LAPAROSCOPIC REPAIR OF VERY LARGE HIATUS HERNIA WITH SUTURES VS. ABSORBABLE VS. NON-ABSORBABLE MESH - A RANDOMIZED CONTROLLED TRIAL

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Key Words:

Hiatus hernia, Mesh repair, Laparoscopy, Randomized controlled trial.

Trial registration – This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12605000725662

ABSTRACT

Objective:

Determine whether absorbable or non-absorbable mesh in repair of large hiatus hernias reduces the risk of recurrence, compared to suture repair.

Summary Background Data:

Repair of large hiatus hernia is associated with radiological recurrence rates of up to 30%, and to improve outcomes mesh repair has been recommended. Previous trials have shown less short term recurrence with mesh, but adverse outcomes limit mesh use.

Methods:

Multicentre prospective double blind randomized controlled trial of 3 methods of repair; sutures vs. absorbable mesh vs. non-absorbable mesh. Primary outcome - hernia recurrence assessed by barium meal X-ray and endoscopy at 6 months. Secondary outcomes - clinical symptom scores at 1, 3, 6 and 12 months.

Results:

126 patients enrolled - 43 sutures, 41 absorbable mesh and 42 non-absorbable mesh. 96.0% were followed to 12 months, with objective follow-up data in 92.9%. A recurrent hernia (any size) was identified in 23.1% following suture repair, 30.8% - absorbable mesh, and 12.8% - non-absorbable mesh (p=0.161). Clinical outcomes were similar, except less heartburn at 3 & 6 months and less bloating at 12 months with non-absorbable mesh, and more heartburn at 3 months, odynophagia at 1 month, nausea at 3 & 12 months, wheezing at 6 months, and inability to belch at 12 months following absorbable mesh. The magnitude of the clinical differences were small.

Conclusions:

No significant differences were seen for recurrent hiatus hernia, and the clinical differences were unlikely to be clinically significant. Overall outcomes following sutured repair were similar to mesh repair.

INTRODUCTION

Laparoscopic surgery for the treatment of patients with a very large hiatus hernia is now standard clinical practice. This problem occurs most commonly in elderly patients, and in the early days of laparoscopic antireflux surgery it represented less than 10% of the antireflux surgery and hiatus hernia repair workload[1]. However, as laparoscopic techniques for repair have become more reliable, surgeons have been referred more patients with very large hiatus hernias, and in recent years the number of patients with this problem has increased greatly, now comprising approximately 50% of the laparoscopic antireflux surgery workload in our practices[1]. In the 1990's, the standard approach to laparoscopic repair of very large hiatus hernias entailed complete dissection of the hernia sac from the mediastinum, hiatal repair with sutures and a fundoplication[2,3]. Whilst good clinical outcomes were reported following laparoscopic repair, and clinical success rates of approximately 90% have been described[2,3], later studies which utilized barium meal X-ray follow-up, demonstrated that suture repair alone is associated with radiological recurrence rates of approximately 25-30%, although only 5% of these patients actually develop symptoms from the recurrent hernia[4]. Nevertheless, concern remains that patients with an asymptomatic recurrence could develop problems later.

Mesh repair has been suggested as a strategy to prevent hernia recurrence, as it applies the principles of groin hernia repair, i.e. tension-free repair with prosthetic reinforcement, and it is technically straightforward to perform laparoscopically. Whilst good results have been reported from case series of mesh repair, some surgeons are concerned that the potential advantages of mesh repair might be offset by the risk of the mesh eroding into the esophageal lumen, and other complications[5]. Difficulties also occur when assessing the outcomes of mesh repair, as there is great variability between mesh types and configurations, and little standardization of surgical techniques.

Three randomized trial have examined the impact of mesh repair of the esophageal hiatus, two in the context of very large hiatus hernia[6,7,8,9]. In one study, Frantzides et al enrolled 72 patients to undergo repair with sutures vs. a piece of polytetrafluoroethylene mesh and the results at median 2.5 years follow-up showed a reduction in hernia recurrence from 22% to 0%[6]. In a second study, Oeschlager et al reported 6 month outcomes from a multicenter trial of 108 patients who underwent repair with sutures vs. an absorbable mesh, and hernia recurrence was reduced from

24% to 9% at short term follow-up[7]. Later follow-up, however, revealed no outcome differences[8].

