their severe NI. The age of the children ranged from 5 months to 6 years (mean 1.8 years).

Indications of surgery included GERD with feeding dysfunction, recurrent respiratory tract infection secondary to repeated aspiration, failure to gain weight, and/or upper GI bleeding.

Preoperative workup of the patients included patient history taking and examination, upper gastrointestinal tract contrast series, upper gastrointestinal tract endoscopy, and a 24-h pH study.

Demographic data of the patients, associated morbidity, preoperative investigations, operative techniques, postoperative investigations, and complications were described.

Nissen fundoplication [21]

This procedure aims to establish a high-pressure zone in the distal esophagus. A relatively large nasogastric tube was placed before incision.

Incision: midline upper abdominal incision. Exposure: by dividing the left triangular ligament to expose the gastroesophageal junction. Mobilization of the fundus of the stomach: the proximal one-third to one-half of the greater curvature of the stomach was liberated from its attachment to the spleen by dividing the short gastric vessels. Alternatively, the long gastric vessels may not be divided (modified Rossetti technique). The esophageal hiatus was then exposed by dividing the phrenoesophageal membrane. Narrowing of the hiatus was performed by suturing with nonabsorbable deep sutures through the crura of the diaphragm allowing the tip of a curved hemostat to pass. Construction of a 360° fundoplication: the mobilized fundus of the stomach is folded behind the esophagus. The length of the wrap varies from 1.0 cm in an infant to 2–2.5 cm in an older child and is performed using 3-4 sutures of nonabsorbable material.

Thal fundoplication [22]

The idea is to preserve at least 2.5 cm of the intra-abdominal esophagus and an acute angle of His. Incision, exposure, mobilization of the esophagus, and narrowing of the hiatus are similar to that in the Nissen procedure. The posterior wall of the esophagus was then sutured to the crural closure using nonabsorbable sutures. Imbrication of the gastroesophageal junction with nonabsorbable sutures was carried out between the stomach and the left side of the esophagus reaching the hiatus. The anterior free wall of the stomach was then sutured to the exposed anterior half of the esophagus to complete the 230–270° anterior fundoplication, which is completed by running the nonabsorbable sutures down the right margin of the esophagus to the cardia.

Stamm's gastrostomy

In 58 patients, a feeding gastrostomy tube was constructed to enable enteral feeding because of the presence of severe oropharyngeal dysmotility. For the remaining 11 patients, such an abnormality did not manifest, thus gastrostomy was not needed.

Follow-up

The postoperative follow-up protocol included evaluation at 3, 6, and 12 months. The parents were asked about the quality of life after antireflux surgery as regards recurrence of vomiting, dysphagia, chest complications, dumping syndrome, gas bloat syndrome, and tolerance to oral feeding. Postoperative 24-h pH-metry was performed for all patients 3 months after surgery (except for eight patients who were lost to follow-up).

Children with symptoms of recurrence like vomiting, weight loss, recurrent pulmonary infection, or choking during gastrostomy feeding were investigated by contrast study and 24-h pH-metry to identify true recurrence (esophageal pH less than 4 more than 4% of the time [23]).

Ambulatory 24-h pH-metry

A GERD pH-monitoring system (Sandhill Scientific, Highlands Ranch, Colorado, USA and Canada) was used. All patients stop taking proton pump inhibitor medications at least 1 week before the study, H_2 blockers and gastric motility drugs were stopped 4 days before the study. No antacids were taken within 6 h of the test or during the study itself [24].

The study was continued for 24 h, following which pH recordings were downloaded into the computer. Results were compared with the preset normal values supplied for GERD pH analysis software, and accordingly, the patients were classified as having normal reflux or acid reflux.

Upper endoscopy and mucosal biopsy

Upper endoscopy and mucosa; biopsy were performed using a Pentax upper GI endoscope (EPM-3500 Pentax video processor model; Asahi Optical Co., Tokyo, Japan) and a standard reusable stainless steel Olympus-FB-25-K mucosal punch biopsy forceps (Olympus, Tokyo, Japan), respectively.

Complete examination of the esophagus, stomach, and the second part of the duodenum was successfully conducted for all patients with no reported major complication. Any abnormal gross endoscopic finding

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.

was reported in detail and routine endoscopic biopsies were performed. The Los Angeles classification was used to report on the gross endoscopic abnormalities in the esophagus [25].

