



Minimal vs extensive esophageal mobilization during laparoscopic fundoplication: a prospective randomized trial

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Abstract

Purpose: Laparoscopic Nissen fundoplication has been traditionally performed with extensive esophageal dissection to create 2 to 3 cm of intraabdominal esophagus. Retrospective data have suggested that minimal esophageal mobilization may reduce the risk of postoperative herniation of the wrap into the lower mediastinum. To compare complete esophageal dissection to leaving the phrenoesophageal attachment intact, we conducted a 2-center, prospective, randomized trial.

Methods: After obtaining permission/assent, patients were randomized to circumferential division of the phrenoesophageal attachments (MAX) or minimal mobilization with no violation of the phrenoesophageal membrane (MIN). A contrast study was performed at 1 year. The primary outcome variable was postoperative wrap herniation.

Results: One hundred seventy-seven patients were enrolled in the study (MIN, n = 90; MAX, n = 87) from February 2006 to May 2008. There were no differences in demographics or operative time. Contrast studies were performed in 64 MIN and 71 MAX patients, respectively. The transmigration rate was 30% in the MAX group compared with 7.8% in the MIN group ($P = .002$). The reoperation rate was 18.4% in the MAX group and 3.3% in the MIN group ($P = .006$).

Conclusions: Minimal esophageal mobilization during laparoscopic fundoplication decreases postoperative wrap transmigration and the need for a redo operation.

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Laparoscopic fundoplication is a commonly performed operation for many pediatric surgeons [1-6]. The most substantial complication of this operation, and the main

reason these patients will require a second operation, is migration of the wrap through the esophageal hiatus [7-9]. Since the development of antireflux procedures, esophageal mobilization to lengthen the intraabdominal esophagus has been felt to be an important tenet for an effective operation [10,11]. However, this concept has been based on the adult experience where migration is less of a problem and foreshortening of the esophagus may be more common. Recently, a retrospective study suggested that minimal esophageal mobilization helps to reduce the risk of

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postoperative transmigration [12]. This concept of minimal esophageal mobilization to reduce the incidence of post-operative wrap transmigration was studied in a 2-center, prospective, randomized trial.

1. Methods

Approval was obtained from the internal review board at both institutions before enrolling patients. Patients were subsequently enrolled only after obtaining consent from the patient's legal guardian. The consent forms and consent process were carefully evaluated by the internal review board on a continual basis. The study was registered with clinicaltrials.gov at the inception of enrollment (NCT# 00287612).

1.1. Participants

The study population consisted of children with gastro-esophageal reflux disease. Inclusion criteria were patients younger than 18 years who were scheduled for laparoscopic fundoplication. Patients with a known hiatal hernia were excluded. A hiatal hernia identified during the operation that required repair was an exclusion criterion, as was conversion to an open procedure.

1.2. Interventions

After obtaining permission/assent, patients were randomized to undergo laparoscopic fundoplication with extensive esophageal mobilization to include circumferential division of the phrenoesophageal membrane (MAX) (Fig. 1) or minimal esophageal mobilization with no violation of the phrenoesophageal membrane (MIN) (Fig. 2).

Photographs were taken of each side of the esophagus before stitch placement to document the absence or presence

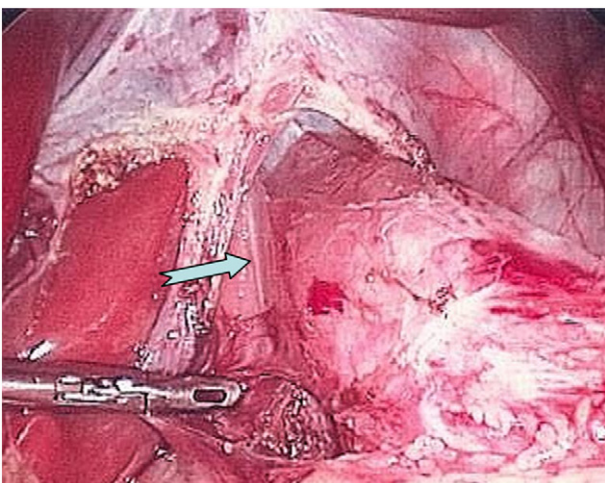


Fig. 1 Complete dissection of the esophagus demonstrating dissociation of the right crus and the esophagus (arrow).