Currently, there remains uncertainty about the preferred technique for repair of very large hiatus hernia, with surgeons disagreeing about whether or not to use mesh, and if mesh is used, what type of mesh and what configuration is optimal. To inform this debate we conducted a multi-center prospective double-blinded randomized trial designed to determine the effectiveness of mesh repair for very large hiatus hernia. In this study we compared a sutured repair technique with 2 different mesh types - absorbable vs. non-absorbable, with posterior placement of mesh for hiatal repair.

METHODS

In this multicentre prospective double blind randomized controlled trial, 3 laparoscopic methods for repair of very large hiatus hernia were compared; repair using sutures alone vs. sutures and absorbable mesh vs. sutures and non-absorbable mesh. The study tested the hypothesis that the incidence of post-operative hiatus hernia would be reduced by the addition of mesh reinforcement to a standardized suture repair technique, with the primary outcome determined by the integrity of the hiatal repair assessed by barium meal X-ray and upper gastrointestinal endoscopy.

Trial design

The trial was undertaken in 4 centers in Adelaide and Melbourne, Australia. All surgery was performed by or directly supervised by one of 9 upper gastrointestinal surgeons, and undertaken within a university teaching hospital or an associated private hospital. All individuals undergoing elective laparoscopic repair of a very large hiatus hernia, irrespective of age, were considered for entry. A very large hiatus hernia was defined as containing at least 50% of the stomach. Patients were excluded if they had undergone previous surgery involving the stomach or the esophago-gastric junction, or if they required any additional procedure in addition to hiatus hernia repair.

Patients were consented before surgery, and randomized 1:1:1 in the operating room after commencing the operation to one of 3 groups;

a) Repair using sutures alone
b) Repair using sutures reinforced by absorbable mesh (4 ply Surgisis® ES, Cook Biotech, Indiana, USA)
c) Repair using sutures reinforced by non-absorbable mesh (Timesh®, PFM Medical, Köln, Germany).

Randomization was undertaken by opening a sealed envelope. The envelopes were prepared before commencing the trial and shuffled independently by 2 research nurses. More envelopes were prepared than needed to ensure that the randomization could not be anticipated by the operating surgeon. Patients were not told which operation variant was performed, and clinical follow-up was undertaken by a research nurse who was blinded to the

surgical procedure. Objective follow-up investigations were also performed in a blinded fashion.

Preoperative workup included endoscopy and barium meal X-ray. Esophageal manometry and pH monitoring was used selectively in patients with significant reflux symptoms, but often omitted in patients in whom the indication for surgery was mechanical symptoms resulting from the very large hernia in whom an anterior partial fundoplication was planned as a gastropexy.

Operating Technique

Before commencing the trial surgical techniques were standardized across sites following a consensus meeting between the participating surgeons, and exchange of videos of the standard operating techniques. Laparoscopic repair was commenced in a similar fashion. The initial steps entailed full dissection of the hiatus hernia sac from the mediastinum, and complete reduction of the sac's contents into the abdomen[10]. An esophageal lengthening procedure was never added. The hiatal defect was narrowed to a diameter of approximately 2.5cm using posterior hiatal sutures, supplemented by additional anterior hiatal sutures if needed to achieve an adequate closure. In patients randomized to one of the 2 mesh repair groups, a rectangular piece of mesh (Surgisis or Timesh) measuring 2-3cm high x 4-5cm wide was cut and placed over the posterior hiatal repair sutures and the hiatal pillars, but not around the esophagus. The mesh overlapped the left and right hiatal pillars behind the esophagus, and did not encircle the esophagus. It was anchored in place using either sutures or a mechanical "tacker" (ProTack, Covidien). The mesh repair aimed to reinforce the sutured hiatal repair, and it applied a similar technique to that reported by Granderath et al[9], but using a larger piece of mesh. A fundoplication was then constructed in all patients, with the choice of the fundoplication type at the operating surgeon's discretion. If any laparoscopic procedure was converted to an open procedure, the randomization schedule was still followed, and if any procedure varied from the trial allocation, the patient remained in the trial and their allocated group for subsequent (intention to treat) analysis.

Postoperative Care

Following surgery patients were allowed oral fluids on the day of surgery, and soft food the next day. A barium meal X-ray was performed routinely before discharge, to detect any early problems amenable to early laparoscopic reintervention, and to confirm integrity of hiatal

repair at the time of discharge. If the appearances were unsatisfactory, the operation site was reinspected laparoscopically and action taken based on the findings.