At least two esophageal biopsy specimens were obtained from the distal esophagus 3–4 cm proximal to the esophagogastric junction [26]. A subjective assessment of the severity as mild, moderate, or severe was made in concordance with the reported histopathologic features.

Data were tabulated and statistically analyzed using SPSS, version13 (SPSS Inc., Chicago, Illinois, USA). Student's *t*-test was used to compare continuous data, whereas the Fisher exact test was used to compare categorical data.

Results

The study included 69 children with NI with severe GERD, who underwent fundoplication between May 2007 and January 2011. The NF group (NFG) included 32 patients and the TF group (TFG) included 37 patients, with construction of a Stamm gastrostomy tube in patients with difficulty in swallowing (58 patients = 84%). The male-to-female ratio was (1.6 : 1). The age of the children ranged from 5 months to 6 years (mean 1.8 years; Table 1). Fifty-two patients were nonambulatory (75.4%). Perinatal asphyxia was the most common cause of NI (30.4%; Table 2). Feeding dysfunction represented the commonest indication of surgery (52.2%; Table 3). Recurrence of symptoms was found in 14 patients (20.3%). Acid pH-metry showed a statistically significant difference between preoperative and postoperative data (Tables 4 and 5); in six included patients, the reported acid pH-metry results did not confirm the presence of acid reflux, meanwhile, the presence of reflux esophagitis was confirmed histologically (nonacidic reflux). However, these differences were insignificant on comparing the postoperative parameters NFG and TFG (Table 6).

Table 1 Patient demographics

	NFG	TFG
Mean age (years)	1.5	1.3
Male/female	20\12	23\14
Associated morbidity		
Heart disorders	4	3
P–R syndrome	2	3
Skeletal disorders	4	2
Gastric herniation	2	4
Nonambulatory patient	24	28

NFG, Nissen fundoplication group; TFG, Thal fundoplication group.

Table 2 Causes of neurological impairment

Causes	*n*
Perinatal asphyxia	21
Prematurity	17
CNS anomalies	3
Meningitis, encephalitis	9
Chromosomal abnormalities	7
Developmental delay without known cause	12

CNS, central nervous system.

Preoperative endoscopic findings showed that 87% of patients had grade A esophagitis, whereas the cardia was incompetent in 84.1% (Table 7); there was no macroscopic evidence of GERD in 13% of patients in spite of evidence of its presence histologically. The severity of reflux esophagitis in the study group was reported as mild, moderate, and severe in nine (13%), 44 (63.8%), and 16 (23.2%) patients, respectively.

Minor preoperative complications occurred in three patients of NFG (one segmental infarction and two minor capsular injuries of the spleen). Perforation of the pleura occurred in two patients, one in each group.

Table 3 Indications of surgery

	NFG	TFG
Aspiration	8	5
Feeding dysfunction	17	19
Failure to thrive	11	13
Upper GIT bleeding	2	2

GIT, gastrointestinal tract; NFG, Nissen fundoplication group; TFG, Thal fundoplication group.

Table 4 Postoperative complications

Complication	NFG	TFG
Recurrence of symptoms	6 (18.7%)	8 (21.6%)
Gastrostomy leakage	1 (3.1%)	0
Subphrenic collection	1 (3.1%)	1 (2.7%)
Adhesive intestinal obstruction	3 (9.4%)	2 (5.4%)
Burst abdomen	0	1 (2.7%)
Intrathoracic herniation	1 (3.1%)	0
Dysphagia	2 (6.2%)	1 (2.7%)

NFG, Nissen fundoplication group; TFG, Thal fundoplication group.

Table 5 Comparison between preoperative and postoperative acid pH-metry parameters reported in the study group

Parameters	Preoperative data ($n=69$)	Postoperative data ($n=61$[a])	*P*-value
Upright time in reflux (%)	10.6 ± 6.5	4 ± 4.2	0.001*
Recumbent time in reflux (%)	11.7 ± 6.3	2.6 ± 5.7	0.018*
Total time in reflux (%)	11.7 ± 5.3	3.2 ± 4.3	0.027*
Number of episodes over 5 min.	8.6 ± 3.6	1.8 ± 3.2	0.007*
Longest episode duration (min)	25.5 ± 10.1	6.1 ± 11.6	0.012*
Total episodes number	91.8 ± 53.7	49.1 ± 42	0.223
Distal channel composite score	40.8 ± 14.8	14 ± 15.2	0.030*

[a]Eight cases lost to follow-up.
*Student *t*-test: significant.

