

Biologic Prosthesis to Prevent Recurrence after Laparoscopic Paraesophageal Hernia Repair: Long-term Follow-up from a Multicenter, Prospective, Randomized Trial

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- BACKGROUND:** In 2006, we reported results of a randomized trial of laparoscopic paraesophageal hernia repair (LPEHR), comparing primary diaphragm repair (PR) with primary repair buttressed with a biologic prosthesis (small intestinal submucosa [SIS]). The primary endpoint, radiologic hiatal hernia (HH) recurrence, was higher with PR (24%) than with SIS buttressed repair (9%) after 6 months. The second phase of this trial was designed to determine the long-term durability of biologic mesh-buttressed repair.
- METHODS:** We systematically searched for the 108 patients in phase I of this study to assess current clinical symptoms, quality of life (QOL) and determine ongoing durability of the repair by obtaining a follow-up upper gastrointestinal series (UGI) read by 2 radiologists blinded to treatment received. HH recurrence was defined as the greatest measured vertical height of stomach being at least 2 cm above the diaphragm.
- RESULTS:** At median follow-up of 58 months (range 42 to 78 mo), 10 patients had died, 26 patients were not found, 72 completed clinical follow-up (PR, n = 39; SIS, n = 33), and 60 repeated a UGI (PR, n = 34; SIS, n = 26). There were 20 patients (59%) with recurrent HH in the PR group and 14 patients (54%) with recurrent HH in the SIS group (p = 0.7). There was no statistically significant difference in relevant symptoms or QOL between patients undergoing PR and SIS buttressed repair. There were no strictures, erosions, dysphagia, or other complications related to the use of SIS mesh.
- CONCLUSIONS:** LPEHR results in long and durable relief of symptoms and improvement in QOL with PR or SIS. There does not appear to be a higher rate of complications or side effects with biologic mesh, but its benefit in reducing HH recurrence diminishes at long-term follow-up (more than 5 years postoperatively) or earlier. (J Am Coll Surg 2011;213:461–468. © 2011 by the American College of Surgeons)
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Abbreviations and Acronyms

HH	= hiatal hernia
LPEHR	= laparoscopic paraesophageal hernia repair
PPI	= proton pump inhibitor
PR	= primary diaphragm repair
QOL	= quality of life
SIS	= small intestinal submucosal
UGI	= upper gastrointestinal series

Paraesophageal hernias are difficult to reduce and difficult to repair because of their size, the large hiatus, the quality of the diaphragm, and the frequency with which the esophagus is foreshortened. In addition, there may be some intrinsic structural or genetic changes in the muscle or suspensory tissues in patients with giant hiatal defects.^{1,2} As a result, repair of the paraesophageal hernia is subject to a high recurrence rate,^{3,4} whether repaired laparoscopically or open, through the chest, or through the abdomen. In 2002, we embarked on a multicenter randomized trial to test the hypothesis that the use of a biologic mesh, small intestinal submucosa (SIS, Cook Biotech Inc), to reinforce the closure of the diaphragmatic hiatus in patients with paraesophageal hernias would lower the recurrence rate and improve outcomes, without increasing the complication rate. In 2006, we reported the results of phase I of this clinical trial: 6 months after the operation there was a significant reduction in recurrent hiatal hernia with use of the SIS mesh (9%) compared with primary repair (24%).⁵ In order to test the durability of biologic mesh in preventing hiatal hernia recurrence, we conducted a systematic follow-up of all patients enrolled in the original study. This article reports the status of the patients entered into this trial at a median follow-up of 5 years postoperatively.

METHODS

In 2002, 4 centers (University of Washington, Oregon Health and Science University, Washington University St Louis, and The Oregon Clinic) embarked on a prospective randomized trial in patients with symptomatic paraesophageal hernias. Eligibility for the trial is outlined in Figure 1. Between September 2008 and August 2009, we endeavored to contact all patients to obtain information regarding symptoms and quality of life, as well as to assess the integrity of the repair with upper gastrointestinal (UGI) series.