Follow-up assessment

The primary outcome for the trial was recurrence of hiatus hernia. Hernia recurrence was determined 6 months after surgery using 2 objective investigations - Barium meal X-ray and upper gastrointestinal endoscopy. A recurrent hiatus hernia was defined as any evidence of stomach above the level of the diaphragm, irrespective of size. A subgroup of patients with a recurrent hernia which was 2cm or greater vertical height was also identified. Barium meal X-rays were reported by radiologists blinded to the details of the hiatal repair technique and reporting was checked by experienced upper gastrointestinal surgeons. Endoscopy was also undertaken in a blinded fashion by upper gastrointestinal surgeons who were experienced in assessing esophago-gastric anatomy after antireflux surgery.

Secondary outcomes were clinical symptom scores, and clinical recurrence of the hernia leading to reintervention. Symptoms were assessed 1, 3, 6 and 12 months after surgery, and analysis and data collection aimed to identify post-operative reflux symptoms, post-operative side effects, and overall satisfaction with the outcome following surgery. To evaluate these outcomes, all patients were interviewed before surgery and at 1, 3, 6 and 12 months after surgery and using a structured questionnaire. Longer term follow-up is continuing and outcomes will be reported when available. The structured questionnaire was similar to a questionnaire used in other studies reported by our group[11]. Follow-up data was collected by telephone interview by research nurses based in Adelaide. The presence or absence of the following symptoms was sought; heartburn, chest pain, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids and liquids, odynophagia, early satiety, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing and wheezing, and diarrhea. The ability to relieve bloating and whether a normal diet was being consumed was also determined.

Zero to 10 analog scales (0 = no symptoms, 10 = severe symptoms) were used to assess heartburn, dysphagia for liquids, and dysphagia for solids. A validated dysphagia score (0 = no dysphagia, 45 = severe dysphagia) which combines information about difficulty swallowing 9 types of liquids and solids was also applied[12]. Overall outcome was determined using 3 previously described scores[11]. Patients ranked the outcome of surgery using a

modified Visick grading (score 1 to 5, 1=no symptoms, 5=worse after surgery), an outcome score (excellent, good, fair, or poor), and an analog satisfaction score (0 = dissatisfied, 10 = satisfied). A quality of life assessment was also performed using the SF-36 questionnaire, but this data will be analyzed and reported elsewhere.

Statistics and Sample size

Before commencing the trial, a power calculation determined that 126 patients (42 per group) would be required to demonstrate a 25% difference (30% vs. 5%) between groups for radiological recurrence of hiatus hernia, at a significance level of $P<0.05$, and power of 80%. The proposed magnitude of difference was based on reported outcome differences from the randomized trial reported by Frantzides et al[6], and objective outcome studies reported by us[4] and others[13]. The sample size was also determined to be sufficient to demonstrate a 13% difference (18% vs. 5%) for a 2-way comparison of mesh vs suture repair. All data were entered into a computerized data base (FileMaker Pro version 12). Data was analyzed within the database or exported to GraphPad Prism Version 6.0 (GraphPad Software Inc.) for statistical testing. Analyses were undertaken on an intention to treat basis with patients classified according to randomization. The 3 groups were compared separately. The Chi-squared test was used to evaluate 3x2 contingency tables. Comparisons of continuous data sets was undertaken using One-way Analysis of Variance (ANOVA).

The protocol for this trial was approved by the Southern Adelaide Clinical Human Research Ethics Committee, and the Clinical Research Ethics Committees for all other participating hospitals.

RESULTS

From February 2006 to September 2012, 126 patients were enrolled in the trial. Forty three were randomized to undergo repair using sutures alone, 41 repair with absorbable mesh (Surgisis) and 42 non-absorbable mesh (Timesh). Of the 126 patients entered, 117 (92.9%) were interviewed 1 month after surgery, 118 (93.7%) at 3 months, 122 (96.8%) at 6 months, and 121 (96.0%) at 12 months. Objective follow-up data was available for 117 (92.9%) at 6 months follow-up. Follow-up is summarized in Figure 1. No patient withdrew from the study. Missing data were the result of an inability to contact patients at specific follow-up intervals. One patient in the suture repair group died 7 days after surgery (see below).

Preoperative Assessment

The preoperative demographic details for the 3 groups of patients were similar, and are summarized in Table 1. Preoperative symptom scores are summarized in Table 2, 3, 4, 5 and 6. Less patients in the Timesh group reported heartburn or chest pain symptoms before surgery. The mean chest pain score was also lower in this group (Table 3), and more patients in the Timesh group reported a Visick score of 1 or 2 before surgery (Table 6). All other preoperative symptoms were similar for the 3 groups.

