



Boix-Ochoa (Partial Fundoplication) Treats Reflux, Even in Neurologically Impaired Patients. Can it Take the Title of “Gold Standard” from Total Fundoplication?

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Abstract

Background In 4–5% of cases of gastroesophageal reflux disease (GERD), surgical treatment is required. The aim of the study was to evaluate the success of Boix-Ochoa antireflux surgery, which is considered more physiologic with a higher failure rate (need for reoperation) than Nissen fundoplication, which is believed to be the gold standard operation.

Method In the 13 years from 2005 to 2018, the medical records of all children who underwent Boix-Ochoa in a single institution by pediatric surgeons were reviewed retrospectively.

Results A total of 133 funduplications were performed, of which patients were divided into four groups: neurologically impaired, structurally impaired, neurologically and structurally impaired, and neurologically and structurally normal; there were 64, 8, 34, and 27 patients in each group, respectively. Structural impairments included hiatal hernia and esophagus atresia, having previously had a gastrostomy and esophageal stenosis. The most common short-term complication was distal esophageal stenosis (13%), which caused vomiting and dysphagia, and was treated by dilatations. There were six (4.5%) recurrences of GER, one in the neurologically and structurally impaired group with a hiatal hernia and five in the structurally impaired group (three esophagus atresias, two caustic esophageal strictures). The mean follow-up period was 5.27 ± 3.43 years. Neurological impairment did not affect the success rate.

Conclusion Although there has not any literature demonstrating significant benefits of one procedure, we detected with this largest study in the pediatric literature about Boix-Ochoa fundoplication (more physiologic and easily performed) that it was successful (95%) in protecting reflux even in neurologically impaired patients (98%). We consider Boix-Ochoa (partial fundoplication) to be an alternative method to Nissen (complete fundoplication), and it can be done safely with a high success rate.

Keywords Fundoplication · Children · Gastroesophageal reflux disease · Boix-Ochoa · Partial fundoplication

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Introduction

Gastroesophageal reflux (GER) is defined as the passage of gastric contents into the esophagus and when it is complicated and pathological symptoms were presented, it is named gastroesophageal reflux disease (GERD). Disorders of esophageal motility, lower esophageal sphincter (LES) location, and function disturbance result in increased acid reflux with poor clearance.¹ When medical treatment fails or cannot be applied, as in infants with life-threatening apneic spells and proven gastroesophageal reflux or young patients with complications related to reflux (e.g., failure to thrive, feeding intolerance, esophagitis, persistent respiratory symptoms, neurobehavioral problems), surgical correction should be undertaken promptly.^{2,3} Structural (after repair of esophageal atresia

(EA) and hiatal hernia) and neurological impairments, gastrostomy, previously performed to feed the patient, may provoke GER.^{4–6}

Fundoplication is one of the most common major surgical procedures performed by pediatric surgeons, and a large portion of children (nearly 40%) undergoing this procedure are infants,⁷ while those with neurological problems are an average of 6 years of age.⁵ Feeding gastrostomy placement in addition to an antireflux procedure also significantly adds to patient growth and survival during infancy.⁸ We analyzed the results of funduplications performed in children who had severe GERD and focused on Boix-Ochoa modification success in children, even in neurologically impaired patients.

Materials and Methods

A retrospective review was conducted of all operated patients with GERD, and children who underwent partial fundoplication (Boix-Ochoa) were included in the study. No patients were excluded from the study. The data review and collection were performed in compliance with the principles of the ethics committee and the Declaration of Helsinki, in 13-year period, from 2005 to 2018, which allowed sufficient time for follow-up assessments. Presenting symptoms, neurological status, medical treatment, preoperative management, and surgical details were among the data collected.

Upper gastrointestinal radiography (UGI) which is non-invasive, inexpensive, and readily available test that can identify reflux and its level, delineate the anatomy of esophagus and GI tract (hiatal hernia etc.), and esophageal peristalsis, was preferred as the diagnostic tests and performed in all patients. Additionally, UGI was used in the evaluation of the postoperative antireflux surgical patient. pH monitoring which has long been considered the gold standard was not able to use as a diagnostic method due to some difficulties such as the disruption of children normal routines by pH probes which require transnasal placement that causes discomfort, decreases appetite and activity and mostly technical problems that belong to our hospital. Endoscopy was performed in limited number of patients that was performed mostly in neurological patients and those who had not been treated properly and had a long treatment period.