Surgical technique

The surgical technique is described in detail in our first report of this trial.⁵ In summary, it entailed a laparoscopic hernia sac resection, reduction of hernia contents, primary crural repair, and Nissen fundoplication, which were per-

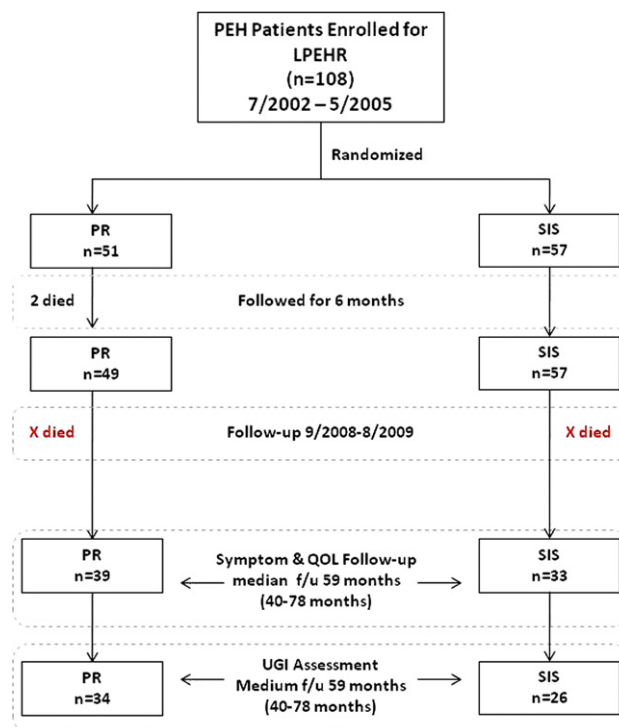


Figure 1. Diagram of the study randomization and follow-up. LPEHR, laparoscopic paraesophageal hernia repair; PEH, paraesophageal hernia; PR, primary diaphragm repair; QOL, quality of life; UGI, upper gastrointestinal.

formed in all patients. For the biologic mesh group, a piece of SIS (4-ply Surgisis, 7 × 10 cm, Cook Biotech Inc) was prepared and cut in a U-shaped configuration. The SIS was placed with the base of the U overlying the posterior hiatal closure and sutured in place.

Outcome variables

Upper UGI series (or barium swallow)

Preoperative and 6-month postprocedural and long-term follow-up UGI series were performed for each patient at their home institutions (University of Washington, Oregon Health and Science University, Washington University St Louis, and The Oregon Clinic) or at a closer facility if the patient was unable to travel to the home institution. Based on the examination protocols at each institution, videofluoroscopic barium UGI was used to assess the esophagus, stomach, and proximal small intestine.

To reduce interobserver variability, hard copies or digitized versions of these examinations were reviewed at the coordinating center (University of Washington) by the same 2 radiologists who, combined, had more than 40 years of experience in gastrointestinal imaging (one of these radiologists read each of the 6-month studies as well). The radiologists were both blinded to the treatment group and

were asked to formulate a consensus interpretation in the following manner. For the purposes of this study we did not assume that any of the recurrences at 6 months carried over to the current study period because this might skew our results toward the group that had a higher recurrence rate at 6 months (ie, the Primary repair group). Therefore, all patients were asked to repeat a UGI at this later phase of the study, and our results are based on these x-rays alone.

Maximum vertical height above the diaphragm

All images for each examination were reviewed and the greatest vertical linear distance from the level of the diaphragm adjacent to the fundoplication to the top of the wrap was recorded (Fig. 2A). Exact pixel measurements were taken and recorded distance conversion scales were used to obtain the measurements in millimeters. In cases received where no calibration scales were found on the fluoroscopic spot images, the height of the nearest vertebral body was estimated from the overhead scout images. We then converted the height (in pixels) above the diaphragm and converted this to a scaled score based on vertebral height (vertical height of the hiatal hernia in pixels/vertebral height in pixels). We then converted this to a measurement (in mm) by using the average vertebral height of the patients in the study with exact scaling ($n = 18$), for which the average height was 27 ± 4 mm.