Surgery

As randomization occurred in the operating room, all patients underwent surgery. One patient randomized to repair with Timesh underwent a sutured repair only and the non-absorbable mesh was not placed. The operating surgeon for that patient encountered a very wide hiatus, with the aorta encompassing the area where the left hiatal pillar is usually found, and was not able to suture a piece of mesh in place. All other patients underwent surgery according to the randomization schedule. Operating time and the number of sutures used for hiatal repair was similar for all 3 groups (Table 7). A fundoplication was added in all patients, and in all but 2 a partial fundoplication was constructed.

Two (1.6%) patients were thought to have a shortened esophagus at surgery - one in the suture repair group and one in the Timesh group. An esophageal lengthening procedure was not performed in any patient enrolled in the trial. Two procedures were converted to open

surgery, both in the suture repair group, due to a bleeding short gastric blood vessel and intra-abdominal obesity respectively. Intra-operative complications are listed in Table 8. One patient in the Surgisis group experienced an esophageal perforation during placement of an esophageal bougie. This was initially sutured, but then managed with a temporary esophageal stent inserted on the 10th day after surgery.

Early Hospital Outcomes

The mean length of stay following surgery was similar for the 3 groups (Sutures - 4.2 days, Surgisis - 4.3, Timesh - 4.3). Post-operative complications occurred in a similar proportion of patients in all groups, and are summarized in Table 8. Four patients underwent early laparoscopic reoperation in the suture repair group, and one patient died suddenly 7 days after surgery following a presumed pulmonary embolus or myocardial infarct. In the Surgisis group one patient experienced an esophageal perforation which was initially repaired with sutures, but eventually required placement of a temporary esophageal stent 10 days later. In the Timesh group 3 patients underwent early reoperation, with one of these converted to an open procedure to excise part of the gastric fundus which was perforated at the site of the fundoplication sutures. Both of the patients thought to have a shortened esophagus developed an acute hiatus hernia and underwent early revision surgery with re-repair of the hiatus, Both subsequently had an excellent clinical outcome, and did not have a hernia when assessed objectively at 6 months. Two (1.6%) late revision procedures were performed, one for a recurrent hiatus hernia following suture repair and one for dysphagia following repair with Timesh.

Objective Postoperative Investigations

The outcomes for the objective assessment with barium meal radiology and endoscopy are summarized in Table 9. There were no statistically significant differences in the rate of recurrent hiatus hernia between the 3 groups for any comparisons. 100 (79.4%) underwent barium meal radiology at 6 months, and 100 (79.4%) underwent endoscopy. 117 (92.9%) underwent at least one of these 2 investigations. Using barium meal radiology, a recurrent hiatus hernia of any size was identified in 22 (22.0%), and a hernia measuring 2 or more cm in length was identified in only 3 (3.0%). Using endoscopy, a recurrent hiatus hernia of any size was identified in 32 (32.0%), and a hernia measuring 2 or more cm in length was identified in 8 (8.0%). The objective outcome data for both tests was combined for a re-

analysis which prioritized the barium meal outcome assessment and supplemented the endoscopy outcome assessment in the patients who had not undergone a barium meal. With this analysis a recurrent hiatus hernia of any size was identified in 26 (22.2%), and a hernia measuring 2 or more cm in length was identified in 5 (4.3%). When this definition of hernia recurrence was used to compare Mesh repair (both mesh types) vs repair with only sutures, the rate of hernia recurrence was 17/78 (21.8%) vs. 9/39 (23.1%; P=1.00, Fisher's exact test), and 3/39 (7.7%) vs. 2/78 (2.6%; P=0.329) for hernias measuring 2 or more cm in length.

One- to 12-Month Postoperative Clinical Outcome

The clinical follow-up outcomes at 1, 3, 6 and 12 months are summarized in Tables 2, 3, 4, 5 and 6. Heartburn analog symptom scores were significantly lower in the Timesh group at 3 and 6 months, with higher scores in the Surgisis group (Table 2). Chest pain and dysphagia scores were similar at all follow-up points (Tables 3 and 5). A range of other symptom scores were significantly worse in the Surgisis group - odynophagia at 1 month, nausea at 3 and 12 months, wheezing at 6 months, and inability to belch at 12 months (Table 4). In addition, the patients in the Timesh group were less likely to report bloating at 12 months. Scores of overall satisfaction were similar for all 3 groups (Table 6). None of the 5 patients with a post-operative hernia of 2 or more cm in length identified primarily by barium meal (supplemented by endoscopy assessment in those who did not undergo barium meal) underwent revision surgery within the follow-up period. Four of the 5 reported an excellent clinical outcome at 12 months, with satisfaction scores of 8, 9, 9, and 10, and no significant symptoms. One of the 5 (Surgisis group) reported bloating and chest pain, and a satisfaction score of 5. At 12 months follow-up this patient was being considered for possible revision surgery.