Table 6 Comparison between postoperative acid pH-metry parameters reported after Nissen ($n=27$) and Thal ($n=34$) procedures

Parameters	Postoperative data after the Nissen procedure ($n=27$)	Postoperative data after the Thal procedure ($n=34$)	*P*-value
Upright time in reflux (%)	4 ± 3.1	4 ± 5.2	0.086
Recumbent time in reflux (%)	2.4 ± 4.9	2.8 ± 5.4	0.128
Total time in reflux (%)	3.1 ± 3.9	3.3 ± 4.2	0.097
Number of episodes over 5 min	1.7 ± 4.7	1.9 ± 4.2	0.324
Longest episode duration (min)	5.1 ± 10.6	7.1 ± 9.6	0.180
Total episodes number	47.1 ± 32	51.1 ± 43	0.243
Distal channel composite score	13 ± 14.2	15 ± 16.2	0.325

*Student *t*-test: significant.

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.

Table 7 Reported gross endoscopic findings of the study group

Parameters	*n* (%)
Esophagus	
No abnormality	**9 (13%)**
Abnormal	**60 (87%)**
Grade A	5 (7.3%)
Grade B	23 (33.3%)
Grade C	20 (29%)
Grade D	12 (17.4%)
Cardia	
Incompetent	58 (84.1%)
Competent	11 (15.9%)
Gastric herniation	6 (8.7%)
Gastric axis malrotation	3 (4.3%)
Other associated endoscopic abnormalities	
Gastric mucosal abnormalities	37 (53.6%)
Gastric ulceration	4 (5.8%)
Antral nodularity	15 (21.7%)
Duodenal mucosal abnormality	31 (44.9%)
Duodenal mucosal ulceration	6 (8.7%)

Bold values represent the total numbers, other values are for subgroups.

All complications were easily controlled at the time of the operation and passed without sequelae.

Recurrence of reflux-associated symptoms occurred in 14 patients (20.3%), six patients belonging to NFG and eight patients belonging to TFG. Recurrence manifested sequentially during the follow-up period (the first case manifested 2 months after operation). These patients were subjected to contrast study and 24-h pH-metry. These investigations confirmed recurrence in 10 patients, of whom four improved spontaneously over 3 months postoperatively, three patients improved on administration of H_2 blockers for 6–8 weeks, whereas three patients did not improve (two patients belonging to TFG and one belonging to NFG; recurrence was caused by intrathoracic herniation of the wrap). These patients were reoperated upon using the NF procedure. Reoperation was performed early in the patient with intrathoracic herniation and late in the other two patients, with no recurrence in any of them in spite of difficult dissection because of adhesion.

The previous work-ups showed normal results in four patients from the symptomatic recurrence group. Recurrence symptoms appeared intermittently over a period of 3 months then totally disappeared. Parents were reassured during these 3 months.

Dysphagia was seen in three patients (two in NFG and one in TFG); one of them was in need of repeated endoscopic dilatations, whereas the other two patients improved spontaneously. Dysphagia may be caused by tight fundoplication.

Patients were operated upon for treatment of leaking caused by gastrostomy (NFG = 1) and burst abdomen (TFG = 1) once diagnosed.

Subphrenic collection (one in each group) was treated by ultrasonic guided tube drainage. Adhesive intestinal obstruction (NFG = 4, TFG = 2) was treated conservatively in three patients, and exploration and adhesiolysis was performed in one patient after failure of conservative treatment.

Ability to swallow was observed postoperatively in six patients (10.3%) and gastrostomy feeding was stopped gradually in these patients (six of 58 patients who were gastrostomy dependent postoperatively). Chest complications, caused by repeated aspiration, were corrected postoperatively in nine of 13 patients (69.2%). Tracheostomy was performed in the other four patients to decrease the incidence of aspiration; however, two of them died as a result of respiratory failure.