Calculated cross-sectional area of the hernia

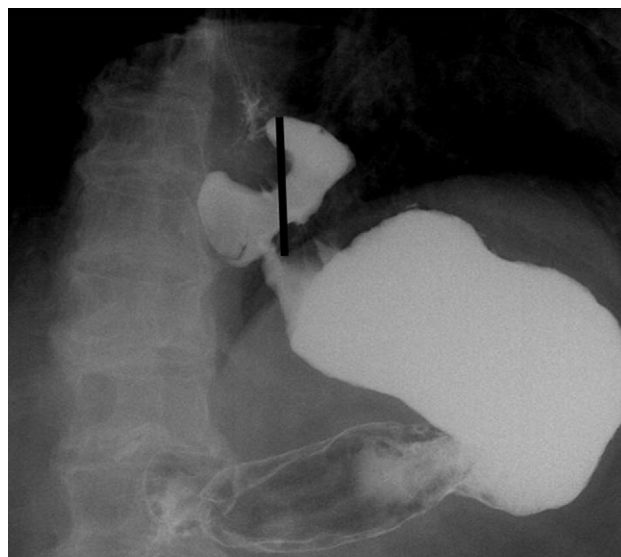
Because the amount and shape of the stomach above the diaphragm in a hiatal hernia are different, we hypothesized that vertical height alone may not be the best way to characterize recurrence. We therefore added a new measure in the second phase of the study, before reviewing any of the UGI examinations. The radiologist and surgeons decided to measure both the maximal vertical and horizontal diameters of the recurrent hernia in the anterior-posterior projection, then use the formula of an ellipse (area = $[\pi \times \text{short axis} \times \text{long axis}] / 4$) as a standardized method of measuring cross-sectional area (Fig. 2B).

Definition of recurrence⁵

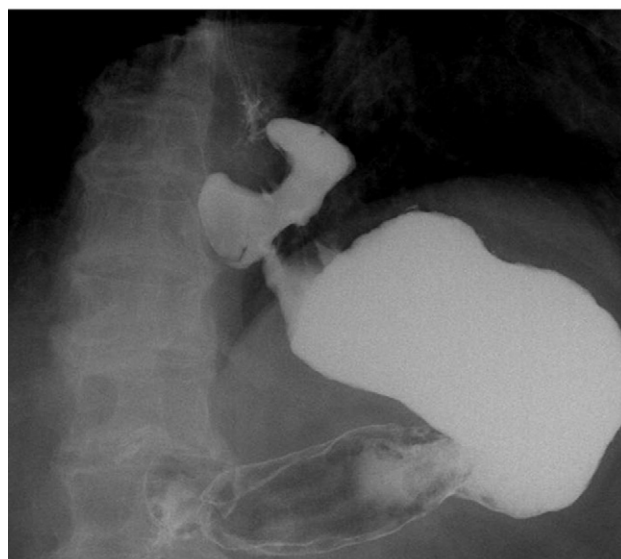
A maximum vertical height >2 cm was chosen as recurrence. The rationale for excluding maximum measurements <2 cm was because of the potential for overestimation of recurrence because of the variability range of x-ray interpretation.

Symptom evaluation and quality of life

A standardized symptom severity questionnaire was administered using a scaled 0 to 10 visual analog score for the following symptoms: heartburn, regurgitation, chest pain, dysphagia, abdominal pain, bloating, nausea, postprandial



A



B

Figure 2. (A) Example of vertical height measurement. (B) Example of hiatal hernia area (ellipse): a = short axis; b = long axis; area = $(\pi * a * b) / 4$.

pain, and early satiety. The 36-item Health Survey (SF-36v2 norm-based scoring) was also administered. The results of the symptom questionnaire and the SF-36 performed during 2008 to 2009 were compared with those reported in the earlier study (REF). This allowed us to compare preoperative and 6-month postoperative data with data obtained long-term.

Primary outcomes measure

Recurrence rate (hiatal hernia > 2 cm, vertical height) was based on the results of a UGI. Need for reoperation sec-

Table 1. Baseline Characteristics of Treatment Groups at Randomization (n = 108) Compared with Those Available at Long-Term Follow-Up (n = 72)