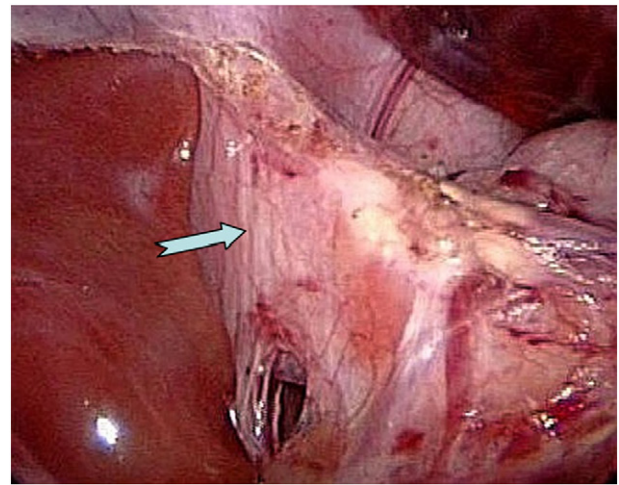


Fig. 2 Minimal dissection of the esophagus resulting in nearly circumferential preservation of the phrenoesophageal membrane (arrow).

of the phrenoesophageal attachments. These photographs were reviewed by both institutions on an annual basis to ensure uniformity in the operative procedure between surgeons and institutions.

1.3. Sample size

The sample size was determined with a power of 0.8 using one stratification for neurologic impairment based on our published retrospective transmigration rates (12% vs 5%) [12]. A sample size of 180 patients in each arm was calculated with an α of .05.

1.4. Assignment

An individual unit of randomization was used in stratified sequence in blocks of 10. Patients were stratified as neurologically impaired or neurologically normal. The family was approached for permission/assent after the staff surgeon had determined that the patient would be scheduled for laparoscopic fundoplication. The randomization sequence was then accessed to identify the next allotment after the permission/assent form was signed.

1.5. Protocol

Laparoscopic Nissen fundoplication was performed using a standard 5-site technique with ligation and division of the short gastric vessels to identify the left crus and incision of the gastrohepatic ligament to identify the right crus. In patients randomized to MAX, the phrenoesophageal membrane was incised circumferentially to separate the esophagus from the crura. In patients randomized to MIN, the phrenoesophageal membrane was left intact. A retro-esophageal window was created in both groups to pass the fundus around the esophagus. In all patients, the crura were

approximated posteriorly with at least single stitch incorporating the esophagus at the 7-o'clock position. Both groups received at least 4 esophagocrural sutures with 2 on each side. The remainder of the fundoplication was similarly performed in the 2 groups. A contrast study was performed at 1 year postoperatively and as indicated for symptoms.

1.6. Data collection

All data were collected prospectively. At the time of operation, variables recorded included age, weight, sex, neurologic status, and documented complications of reflux. Operative variables collected included the operative time and the intra- and postoperative complications. Complications of reflux at the time of operation were recorded. Because of the inability to prove reflux as the cause of pneumonia, weight loss, or acute life-threatening event (ALTE) spells, all documented events were recorded as a reflux complication before and after the operation. The primary outcome variable was herniation of the wrap through the esophageal hiatus. The other outcome variables included redo fundoplication, esophageal dilation, retching, mortality, and recurrence of reflux complications.

1.7. Statistical analysis

Continuous variables were compared using an independent-sample, 2-tailed Student *t* test. Discrete variables were analyzed with χ^2 test with Yates correction where appropriate. Significance was defined as *P* value < .05. Descriptive statistics are expressed as mean \pm standard deviation. All patients were analyzed in an intention-to-treat manner. An interim analysis was performed annually.

3. Results

From February 2006 to May 2008, 177 patients were enrolled in the study. Accrual of patients was terminated after an interim analysis when the primary outcome variable was found to be significantly different between groups.

Table 1 Patient characteristics at operation

	Maximal esophageal mobilization (n = 87)	Minimal esophageal mobilization (n = 90)	<i>P</i> value
Age (y)	1.9 \pm 3.3	2.5 \pm 3.5	.30
Weight (kg)	10.7 \pm 11.9	12.6 \pm 18.2	.44
Sex (% male)	59.8%	55.6%	.65
Neurologically impaired (%)	51.7	54.4	.76

3.1. Demographics

There was no difference between the 2 groups in age, weight, or percentage of patients who were neurologically impaired (Table 1). There were no differences in the documented preoperative complications of reflux (Table 2).