We had no procedure-related mortality in the series; however, 10 patients (14.5%) died within 4 to 24 months of follow-up because of respiratory failure.

Discussion

In neurologically impaired patients with GERD, medical treatment is often ineffective and surgical management is mandatory to control symptoms and to improve quality of life even in the presence of high postoperative failure rate.

Eposito and colleagues [27] studied postoperative complications in 80 neurologically impaired children after antireflux surgery. The total postoperative complication rate was 30%, of which redo surgery was necessary in 6.2%. In our series, the total complication rate was 39.1% and redo surgery was indicated in 4.3%. This high rate of complications is another issue to be solved. Several characteristics of children with NI, such as concomitant malnutrition, spasticity, epilepsy, and chronic respiratory disease, have been suggested as factors possibly contributing to the recurrence of GERD [28].

Improvement of respiratory symptoms was observed in 69.2% of our patients at 3 months after operation. In the study by Capito *et al.* [23], the incidence of respiratory symptom improvement was 89% at 3 months after operation. The other four patients with persistent respiratory symptoms in our study needed tracheostomy to control persistent aspiration; however, two patients from this group died because of progressive deterioration of respiratory status. Takamizawa *et al.* [29] concluded that respiratory resuscitation should include tracheostomy or laryngotracheal separation in the treatment of handicapped children with respiratory symptoms when fundoplication has been indicated or respiratory symptoms persist after fundoplication.

In our series, dysphagia occurred in three patients (4.3%). In the study by Mathei *et al.* [30] on 49 patients with NI, the incidence of dysphagia following NF was 10.2%. The lower incidence in our study may be because of the number of patients operated upon using the TF procedure, which is associated with a decreased incidence of dysphagia. The lower incidence of dysphagia after anterior 270° fundoplication was also confirmed by Engelmann *et al.* [31] through their study on the effect of fundoplication on the quality of life of NI and neurologically healthy children having GERD.

Similar to the results obtained by Capito *et al.* [23], postoperative 24-h pH monitoring showed a significant decrease in the prevalence of acid reflux compared with that observed preoperatively in both NFG and TFG. These parameters parallelize the resulting clinical improvement.

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.

Mathei *et al.* [30], in their study, reported that mechanisms other than anatomical failure may play a role in symptom recurrence after antireflux surgery; this was because three patients in their study showed wrap failure and were still asymptomatic; however, in our study we found the opposite, in which there were four patients with symptomatic recurrence without evidence of anatomical failure. This may be due to many other putative mechanisms that contribute to the symptomatic recurrence in this group of patients – namely, abnormalities of lower esophageal function [8,9]; delayed gastric emptying [10,11]; and antroduodenal dysmotility [12].

In the present study, the incidence of symptomatic reflux was 20.3%, of which NFG represented 8.7% and TFG represented 11.6%; all patients except three were managed conservatively. The patient with wrap migration was treated, after diagnosis with contrast study and 24-h pH-metry, by reduction of the wrap, repair of the crura, and fixation of the wrap to the diaphragm. The other two patients were operated upon 3 months after diagnosis; these patients showed disruption of fundoplication after the Thal procedure and were reoperated upon using the NF procedure. The incidence of symptomatic recurrence in the study by Mathei *et al.* [30] was 18.4% in patients with NI, in whom postoperative work-up was completely normal and who improved conservatively without the need for reoperation. Capito *et al.* [23] performed NF on 73 children with NI among whom 12% had GERD recurrence and 8.2% were reoperated upon. Pimpalwar and Najmaldin [32], after performing NF on 54 children with NI, found that the recurrence rate was 16%. In the TFG of our study, the incidence of postoperative recurrence was 11.6%, which is statistically insignificant when compared with postoperative recurrence after NFG in our study and also in the studies mentioned previously [23,32]. Moreover, Ramachandran *et al.* [33] reported that TF retains the ability to vomit, is easier to perform, and involves less dissection, less blood loss, and fewer small-bowel adhesions postoperatively.

Tuggle *et al.* [34] found that eight of 48 patients with central nervous system disorders had recurrent reflux with gastrostomy feedings after TF (16%), whereas only two of 68 neurologically normal children had a failure of operation (2.9%). Van der zee *et al.* [35] performed NF on 23 patients and TF on 21 patients. They found the postoperative recurrence rate to be much higher for NF (37%) compared with TF (4%). In our series, it was 8.7% for NFG and 11.6% for TFG.