Characteristic	PR, all (n = 57)	PR, long-term follow-up (n = 39)	SIS, all (n = 51)	SIS, long-term follow-up (n = 33)
Age, y, mean $\pm$ SD	64 $\pm$ 13	63 $\pm$ 10	67 $\pm$ 11	64 $\pm$ 10
Female, n (%)	43 (75)	32 (82)	38 (75)	25 (76)
BMI, kg/m ² , mean $\pm$ SD	31.3 $\pm$ 4.9	31.5 $\pm$ 4.5	30.2 $\pm$ 5.6	31.1 $\pm$ 5.8
Symptoms, n, mean $\pm$ SD *				
Heartburn	5.3 $\pm$ 3.5	5.2 $\pm$ 3.9	5.3 $\pm$ 3.1	6.0 $\pm$ 3.2
Regurgitation	5.4 $\pm$ 3.2	5.4 $\pm$ 3.4	5.2 $\pm$ 3.1	5.3 $\pm$ 3.4
Chest pain	4.4 $\pm$ 3.7	4.3 $\pm$ 3.9	3.7 $\pm$ 3.6	4.1 $\pm$ 3.8
Dysphagia	3.1 $\pm$ 2.9	2.5 $\pm$ 2.7	3.1 $\pm$ 3.1	3.4 $\pm$ 3.0
Hiatus (R-L), cm, mean $\pm$ SD	4.3 $\pm$ 2.4	4.1 $\pm$ 1.7	4.2 $\pm$ 1.8	4.1 $\pm$ 2.0
Hiatus (A-P), cm, mean $\pm$ SD	5.8 $\pm$ 1.5	5.7 $\pm$ 1.6	6.4 $\pm$ 2.0	6.4 $\pm$ 2.2
Esophageal length, cm, mean $\pm$ SD	3.4 $\pm$ 0.9	3.4 $\pm$ 1.0	3.2 $\pm$ 1.0	3.3 $\pm$ 0.9
Collis gastroplasty, n (%)	3 (5)	1 (3)	2 (4)	1 (3)

*Symptom severity scored by visual analog scale (0-10).

A-P, anterior-posterior; BMI, body mass index; PR, primary diaphragm repair; R-L, right to left; SIS, small intestinal submucosa.

ondary to wrap disruption, migration, or herniation at any time during the study period was assumed to constitute a recurrence.

Secondary outcomes measures

Secondary outcomes measures include vertical height of the hiatal hernia, cross-sectional area of the hiatal hernia, symptom frequency and severity, and quality of life (QOL) (SF-36).

Statistical considerations

Data were collected and stored in a database developed at the University of Washington. Data compilation, entry, and organization were performed electronically by the study coordinator. Outcomes scores and their changes over time were compared between the primary and small intestinal submucosal (SIS) groups. We tested for differences between pairs of groups as well as for differences over time within each of the groups. Two- and 1-sample *t*-tests were used for symptom severity scores, QOL scores, and all quantitative operative outcomes to test for differences between groups and temporal changes within groups, respectively. We examined the distributions of the outcomes where the *t*-test was used and found no outcome where the *t*-test would not be justified. Likewise, we used the chi-squared test to compare presence of hernia between groups. Baseline patient characteristics (about 60 variables on treatment, body mass index, patient symptoms, and QOL) were compared between those with and without the long-term assessment. A *p* value < 0.05 was accepted to denote statistical significance. All analyses were carried out using R version 2.11.0.

The study was approved by the University of Washington Human Subjects Division as well as by each of the participating institution's institutional review board. Patients who agreed to participate provided written informed consent. All data were protected according to HIPPA guidelines.

RESULTS

Of the original 108 patients, 51 randomized to the SIS arm and 57 to the primary diaphragm repair (PR) arm, operated on between July 2002 and May 2005, we were able to contact 72 patients. Two patients died in the immediate postoperative period, and 10 additional patients died in the follow-up interval. Twenty-six patients could not be found. All 72 patients (PR, 39; SIS, 33) we contacted agreed to provide symptom and QOL assessments. Sixty of the 72 patients (PR, 34; SIS, 26) also consented to a repeat UGI (Fig. 1). There were no statistically significant differences between PR and SIS in clinical and UGI follow-up participation. The median follow-up was 58 months (range 40 to 78 months). Baseline characteristics are included in Table 1, and those with long-term follow-up appear representative of the overall cohort.

UGI symptoms and quality of life symptoms

There were no statistically significant differences in the frequency or severity of UGI symptoms (heartburn, regurgitation, chest pain, dysphagia, abdominal pain, bloating, postprandial pain, and early satiety) between patients in the PR vs the SIS group at long-term follow-up (Table 2). Furthermore, there remained a large and statistically significant reduction in the severity of most symptoms (in both

Table 2. Comparison of Symptom Severity Between Primary and Small Intestinal Submucosa Groups at Long-Term Follow-Up