3.2. Operation

Excluding all combination cases except gastrostomy, the mean operative time was 82.5 \pm 22.2 minutes in the MAX group and 83.9 \pm 21.0 minutes in the MIN group (*P* = .80) when gastrostomy was performed. The mean operative time was 80.5 \pm 18.3 minutes in the MAX group and 79.9 \pm 20.4 minutes in the MIN group (*P* = .97) when a gastrostomy was not performed. A gastrostomy was placed in 55 patients (63.2%) in the MAX group and 57 patients (63.3%) in the MIN group (*P* = 1). There were no significant intraoperative or immediate postoperative complications.

3.3. Outcome

Follow-up contrast studies were performed in 64 MIN patients and 71 MAX patients (*P* = .11). The mean time from the operation to the most recent contrast study was 13.4 \pm 6.4 months in the MAX group and 13.7 \pm 6.2 months in the MIN group (*P* = .79). There were 26 patients (21 MAX, 5 MIN) with some herniation documented on the contrast study, which led to a reoperation in 19 patients (16 MAX, 3 MIN). The differences were both highly significant (Table 3). Mean time to redo operation was 16.9 \pm 5.3 months in the MIN group and 14.3 \pm 10.0 months in the MAX group (*P* = .68). Redo operations were performed in the presence of substantial hernia and/or the development of symptoms such as worsening retching, swallowing difficulty, and recurrent reflux. Small asymptomatic hernias are being observed.

Table 2 Complications of reflux pre- and postoperatively

	Maximal esophageal mobilization (n = 87)	Minimal esophageal mobilization (n = 90)	<i>P</i> value
At presentation			
Weight loss	55.7%	59.3%	.75
Pneumonia	20.0%	23.8%	.57
ALTE spells	23.0%	18.9%	.46
At 1 mo			
Weight loss	6.9%	1.3%	.18
Pneumonia	4.2%	2.5%	.89
ALTE spells	4.2%	1.3%	.54
At 1 y			
Weight loss	14.0%	7.0%	.37
Pneumonia	16.7%	12.0%	.59
ALTE spells	8.2%	5.2%	.81

Table 3 Outcome data

	Maximal esophageal mobilization (n = 70)	Minimal esophageal mobilization (n = 64)	<i>P</i> value
Postoperative wrap transmigration by upper GI contrast study (%)	30.0%	7.8%	.002
Need for redo fundoplication (%)	18.4%	3.3%	.006

GI indicates gastrointestinal.

There were 2 patients in the MAX group who underwent a second redo operation and none in the MIN group. One patient underwent a third redo fundoplication combined with resection of an epiphrenic esophageal diverticulum.

In addition to redo fundoplications, there were 6 patients who underwent a total of 10 esophageal dilations in the MAX group compared with no dilations in MIN group ($P = .04$). Only one of these patients required dilation without the finding of herniation or the need for redo fundoplication, and 2 dilations were performed for swallowing difficulties. There were 2 patients who underwent pyloroplasty, both of whom were in the MAX group; one was done in combination with redo fundoplication, and the other was performed subsequent to a redo fundoplication.

Herniation occurred in 14.9% of those neurologically impaired and 14.5% of neurologically normal patients ($P = 1$). One-year mortality was 7.8% in the MIN group and 6.9% in the MAX group ($P = .99$). None of these deaths were related to the operation or identifiable reflux-related complications. At 1 year, the presence or absence of retching was recorded in 51 of the MAX group and 60 of the MIN group. Retching was documented in 18% of the MAX group and 11% of the MIN group ($P = .05$). There was a substantial decrease in reflux complications in both groups after fundoplication. However, there was no difference in persistent complications of reflux between groups (Table 2).

4. Discussion

Transhiatal wrap migration is the dominant mode of failure after laparoscopic Nissen fundoplication, with relatively high rates of reoperation reported in large case series [5,7-9]. Prevention of this anatomical failure of the operation is essential to improving outcomes. Most reports in adult general surgery emphasize the importance of complete esophageal mobilization to bring the lower 2 to 3 cm of esophagus into the abdomen [13-15]. This operative concept has naturally translated to pediatric surgical practice. However, there may be important differences between adults and children, including differences in the occurrence of esophageal foreshortening. The results of this

trial provide compelling evidence that minimal esophageal mobilization can reduce the risk of transhiatal migration and support a different approach in children. It is noteworthy that the clinical symptoms of reflux appeared to be similarly controlled in both groups and that there were no patients who had undergone minimal mobilization who required revision fundoplication for control of symptoms. The natural question will be whether this is an adequate antireflux procedure.