The treatment of GERD was typically started by pediatric surgery, pediatrics, and pediatric gastroenterology clinics with dietary modifications and postural changes. For infants, the elevation of the head of the bed and frequent small volume meals with thickened formulas or agents was recommended. The main acid suppressant agents (H_2 -receptor antagonists and proton pump inhibitors) and motility medications such as metoclopramide were added if necessary as pharmacologic agents.

Indications for operative management in our patients include failure of medical therapy with failure to thrive (feeding and vomiting-related complications); continued respiratory symptoms such as pneumonia, apneas, and chronic lung damage (aspiration-related complications); and esophagitis-related symptoms such as pain, bleeding, anemia, and dysphagia. Situations in which a trial of medical treatment may not be necessary include structurally impaired patients such as hiatal hernia. In addition, neurologically impaired patients who require gastrostomy for feeding and concerns for GERD were routinely investigated for reflux before surgery and underwent fundoplication at the same time.

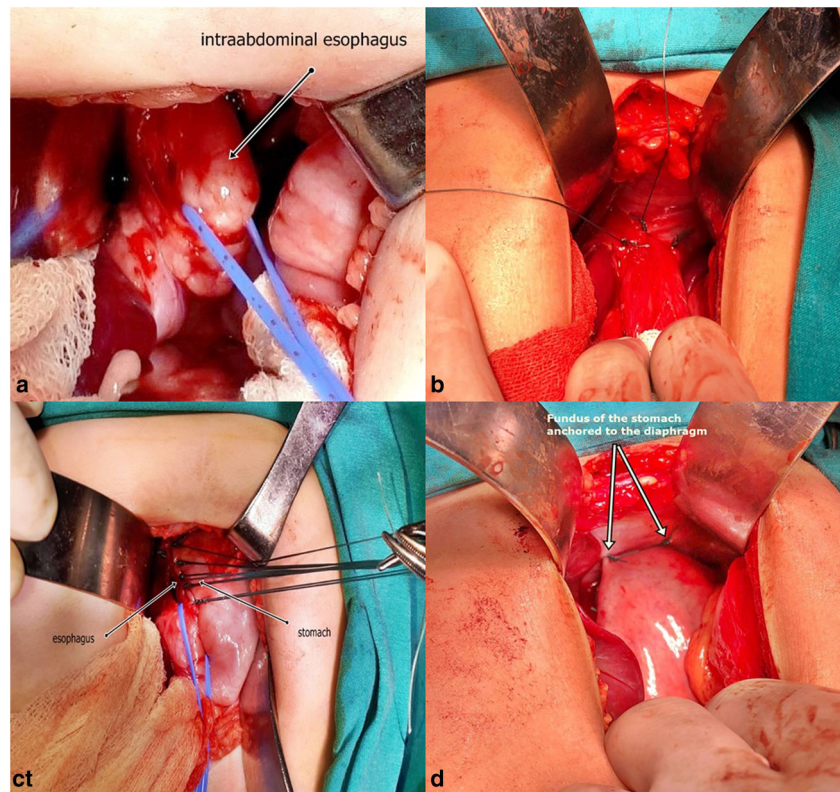
The children included in the study were distributed into four groups, according to their preoperative status: neurologically impaired, structurally impaired, neurologically and structurally impaired, and neurologically and structurally normal.

The Boix-Ochoa (partial fundoplication) operation was preferred and performed by experienced pediatric surgeons with an open manner not laparoscopically. In this procedure, the intra-abdominal esophagus was mobilized to lengthen the intra-abdominal part of the esophagus. The lower esophagus was anchored to the esophageal hiatus. The crural was musculature to form the esophageal hiatus by suturing the diaphragmatic crurals. Restoration of the angle of HIS was done. Approximation of the right crural fibers was followed by anchoring an anterior wrap of the fundus across the anterior aspect of the esophagus and to the margins of the right crus and diaphragm. Boix-Ochoa defined suturing the fundus to the right anterior wall of the esophagus with diaphragmatic fixation of both the esophagus and fundus. Partial anterior plication was done and the fundus was stitched to the diaphragm (Figs. 1 and 2).