Symptom*	Primary, n, mean $\pm$ SD	SIS, n, mean $\pm$ SD	p Value†
Heartburn	1.4 $\pm$ 2.4	2.3 $\pm$ 3.1	0.2
Regurgitation	1.5 $\pm$ 2.5	0.8 $\pm$ 1.7	0.2
Dysphagia	1.6 $\pm$ 2.8	1.4 $\pm$ 2.5	0.7
Chest pain	1.0 $\pm$ 2.4	0.6 $\pm$ 1.4	0.5
Abdominal pain	2.1 $\pm$ 2.7	2.0 $\pm$ 2.8	0.8
Bloating	2.3 $\pm$ 2.6	2.1 $\pm$ 2.5	0.7
Postprandial pain	1.4 $\pm$ 2.5	0.8 $\pm$ 2.2	0.4
Early satiety	2.1 $\pm$ 2.5	1.2 $\pm$ 2.0	0.2

There were 32 primary patients and 26 SIS patients (except for chest pain; 3 primary and 5 SIS patients). Limited to patients with data at all 3 of the time points (baseline, 6 months and long term).

*Symptom severity scored by visual analog scale (0-10).

†*t*-test.

SIS, small intestinal submucosa.

groups) when preoperative symptoms were compared with long-term follow-up symptoms (Table 3).

SF-36

There were no statistically significant differences in QOL as measured by the SF-36 (either summary scores of individual domains) between patients in the PR or SIS group at long-term follow-up (Table 4). Moreover, there remained improvements in most areas of the SF-36 at long-term follow-up compared with baseline, including statistically significant improvements in the SF-36 bodily pain for PR patients and SF-36 vitality for SIS patients (Table 5).

Table 3. Change in Symptom Severity from Preoperative to Long-Term Follow-Up

Symptom*	Primary		SIS	
	Mean $\pm$ SD	p Value†	Mean $\pm$ SD	p Value†
Heartburn	-3.6 $\pm$ 4.0	<0.001	-3.2 $\pm$ 4.6	0.002
Regurgitation	-4.3 $\pm$ 3.5	<0.001	-4.2 $\pm$ 4.0	<0.001
Dysphagia	-1.0 $\pm$ 4.3	0.200	-2.0 $\pm$ 3.2	0.009
Chest pain	-3.2 $\pm$ 4.1	<0.001	-3.8 $\pm$ 3.6	<0.001
Abdominal pain	-1.9 $\pm$ 3.8	0.007	-1.8 $\pm$ 3.5	0.020
Bloating	-1.6 $\pm$ 3.6	0.020	-2.7 $\pm$ 3.2	0.000
Postprandial pain	-2.9 $\pm$ 3.3	<0.001	-3.6 $\pm$ 3.7	<0.001
Early satiety	-1.2 $\pm$ 2.7	0.020	-2.6 $\pm$ 3.1	<0.001

There were 32 primary patients and 26 SIS patients (except for chest pain; 3 primary and 5 SIS patients). Limited to patients with data at all 3 of the time points (baseline, 6 months and long term).

*Symptom severity scored by visual analog scale (0-10).

†*t*-test

SIS, small intestinal submucosa.

Table 4. SF-36 (Normalized Values) in Primary and Small Intestinal Submucosa Groups at Long-Term Follow-Up

SF-36	Primary, mean $\pm$ SD	SIS, mean $\pm$ SD	p Value*
Physical functioning	43 $\pm$ 13	45 $\pm$ 12	0.6
Role limitations due to physical health (role physical)	43 $\pm$ 14	42 $\pm$ 14	0.7
Bodily pain	45 $\pm$ 12	43 $\pm$ 10	0.6
General health perceptions	47 $\pm$ 11	46 $\pm$ 10	0.8
Vitality	46 $\pm$ 11	47 $\pm$ 13	0.8
Social functioning	46 $\pm$ 14	43 $\pm$ 14	0.4
Role limitations due to emotional health (role emotional)	47 $\pm$ 14	43 $\pm$ 15	0.4
Mental health	48 $\pm$ 12	49 $\pm$ 12	0.8
Physical component summary score	44 $\pm$ 13	44 $\pm$ 11	1.0
Mental component summary score	49 $\pm$ 13	47 $\pm$ 15	0.6

There were 32 primary patients and 26 SIS patients (except for chest pain; 3 primary and 5 SIS patients). Limited to patients with data at all 3 of the time points (baseline, 6 months, and long-term).

**t*-test.

SIS, small intestinal submucosa.