Conclusion

GERD in neurologically impaired children is a very common problem associated with a high failure rate after properly performed fundoplication. The outcome of TF is similar to that of NF with less dissection, decreased incidence of intestinal adhesion, and less dysphagia or gas bloat. Long-term evaluation is required as incidence of recurrence increases with time secondary to the persistent comorbidities. Further refinement of management strategies is needed to decrease incidence of recurrence and improve the overall quality of life.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Spitz L, Roth K, Kiely EM, Brereton RJ, Drake DP, Milla PJ. Operation for gastro-oesophageal reflux associated with severe mental retardation. *Arch Dis Childhood* 1993; **68**:347–351.
2 Walker WA, Durie PR, Hamilton JR, Walker-Smith JA, Watkins JB. *Pediatric gastrointestinal disease.* vol.1. St Louis: Mosby; 1996. p. 467.
3 Fonkalsrud EW, Ashcraft KW, Coran AG, Ellis DG, Grosfeld JL, Tunell WP, Weber TR. Surgical treatment of gastroesophageal reflux in children: a combined hospital study of 7467 patients. *Pediatrics* 1998; **101 (I)**: 419–422.
4 Inge TH, Carmeci C, Ohara LJ, Berquist WB, Cahill JL. Outcome of Nissen fundoplication using intraoperative manometry in children. *J Pediatr Surg* 1998; **33**:1614–1617.
5 Rice H, Seashore JH, Touloukian RJ. Evaluation of Nissen fundoplication in neurologically impaired children. *J Pediatr Surg* 1991; **26**:697–701.
6 Pacilli M, Chowdhury MM, Pierro A. The surgical treatment of gastro-esophageal reflux in neonates and infants. *Semin Pediatr Surg* 2005; **14**:34–41.
7 Wilkinson J, Dudgeon DL, Sondheimer JM. A comparison of medical and surgical treatment of gastroesophageal reflux in severely retarded children. *J Pediatr* 1981; **99**:202–205.
8 Staiano A, Cucchiara S, Del Giudice E, Andreotti MR, Minella R. Disorders of oesophageal motility in children with psychomotor retardation and gastro-oesophageal reflux. *Eur J Pediatr* 1991; **150**:638–641.
9 Gustafsson PM, Tibbling L. Gastro-oesophageal reflux and oesophageal dysfunction in children and adolescents with brain damage. *Acta Paediatr* 1994; **83**:1081–1085.
10 Ravelli AM. Diagnostic and therapeutic approach to vomiting and gastroparesis in children with neurological and neuromuscular handicap. *J Pediatr Gastroenterol Nutr* 1997; **25 (Suppl 1)**:S34–S36.
11 Ravelli AM, Milla PJ. Vomiting and gastroesophageal motor activity in children with disorders of the central nervous system. *J Pediatr Gastroenterol Nutr* 1998; **26**:56–63.
12 Werlin SL. Antroduodenal motility in neurologically handicapped children with feeding intolerance. *BMC Gastroenterol* 2004; **4**:19–23.
13 Richards CA, Milla PJ, Andrews PLR, Spitz L. Retching and vomiting in neurologically impaired children after fundoplication: predictive preoperative factors. *J Pediatr Surg* 2001; **36**:1401–1404.
14 Di Lorenzo C, Flores A, Hyman PE. Intestinal motility in symptomatic children with fundoplication. *J Pediatr Gastroenterol Nutr* 1991; **12**:169–173.
15 Morton RE, Wheatley R, Minford J. Respiratory tract infections due to direct and reflux aspiration in children with severe neurodisability. *Dev Med Child Neurol* 1999; **41**:329–334.
16 Martinez DA, Ginn-Pease ME, Caniano DA. Sequelae of antireflux surgery in profoundly disabled children. *J Pediatr Surg* 1992; **27**:267–273.
17 Pearl RH, Robie DK, Ein SH, Shandling B, Wesson DE, Superina R, *et al.* Complications of gastroesophageal antireflux surgery in neurologically impaired versus neurologically normal children. *J Pediatr Surg* 1990; **25**:1169–1173.
18 Justo RN, Gray PH. Fundoplication in preterm infants with gastro-oesophageal reflux. *J Paediatr Child Health* 1991; **27**:250–254.
19 Fonkalsrud EW, Bustorff-Silva J, Perez CA, Quintero R, Martin L, Atkinson JB. Antireflux surgery in children under 3 months of age. *J Pediatr Surg* 1999; **34**:527–531.
20 Islam S, Teitelbaum DH, Buntain WL, Hirschl RB, Wulkan M, Martinez L. Esophagogastric separation for failed fundoplication in neurologically impaired children. *J Pediatr Surg* 2004; **39**:287–291.
21 Nissen R, Rossetti M. Surgery of hiatal hernia and the reflux syndrome. Fundoplication and gastropexy [in French]. *J Chir (Paris)* 1962; **83**:659–671.
22 Ashcraft KW, Holder TM, Amoury RA. The Thal fundoplication for gastroesophageal reflux. *J Pediatr Surg* 1984; **19**:480–483.
23 Capito C, Leclair M-D, Piloquet H, Plattner V, Heloury Y, Podevin G. Long-term outcome of laparoscopic Nissen-Rossetti fundoplication for neurologically impaired and normal children. *Surg Endosc* 2008; **22**:875–880.
24 Postma GN. Ambulatory pH monitoring methodology. *Ann Otol Rhinol Laryngol* 2000; **109 (Suppl)**:10–14.
25 Lundell LR, Dent J, Bennett JR, Blum AL, Armstrong D, Galmiche JP, *et al.* Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. *Gut* 1999; **45**:172–180.
26 Takubo K, Honma N, Aryal G, Sawabe M, Arai T, Tanaka Y, *et al.* Is there a set of histologic changes that are invariably reflux associated? *Arch Pathol Lab Med* 2005; **129**:159–163.