Postoperatively, patients received follow-up in our clinic. Complications, if any, were recorded along with any symptoms of recurrence of gastroesophageal reflux. UGIs were performed in all patients for the control of recurrent reflux in the first postoperative year and at any time when patients presented with symptoms that were clinical suspicions of recurrence. In the short-term postoperative period, symptomatic patients such as vomiting, coughing, and retching underwent UGI and treated with balloon dilatations whether distal esophageal stenosis was observed. If an esophageal dilator is needed, we use a balloon dilator as large as the diameter of the patient's thumb.

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows version 15 package software (SPSS, Inc., Chicago, IL, USA). Data were expressed as medians (min–max). Categorical variables were analyzed with a chi-square test or, where appropriate, a Fisher's exact test. Continuous variables were analyzed with the Mann–Whitney *U* test. A *P* value lower than 0.05 was accepted as statistically significant for all analyses.

Fig. 1 Intraoperative pictures showing of the procedure. **a** Mobilization of intra-abdominal esophagus. **b** Anchoring of intra-abdominal esophagus to the crura of the diaphragm. **c** Partial anterior plication. **d** Fundus of the stomach anchored to the diaphragm



This study was approved by the Başkent University Ethical Committee.

Results

During the period from 2005 to 2018, 133 primary partial fundoplications (Boix-Ochoa) were performed by pediatric surgeons. Preoperative studies included UGIs in all 133 cases (100%) and endoscopy with biopsy in 43 cases (31%). All children had proven severe GERD with significant

complications of the disease. Aspiration-related, esophagitis-related, and feeding- and vomiting-related complications were indications for surgery in patients, 28%, 16%, and 56%, respectively. Six children had esophageal strictures that required serial balloon dilatations both pre- and post-fundoplication. Gastrostomy was performed in 49% of patients for feeding purposes at the time of fundoplication. The mean operation time was 116 ± 39 min and patients were discharged in a median of 7 days (ranging between 1 and 56 days).

All patients' clinical characteristics were summarized in Table 1.

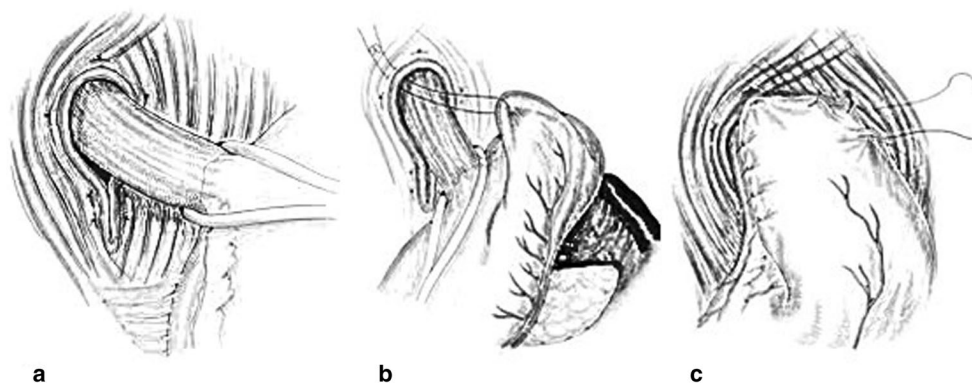


Fig. 2 Cartoon showing the steps of fundoplication. **a** Mobilization of intra-abdominal esophagus and anchoring of intra-abdominal esophagus to the crura of the diaphragm. **b** Fundus of the stomach anchored to the diaphragm with the first suture of the plication (fundus-esophagus-diaphragm). **c** Partial anterior plication (Fig. 5 reference: Ochoa J.B., Broto

J.¹⁰ IBoix-Ochoa Procedure. In: Esposito C., Montupet P., Rothenberg S. (eds) *The Gastroesophageal Reflux in Infants and Children*. Springer, Berlin, Heidelberg doi.org/10.1007/978-3-642-18906-7_29