Proton pump inhibitor use

Thirty-two (44%) of the 72 patients contacted were currently using a proton pump inhibitor (PPI) (17 [44%] PR and 15 [45%] SIS). This compared with 55 (77%) patients using a PPI preoperatively (29 [76%] PR and 26 [79%] SIS) and 12 (17%) patients using a PPI 6 months after their PEH repair (4 [11%] PR and 8 [25%] SIS).

Hiatal hernia recurrence

Using our study definition of hiatal hernia recurrence (vertical height > 2 cm), the PR group had 20 recurrences (59%) and the SIS group had 14 (54%) (*p* = 0.7) at long-term follow-up. The average size of the hernia (vertical height) was 24 $\pm$ 21 mm in the PR group and 24 $\pm$ 20 mm in the SIS group (*p* = 1.0). The average cross-sectional area of the hernia (area above diaphragm) was 887 $\pm$ 1,073 mm² in the PR group and 926 $\pm$ 1,021 mm² in the SIS group (*p* = 0.8). The follow-up duration (surgery date to long-term follow-up UGI) was similar between the 2 groups: 4.9 $\pm$ 0.8 years (range 3.6 to 6.5 years) for the PR group and 5.0 $\pm$ 0.8 years (range 3.7 to 6.2 years) for the SIS group.

At 6 months after repair, 41 (91%) patients in the SIS group and 37 (76%) patients in the PR group did not have a recurrence.⁵ Of those without recurrence at 6 months, 24 patients in each group had long-term evaluation with UGI. Twelve patients (50%) in each group had a recurrent hernia at an average of 5 years after the repair.

Table 5. Change in SF-36 (Normalized Values) in Primary and Small Intestinal Submucosa Groups at Long-Term Follow-Up

SF-36	Primary		SIS	
	Mean $\pm$ SD	p Value*	Mean $\pm$ SD	p Value*
Physical functioning	0.7 $\pm$ 13.3	0.800	3.9 $\pm$ 11.5	0.080
Role limitations due to physical health (role physical)	-1.2 $\pm$ 11.4	0.500	3.8 $\pm$ 14.2	0.200
Bodily pain	5.4 $\pm$ 10.3	0.004	3.2 $\pm$ 11.7	0.140
General health perceptions	-0.9 $\pm$ 9.7	0.600	0.2 $\pm$ 9.5	0.900
Vitality	0.4 $\pm$ 9.3	0.800	6.7 $\pm$ 13.0	0.009
Social functioning	2.3 $\pm$ 16.0	0.400	3.1 $\pm$ 14.0	0.200
Role limitations due to emotional health (role emotional)	-0.8 $\pm$ 11.5	0.700	2.4 $\pm$ 12.1	0.300
Mental health	-1.5 $\pm$ 10.7	0.400	3.9 $\pm$ 11.9	0.080
Physical component summary score	2.1 $\pm$ 9.3	0.200	3.5 $\pm$ 10.5	0.080
Mental component summary score	-0.7 $\pm$ 12.5	0.800	4.0 $\pm$ 12.5	0.100

There were 32 primary patients and 26 SIS patients (except for chest pain; 3 primary and 5 SIS patients). Limited to patients with data at all 3 of the time points (baseline, 6 months, and long term).

*t-test.

Effect of surgical date

Table 6 describes the long-term recurrence rates by date of operation. There was no statistically significant difference between SIS and PR in recurrence rates over time ($p = 0.5$).

Predictors of long-term recurrence

Univariate regression analysis was performed to investigate the following as potential factors in recurrence: use of SIS mesh, time since surgery, weight, body mass index, esophageal length, hiatal hernia size (right to left and anterior to posterior measurements), surgical institution, PPI use at baseline, severity of baseline symptoms, and quality of life (SF-36 factors). None of these was a statistically significant predictor of long-term recurrence, so no multivariate analysis was conducted.

Reoperation for hiatal hernia recurrence

Two patients (3.5%) in the PR group and none in the SIS group required reoperation for a symptomatic recurrent hiatal hernia.