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.

27 Esposito C, Van Der Zee DC, Settimi A, Doldo P, Staiano A, Bax NMA. Risks and benefits of surgical management of gastroesophageal reflux in neurologically impaired children. *Surg Endosc* 2003; **17**:708–710.
28 Kawahara H, Okuyama H, Kubota A, Oue T, Tazuke Y, Yagi M, Okada A. Can laparoscopic antireflux surgery improve the quality of life in children with neurologic and neuromuscular handicaps? *J Pediatr Surg* 2004; **39**:1761–1764.
29 Takamizawa S, Tsugawa C, Nishijima E, Muraji T, Satoh S. Laryngotracheal separation for intractable aspiration pneumonia in neurologically impaired children: experience with 11 cases. *J Pediatr Surg* 2003; **38**:975–977.
30 Mathei J, Coosemans W, Nafteux P, Decker G, De Leyn P, Van Raemdonck D, *et al*. Laparoscopic Nissen fundoplication in infants and children: analysis of 106 consecutive patients with special emphasis in neurologically impaired vs. neurologically normal patients. *Surg Endosc* 2008; **22**:1054–1059.
31 Engelmann C, Gritsa S, Ure BM. Impact of laparoscopic anterior 270° fundoplication on the quality of life and symptoms profile of neurodevelopmentally delayed versus neurologically unimpaired children and their parents. *Surg Endosc* 2010; **24**:1287–1295.
32 Pimpalwar A, Najmaldin A. Results of laparoscopic antireflux procedures in neurologically impaired children. *Semin Laparosc Surg* 2002; **9**:190–196.
33 Ramachandran V, Ashcraft KW, Sharp RJ, Murphy PJ, Snyder CL, Gittes GK, Bickler SW. Thal fundoplication in neurologically impaired children. *J Pediatr Surg* 1996; **31**:819–822.
34 Tuggle DW, Tunell WP, Hoelzer DJ, Smith EI. The efficacy of Thal fundoplication in the treatment of gastroesophageal reflux: the influence of central nervous system impairment. *J Pediatr Surg* 1988; **23**:638–640.
35 Van Der Zee DC, Rovekamp MH, Pull Ter Gunne AJ, Bax NMA. Surgical treatment of reflux esophagitis: Nissen versus Thal procedure. *Pediatr Surg Int* 1994; **9**:334–337.

Copyright © Annals of Pediatric Surgery. Unauthorized reproduction of this article is prohibited.