Table 1 Clinic characteristics of patients

	Patient number	M/F ratio	The median age (year)	Surgery indication	Weights (lower than 25th percentile)	Postoperative short-term period distal esophageal stenosis	Recurrent reflux	Treatment	Follow-up period (year)
Neurologically impaired patients	64	5/4	2,5	Failure to thrive (62%)	67%	2 patient	No	-	4.77±3.15
Neurologically and structurally impaired patients	8	1/1	2	Failure to thrive (75%)	94%	2 patient	1 patient	Re-operation	4.87±2.69
Structural impaired patients	10	9/1	2	Failure to thrive (70%)	90%	1 patient	No	-	5±3.9
Operated esophagus atresia	20	12/10	2	Failure to thrive (55%)	95%	6 patient	3 patients	2 medical treatment	6±2.9
Esophageal stenosis	3	2/1	6	Refractory to treatment (100%)	0%	-	2 patients	1 re-operation 2 medical treatment	5±1.2
Previously performed antireflux surgery/failed	1	1/0	4.2	Failure to thrive (100%)	100%	-	No	-	3
Neurologically and structurally normal patients	27	17/11	2	Failure to thrive (48%)	81%	7 patient	No	-	5.9±4.3

*surgery indication: failure of medical therapy with poor weight gain or failure to thrive

In the 64 neurologically impaired patients, the M/F ratio was 5/4. The median age was 2.5 years (ranging between 1 month and 16.5 years). Aspiration-related complications, esophagitis-related complications, and failure to thrive were the surgery indication in 27%, 11%, and 62% of patients, respectively. In 22 (34%) patients, the diagnosis was supported with endoscopic biopsy. Twenty-three patients (36%) received reflux therapy within a mean of 10.5 ± 6.7 months before surgery. In 45 of the 64 neurologically impaired patients, the main operation goal was feeding gastrostomy, but fundoplication was subsequently added with diagnosing reflux. In the short-term postoperative period, four patients presented symptoms such as vomiting, coughing, and retching. However, in two of these patients, distal esophageal stenosis was observed and treated with balloon dilatation two times. Recurrent reflux was not seen in any patients during the follow-up period, which had a mean of 4.77 ± 3.15 years (range 1 to 13 years). Eighteen patients died due to neurological disease progression within 5 years of pediatric neurology clinical follow-ups.

In the eight neurologically and structurally (hiatal hernia and performed gastrostomy [via percutaneous or open]) impaired patients, the M/F ratio was 1/1. The median age was 2 years (ranging between 1 month and 9 years). Half (50%) of the patients received reflux therapy within a mean of 8 months before surgery. In three of eight patients, gastrostomy had provoked the reflux, with no evidence of reflux before surgery, even with barium upper studies. In the short-term postoperative period, two patients presented symptoms such as vomiting, and in one patient, distal esophageal stenosis was observed, which was treated with balloon dilatation two times. In one patient with hiatal hernia, recurrent reflux was detected in the second year after the operation and, therefore, reoperation was performed. One patient died due to neurological disease progression. The mean follow-up period was 4.87 ± 2.69 years.

Thirty-four structural impairments, including hiatal hernia, esophagus atresia, and esophagus stenosis due to reflux or caustic ingestion and previously performed antireflux surgery, were detected in 10, 20, 3, and, 1 patients (who had previously undergone Thall (partial) fundoplication in another center and had failed), respectively. Of the 10 hiatal hernia patients, a male predominance was seen, with an M/F ratio of 9/1 and a median age of 2 years (ranging between 1 month and 4 years). Half (50%) of the patients received reflux therapy with a mean of 6 months. One patient presented distal esophageal stenosis, which was treated once with balloon dilatation. Recurrent reflux was not detected in any patient during the follow-up period, which had a mean of 5 ± 3.9 years.

Reflux associated with operated esophagus atresia was seen in 20 patients, with a male predominance, an M/F ratio of 12/10, and a median age of 2 years (ranging between 2 months and 6 years). The most common surgery indication

was failure to thrive, seen in 55% of patients. All patients received reflux therapy within a mean of 10.5 ± 5.9 months. Ten (50%) patients presented with symptoms in the short-term postoperative period, but distal esophageal stenosis was detected in six patients, which was treated by balloon dilatation maximum four times. Recurrent reflux was detected in three (15%) patients during the follow-up period, which had a mean length of 6 ± 2.9 years.