Although the results of this study may contradict historical assumptions about the source of lower esophageal sphincter pressure offered by fundoplication, more recent data shed light on the effectiveness of fundoplications in the MIN group [16]. Simultaneous combined endoscopic ultrasound/manometry studies have demonstrated that the normal high pressure zone of the lower esophagus is composed of 3 components, 2 of which are smooth muscle intrinsic sphincter components (upper and lower) and the other is the effect of the crural sling [17]. The proximal intrinsic component is aligned with the crura and moves during respiration, implicating the importance of the phrenoesophageal membrane [18]. The lower intrinsic component lies at the junction of the gastric cardia and esophagus. Adult patients with reflux have been shown to have an abnormality in the lower intrinsic component [19]. Pharmacologic manipulation in patients who have undergone Nissen fundoplication has demonstrated that tonic contraction of the gastric smooth muscle in the wrap augments the lower intrinsic component [16]. Therefore, it would argue against disrupting the anatomical association between the top intrinsic component and the crural sling in patients without a hiatal hernia. Such anatomical disruption was performed in the MAX group. Augmenting the lower intrinsic component with a wrap around the distal esophagus in its native position, as done in the MIN group, should overcome the physiologic deficit while preserving the function and relationship of the 2 upper components. A model for the efficacy of maintaining the anatomical alignment of the esophagus and hiatus while performing an antireflux operation is seen in the emerging endoscopic technologies that have little to no impact on the hiatus [20-23].

The authors recognize the limitation of not having postoperative pH or impedance monitoring to prove equal efficacy of the 2 techniques. The practice at both institutions has been to use these postoperative studies selectively because reflux complications are often readily apparent in children. Furthermore, although pH studies adequately depict risks for peptic complications, they are only a surrogate measure for nonpeptic complications such as failure to thrive, aspiration, and ALTE spells. Because most of the operations were required for complications felt to be secondary to reflux, the follow-up data in Table 2 suggest that minimal dissection does not compromise the efficacy of the wrap. Most importantly, there is a clear advantage in preventing postoperative complications requiring redo fundoplication.

The rate of transmigration was higher in this study compared with our own historical retrospective data [5]. This is likely because of the fact that an upper gastrointestinal contrast study at 1 year postoperatively was part of the study protocol. This also likely accounts for the reduced number of redo operations, as not all the patients with transmigration seen on the contrast study were symptomatic. Moreover, the contrast study at 1 year is likely the explanation for the unique finding in this study that rate of transmigration is the same between neurologically normal and neurologically impaired patients.

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Discussion

Unidentified Speaker: So, Shawn, I have to ask you – first of all I want to congratulate you guys for being very honest about your outcomes.

My question is this. I know that there was a paper presented here a couple of years ago I think on open fundoplication, which is a much greater scar inducing operation, and largely with the collar sutures this is a very similar operation to the one you are doing. The failure there that was reported was like 1-2%. It was relatively low. My question is not so much about mobilization but are we reaching the limits of laparoscopy because it does not induce scar for this particular operation?

Dr St. Peter: I am not sure about that because I think we can get to the point that our recurrence rates are going to be just as low. The overall morbidity that is induced on every single patient when you make the commitment to open probably is not worth it in the entire population if there are a few more patients that have a redo operation if they all have a primary laparoscopic procedure. Having said that, there are some longer term followup studies after open fundoplication that have herniation rates of upwards of 8-11%. I think it become even higher than that if people do more careful long-term followup studies because I probably see at least two patients a year that had an open fundo as an infant and now they are teenagers and they have a big hiatal hernia.

Ann Kosloske, MD (Sanibel, Florida): You are to be congratulated for an epidemiologically solid study. I like your power of 0.8 and look forward to the time when all the studies that are presented here comparing two groups will give the power because that tells you a lot about truth or anecdote.

I have one question. Did individual surgeons randomize or did you divert patients who were going to have maximal mobilization to one surgeon who did it and minimal to another surgeon?

Dr St. Peter: That is an excellent question. There were two randomization sequences at each institution. For the Alabama surgeons, there were three participating

surgeons. They had a randomization sequence and so did we. All six surgeons did both groups. We did not have to randomize by surgeon because with a volume that large we would anticipate each individual surgeon would do enough that they should have roughly equal numbers and that did turn out to be the case. No individual surgeon was separated by more than three cases in one arm or the other.