Predictors of drop-out

Long-term follow-up data on the recurrence of hiatal hernia were available for 60 patients (56%). We compared

about 60 baseline patient characteristics between patients with the data and patients who dropped out as an indirect way to determine if the results could be influenced by those who had dropped out. Among these, only the type of hernia (2, 3, and 4) and the frequency of regurgitation on medications were statistically significant predictors of dropout ($p = 0.02$ and 0.03 , respectively, no adjustment for multiple comparisons). Patients with type 2 hernias were less likely to have the long-term assessment missing (21%) than patients with type 3 hernias (45%) and patients with type 4 hernias (86%). There was only a small and statistically nonsignificant difference between SIS and PR in the pattern of dropout percentages across types of hernia ($p = 0.6$, based on the interaction term in logistic regression of a binary missing status variable on treatment, hernia category, and treatment-category interaction).

DISCUSSION

Our study shows that the recurrence of a hiatal hernia, after laparoscopic repair of paraesophageal hernia, is more frequent than suspected, even when repair is performed by experienced surgeons. Furthermore, it shows that although the use of a biologic mesh conferred an advantage at 6 months, that advantage is erased by the end of 5 years. Despite this, patients did very well clinically after LPEHR with long-term improvements in symptom relief and QOL. Moreover, the use of mesh was not associated with any adverse side effects, either short- or long-term.

Recurrence rate

The main reason for using mesh to reinforce the hiatus is to minimize the chance of hernia recurrence. Indeed, other series had shown recurrence rates as high as 42% when LPEHR was performed with primary suture repair only.³ It has been shown that nonabsorbable mesh seems to reduce

Table 6. Long-Term Assessment for Patients According to Date of Surgery

Repair type	Surgery date		
	July 24, 2002–July 29, 2003	August 6, 2003–May 25, 2004	June 8, 2004–May 2, 2005
Primary, n (%)	3/7 (43)	8/11 (73)	8/15 (53)
Mesh, n (%)	5/9 (56)	5/8 (63)	4/9 (44)

n = 33 (the date of surgery was last for 1 patient in the primary group) for primary and 26 for mesh. $p = 0.6$ (logistic regression) for dependence of treatment difference on surgery date (a statistical interaction).

recurrences,^{6,7} but given the known complications associated with its use,^{8,9} we deliberately chose a biologic, absorbable product to determine whether we could reduce recurrence and at the same time not increase complications. Perhaps the most striking aspect of our results is the very high rate of anatomic recurrence whether or not biologic mesh was used. Although it was surprising to find that more than half of our patients had a recurrent hiatal hernia, other studies by experienced, high volume groups have reported recurrence rates in the 20% to 30% range in retrospective case series.^{4,10} Nevertheless, it was surprising to find that the addition of a biologic mesh to a primary repair did not significantly affect recurrence at all by the end of 5 years. Our study differs from all other reports of outcomes with both laparoscopic and open repair in several important ways. First, we prospectively followed patients over a long period of time (average of 5 years). Second, we used consistent and objective studies (UGI) to monitor recurrence and we defined a priori what we would consider a recurrence. Third, we had a meticulous, expert, blinded, and objective third party (2 radiologists) evaluate all x-rays. Fourth, we empowered these radiologists to be the final arbiter as to whether a recurrence had occurred. So any study read by them that had >2 cm of vertical height of any portion of stomach above the diaphragm was categorized as "recurrent." Finally, all surgeons and sites performed a high volume of esophageal surgery and the surgeons were experts at minimally invasive procedures. As a result, we think that these results probably represent the best that can be expected using the techniques and materials we used. At the same time, it is possible that the "strictness" of our criteria, and the fact that it was based solely on the radiographic appearance of the esophagogastric junction, may have led to the identification of more recurrent hernias than previous studies had shown.

Symptoms and quality of life

We have previously reported that presenting symptoms and QOL improved significantly 6 months after LPEHR.⁵ Early symptom improvement was equivalent whether patients had undergone primary or SIS repair. Surprisingly, and despite the high rate of anatomic recurrence nearly 5 years after the repair, most presenting symptoms remained under control, regardless of whether or not SIS was used to buttress the hiatal repair. Furthermore, there was no statistically significant difference in the frequency or severity of these symptoms between the SIS and PR groups. There was a less substantial and nonsignificant difference in health-related QOL (SF-36) overall than was seen in symptoms, and although there were some trends in SIS group showing greater improvement, this was not statistically signifi-

cant except for the "vitality" domain. The explanation for the persistence of improvement despite the anatomic recurrence may lie in the fact that the average recurrence is relatively small when compared with the initial anatomic defect, and the fact that postoperative adhesions probably prevent the stomach from twisting in an axial rotation as it did before surgery.