It was unclear whether patients with corrosive esophageal stenosis had previously refluxed. The ages of these patients were 5.5, 6, and 6.5 years; all of them were male. They received at least 1.5 years of reflux therapy. Because of the insufficient response of esophagus dilatations, antireflux surgery was added to their treatment. Recurrent reflux was detected in 2/3 (66%) patients during the follow-up period, which had a mean length of 5 ± 1.2 years.

Of the 27 neurologically and structurally normal patients, 17 were male. The median age was 2 years (ranging between 1 month and 18 years). Aspiration-related complications, esophagitis-related complications, and failure to thrive were the surgery indications in 34%, 18%, and 48% of patients, respectively. All patients received reflux therapy, with a mean of 11.3 ± 6.2 months. Eleven patients were symptomatic in the postoperative period, with symptoms such as vomiting and dysphagia; however, in seven patients, distal esophageal stenosis was detected and treated with balloon dilatation up to four times. There was no recurrent reflux during the follow-up period, which had a mean of 5.9 ± 4.3 years.

All patients overall mean follow-up period was 5.27 ± 3.43 years.

Discussion

Although there are no randomized studies comparing partial or complete fundoplication, increased risk of recurrent GER has been the primary concern with the various partial fundoplications compared with Nissen.⁹ From the current study, we can conclude that partial fundoplication is beneficial to children with GERD with low recurrent GER, irrespective of their neurological status. We detected that the recurrence of reflux is more often associated with esophageal lengthening that may be shortened in either operated esophagus due to atresia or stenosis and also our study strongly supports the theories: “a sufficient length of the intra-abdominal segment of the esophagus as the key to preventing the reflux system” and “lengthening the intra-abdominal part of the esophagus is the main important step of the operation”⁽¹⁰⁾ by detecting five of the six recurrent reflux cases were seen in structurally impaired patients.

Principles of the Operation, reported by Boix-Ochoa in his classic paper in 1986, has identified six factors which comprise the antireflux barrier.¹⁰ These are all performed on the

lower esophageal sphincter: (1) The length of intra-abdominal esophagus (> 2 cm), exposed to intra-abdominal pressure, is the key to LES and has a main role on the successfulness of fundoplication. The length of esophageal valve that cannot hold back potential refluxate has an abdominal length of < 1 cm, or an overall sphincter length of < 2 cm. (2) The right crura of the diaphragm, a sling-shaped orifice around the esophagus, has a pinchcock action by pulling the esophagus to the right and downward with deep inspiration. (3) The angle of His, which locates the junction of esophagus and the stomach, is acute in a child with the normal-sized intra-abdominal esophagus. (4) The mucosal rosette, redundant folds of mucosa at the gastroesophageal junction, is present only when the angle of His is normal and forms a weak valve when increased intra-gastric pressure. (5) Near the gastro-esophageal junction, there is an area that presents increased muscular thickness called high-pressure zone (HPZ). The basal tone of HPZ increases until 45 days of age, at which maturation is complete; 6–8-cm H₂O or 10–30-mmHg intra-abdominal pressure is necessary to maintain competent lower esophageal sphincter (LES) by collapsing the intra-abdominal segment.

Fundoplication was first described in adults by Nissen in 1956.¹¹ In this operation, the fundus is wrapped to the esophagus posteriorly to complete 360°.¹² Early complications are uncommon in the recovery period, but a minority of patients develop dysphagia (2–12%) and gas bloat (4–10%).¹³ Dysphagia generally settles in most patients by 2 to 4 weeks.¹³ Anatomic complications, such as disrupted (8–12%) or slipped wraps, a herniated wrap, too tight or too long a fundoplication, a twisted wrap, or a two-compartment stomach, are associated with surgeon experience and qualification.¹³ To offset the known adverse effects associated with a complete circumferential wrap, several different antireflux procedures with numerous modifications (Toupet, 270° posterior fundoplication; Thal-Aschcraft, 270° anterolateral fundoplication; Dor, 180° anterior fundoplication; Boix-Ochoa, 180–270° anterolateral fundoplication) have been reported.¹⁴ In the Boix-Ochoa procedure, the fundoplication is completed by 3–5 sutures from the top to the right anterior wall of the esophagus.¹⁵ Generally, partial fundoplication (for all procedures) is considered more physiologic and reduces the rate of adverse effects of a total fundoplication by allowing the venting of air from the stomach.¹⁴ Many reports show that the efficacy and complications of partial and complete fundoplication are similar, even though there are no randomized studies that compare them.¹⁴ Therefore, the main concern is recurrent GER that is considered much higher in partial fundoplication. Recurrent GER, also a significant problem after Nissen fundoplication, must be differentiated from transient symptoms that require medical therapy for up to 2 months, known as GERD-related squeal.¹⁶ Recurrent reflux mostly occurs as a result of wrap disruption and/or transmigration, especially in children younger than 6 years,

preoperative HH (0–11%), and neurologically impaired children.¹⁷ Additionally, it was identified by Glen et al. that any evidence to indicate that the extent of the wrap (partial or complete) results in a superior correction of GERD symptoms.¹¹

The success rate of Boix-Ochoa fundoplication was reported to be 88.4% in the author's own series,¹⁸ while the long-term success of Nissen fundoplication is reported to be 90%.¹⁹ In our study, the success rate of the partial fundoplication was 95%, irrespective of the neurological status of the patient. The Boix-Ochoa procedure relies on the anterior wrap and the crural musculature.¹⁰ In children with GER, particularly in the neurologically impaired group, which formed 54% of our study, the right crus and muscles of the diaphragm are weak because of malnutrition and distorted anatomy.²⁰ It is reported that if the crural muscles are weak, there is a significant chance for reflux to recur because (a) the angle of His is not maintained after failure of the wraps to maintain its position anchored to the diaphragm and (b) the whole wrap is liable to prolapse through the hiatus. The fundus is sutured and fixed to both the esophagus and itself and just to the diaphragm and esophagus in the Nissen and Boix-Ochoa procedures, so the integrity of the crus does not seem to be a key factor in determining the long-term outcome of these procedures.¹⁰ There is also a functional disorder, not just anatomically, in these patients.²¹ When refractory retching was added to the underlying diffuse gastrointestinal dysmotility, the risk of recurrent reflux increases.²¹ In our study, we noted a 98% success rate of the operation in neurologically impaired patients and considered that it may be the reason of gastrostomy (82%, $n = 52$) that both relieves the retching episodes by allowing the passage out of gas and letting the stomach fixate to the abdominal wall with protecting the wrap prolepses.

In many cases that lead to the malnutrition and failure to thrive, alternative measures should be taken to ensure adequate nutrition, such as an enteral feeding tube. When the other efforts to increase nutritional intake, such as dietary supplementation, have failed, enteral feeding is considered effective to prevent or reverse growth failure. Children with neurological impairments frequently have feeding difficulties, which mostly results in malnutrition and growth failure. Currently, gastrostomy feeding is the preferred method of providing nutritional support to children with neurological impairment. The prevalence of GER among children with neurological impairments has been reported to be 14–75% and the role of reflux is not well understood. Performing gastrostomy feeding tube in these patients arises complications, and the development or worsening of GER has been widely reported. So, this undesirable result has led to the frequent use of surgical antireflux treatment in the form of fundoplication, or other antireflux procedures, at the same time with gastrostomy feeding.²²

In our study, gastrostomy feeding was performed in 65 of 133 patients at the same time with fundoplication. Of these, 55 were neurologically impaired.