Benefit of the use of mesh

There was much enthusiasm generated by our initial phase study because there was nearly a 3-fold reduction in recurrence rates at 6 months (PR, 24% and SIS, 9%).⁵ We knew we needed to document long-term results before confirming success for this strategy, especially since biologic mesh is designed to be "incorporated" into the repair and may only confer short-term benefits. Because other studies had suggested that most recurrences after PEH repair occur early,⁷⁻¹¹ we had hoped that the use of this type mesh would reinforce the repair during that critical period and by that mechanism reduce hiatal hernia recurrence. Having now found that anatomic recurrence long-term is similar between mesh and primary repair, we are inclined to believe that what appeared to be the biggest benefit of biologic mesh, its absorbability, may be a downside as well. There could be a small difference in recurrence rates that this study is not powered to detect; as such we have been careful to state that there is no statistical difference between the groups rather than no difference. It is possible that mesh, although not protecting against recurrent hernias, may reduce the risk of severe hernias, at least severe enough to require reoperation. Indeed, only 2 patients in our study required reoperation and both were in the PR group. To provide stronger evidence that this difference is real would require a much larger study. A power analysis for a comparison of 3.5% vs 0% rates in 2 groups showed that a study with at least 438 patients (219 per group) would be needed to likely yield a statistically significant difference (assuming 80% power, 0.05 significance level, and a 2-sided test).

Assuming an early benefit to SIS buttressing of the hiatal repair, one might want to know when the early benefit of mesh is lost. The answer from this study is: sometime between 6 months and 5 years. Our study was neither designed nor conducted to accurately measure the "time to recurrence." For practical reasons, patients were accrued over a 2½ year period and the long-term follow-up was conducted in less than 1 year. As a result, patients have a variable length of follow-up, between nearly 4 and more than 6 years. One of the main theoretical benefits of a biologic mesh over the synthetic mesh alternative is a lower risk of complications. There is a known risk of synthetic

mesh erosion into adjacent structures (eg, esophagus or stomach) and association of this complication with severe dysphagia.^{8,9,12} The results of this study suggest that biologic mesh at the hiatus does not have any long-term negative sequelae. Indeed, no patient developed strictures or erosions in the SIS group. Moreover, there was no statistically significant difference in the frequency or severity of dysphagia between PR and SIS repair. As a result, it would appear that, other than cost, there is no downside to the use of biologic mesh for LPEHR.

So where does this leave us? There is a clear short-term benefit using SIS buttressing to prevent hiatal hernia recurrence, but no long-term benefit. Our impression is that many surgeons have already incorporated the use of biologic mesh in the repair of paraesophageal hernias. In light of these findings, does the short-term benefit justify its use? We believe that it does, or at least it justifies continued investigation. Since we designed this study there has been an explosion in the development of biologic mesh materials and redesign of existing materials (including modifications of the small intestinal submucosa used in this study). These newer materials may be more effective in preventing long-term recurrence than the SIS mesh used in this study; they may be more durable or create greater or stronger tissue remodeling. In addition, many techniques of hernia closure and mesh application have been developed in an attempt to obtain better results. There are different suturing techniques, and some surgeons are securing the mesh with other materials like biologic "glues." We also continue to use these materials as a "buttress" of a primary closure, when in all other hernia types, mesh is used to "bridge" a gap in order to relieve tension (which seemed to be the biggest contributor to recurrence). There are clearly many aspects that need ongoing investigation in our quest to reduce recurrence. At the very least, the field deserves a follow-up to this study to compare the efficacy of other types of biologic mesh and operative techniques. Moreover, we need to determine more clearly the patterns of recurrence, time to recurrence, and clinical significance of recurrence, which were not addressed by this study.

CONCLUSIONS

When measured prospectively and with strict predetermined criteria, it appears that the anatomic recurrence rate of a hiatal hernia after LPEHR is much higher than previously appreciated. The use of biologic mesh during LPEHR is safe and confers a clear benefit at 6 months. However, 5 years after the repair, the radiologically determined anatomic recurrence was observed to be similar between mesh-treated patients and

those treated with primary closure. More studies will be needed to determine what, if any, role biologic mesh should have in the future of these difficult repairs.

Author Contributions

Study conception and design: Oelschlager, Pellegrini, Hunter, Soper, Swanstrom
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