Poor esophageal motility, inadequate clearance of acid from the esophagus shortening of the esophagus and abnormal LES pressures, occurs with an incidence of 6 to 45% and let GERD require fundoplication in patients after EA repair.¹ Partial fundoplication is considered more attractive and offers substantially better results than complete wrap fundoplication.¹ However, when the EA and non-EA patients were compared, the failure rate for GERD in EA patients is substantially higher (4.2–15%). Dysphagia is commonly presented during the postoperative period in total fundoplication because of the underlying dysmotility, especially against the increased resistance caused by the complete wrap.¹ But in our study with antireflux by partial wrap, 50% of patients presented with dysphagia and 30% ($n = 6$) needed dilatation due to distal esophageal stenosis. We considered the shortening of the esophagus to be the most important feature of failure, as in either EA patients or due to the upward tension on the wrap, as is reported in the literature.¹ Additionally, during the operation of these patients, the length of the esophagus does not allow the surgeon to make an adequate intra-abdominal esophagus that is tension free. In the literature, the rate of recurrent reflux was reported to be 31%, regardless of the type of fundoplication, 30% for total fundoplication, and 15% for partial fundoplication.^{1,6} Defining failure strictly as a need for reoperation, the failure rate in our series was 15% (3 of 20 children), which is compatible with the literature.

Regardless of the approach, there are four important surgical tenets to consider when treating hiatal hernias: (a) reduction of hernia contents; (b) excision of hernia sac; (c) crural closure; and (d) performance of an antireflux procedure.²³ In the literature, recurrent reflux is reported in 15% of patients,²³ whereas in our study, any patient during the follow-up period had a mean duration of 5 ± 3.9 years.

The main limitations of our study are its retrospective format and the lack of a random comparison of both methods. Additionally, in recent years, most of the total fundoplication studies have been performed laparoscopically, whereas in our study, for a limited number of patients, total fundoplication was performed laparoscopically and excluded from the study. Therefore, all patients were operated using open fundoplication, and further randomized studies are required. Compared with open procedures, laparoscopic fundoplication is considered to have the advantage to reduce hospital stay and operation time. However, our mean operation time was 116 ± 39 min (even 49% had performed gastrostomy feeding tube at the same time with fundoplication), not higher when compared with laparoscopic fundoplication reported in the literature. Capito et al.,²¹ reviewing children with a median age 3.5 years, reported 80 min (range, 40–220 min); Thatch et al.,⁸ reviewing neonatal patients, reported 113 ± 4 min; Rosales

et al.,²⁴ reviewing 106 children, reported 116.26 ± 44.99 min; Leung et al.,²⁴ reviewing 86 patients and all children who had gastrostomy performed in the same operative session, reported 157 ± 55 in under 1 year of age vs. 169 ± 52 min in over 1 year of age. Additionally, the median length of hospital stay was comparable with the literature. In our study, all patients were discharged in a median of 7 days (1–56). We consider that the result is in the acceptable range closer to the good side compared with the literature of laparoscopic fundoplication, as reported by Capito et al.²¹ as 4 days (range, 2–20 days), by Rosales et al.²⁴ as 14 days (2–70), and by Leung et al.²⁵ as 10 ± 11.69 (day) in under 1 year of age vs. 9 ± 11.7 (2.0–72) (day) in over 1 year of age. In fact, the length of hospital stay in our study was a little longer than we expected, because more than half of our patients had neurological disease and we know that neurological diseases increase the time of postoperative hospital stay. Neurologically and structurally normal patients' average hospital stay was 5 days vs. neurologically impaired patients 6 ± 4.76 days.

Conclusion

Belching, retching, inability to vomit, and gas bloat syndrome are the most common problems with the Nissen fundoplication reported in the literature. Vomiting, belching, and the natural release of the neo-valve during deglutition are important in children, and Boix-Ochoa induces these more physiological results, as it enables them. According to our study, we conclude that fundoplication-modified Boix-Ochoa, easily performed, is also beneficial in children with GERD, irrespective of their neurological status. Therefore, with a 95% success rate, this procedure may be preferred for antireflux surgery as an alternative to complete fundoplication. Finally, we consider that recurrent reflux is more often associated with esophageal lengthening, which is shortened in the esophagus when operating for atresia or strictures (reflux or caustic ingestion).

Contributions - Substantial contributions to the conception or design of the work or the acquisition, analysis, or interpretation of data for the work;
- Drafting the work or revising it critically for important intellectual content;

- Final approval of the version to be published; and
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

All authors meet all the four criteria mentioned above.

Compliance with Ethical Standards

The data review and collection were performed in compliance with the principles of the ethics committee and the Declaration of Helsinki. This study was approved by the Başkent University Ethical Committee.

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