DISCUSSION

The reports of good early outcomes for hiatal repair with mesh in randomized trials of mesh vs. sutured repair of large hiatus hernias has encouraged the wider use of mesh for repair for very large hiatus hernias, despite concerns about the risk of mesh erosion and added difficulties if subsequent surgical revision is required. At follow-up of up to 12 months, our trial identified no major differences for mesh vs. sutured repair of very large hiatus hernias. In particular, no significant differences were seen between the 3 repair types for the primary study outcome of hernia recurrence measured by barium meal radiology and endoscopy. The secondary outcomes which were measured by the clinical questionnaire also revealed no major differences in overall outcome, although there were some statistically significant differences between heartburn scores, and the incidences of nausea and bloating, with the outcomes pointing towards a somewhat poorer clinical outcome following repair with Surgisis, and a better outcome for Timesh due to less bloating issues. However, most clinical outcomes were similar for all 3 repair types, and the differences were probably insufficient to support any claim that one particular technique was better then the others.

The outcomes from our study differ from those reported in the 3 other published randomized trials of mesh vs. sutured repair, which all reported a reduced incidence of hiatus hernia after mesh repair. In the study reported by Frantzides et al the incidence of hernia recurrence at median 2.5 years follow-up was reduced from 22% to 0%[6]. Oelschlager et al reported a reduction from 24% to 9% at 6 months follow-up[7], and Granderath et al reported a reduction from 26% to 8% at 12 months[9]. In Frantzides et al's trial patients underwent repair using a piece of polytetrafluoroethylene mesh that encircled the esophagus. The 0% recurrence rate after mesh repair in this study was not replicated in the other trials, perhaps reflecting the encirclement of the esophagus by the mesh prosthesis. However, many surgeons remain reluctant to place mesh fully around the esophagus because of the perceived risks of mesh erosion and hiatal fibrosis at longer term follow-up[5]. Unfortunately, because late follow-up from this study has not been reported, Frantzides et al's results have not addressed this issue.

Oelschlager et al used Surgisis to reinforce the hiatus posteriorly and around the sides of the esophagus[7]. In their trial, the early results at 6 months follow-up appeared promising[7]. However, a subsequent report of 5 years follow-up revealed very high recurrence rates of 59% vs. 54% in the two groups, and provided little support for repair with absorbable mesh[8]. In this trial

Oelschlager et al defined a hiatus hernia to be present if it exceeded 2cm in vertical length. This was different to our study, in which as we included all hernias, irrespective of their size. When a similar definition of hernia size ≥2cm was applied in our trial, the "hernia" recurrence rate was substantially lower (Table 9), and only 5 patients were identified by barium meal radiology (supplemented by endoscopy) to have a hernia larger than 2cm.

Granderath et al's randomized trial included patients undergoing laparoscopic Nissen fundoplication for gastro-esophageal reflux with or without a hiatus hernia, and enrolled a different set of patients to those included in the other 2 trials and our current trial[9]. Hence, it did not directly address the issue of how best to repair a large hiatus hernia. Their technique did, however, entail a posterior hiatal repair with sutures which was reinforced by an on-lay of a 3x1cm piece of polypropylene mesh, a similar approach to that used in our trial, although we used a larger piece of mesh. Their main outcome measure was the incidence of fundoplication migration into the mediastinum, and in their control group this occurred in 26% of patients. In a report from an earlier randomized trials conducted in our Departments, we identified a much lower 6% incidence of fundoplication migration using barium meal X-ray 6 months after surgery in patients who underwent a sutured hiatal repair with no mesh[11].

Three patients in the suture repair group in the current trial underwent early laparoscopic reoperation for an acute hiatus hernia, and one required revision for a hiatus hernia at 7 months, compared to one early recurrence in the non-absorbable mesh group and none in the absorbable mesh group. This was offset, however, by a higher number of patients in the absorbable mesh groups found to have a hiatus hernia at 6 months, and a more revision procedures for a tight hiatal repair in the non-absorbable mesh group. When all of these outcomes are considered together, the risk of adverse outcomes appeared to be similar for all repair types. Further, we have always applied a low threshold for early laparoscopic re-exploration of the operative site within the first few days, and our experience has confirmed that correction of potential problems identified by contrast radiology in the first few days, has a minimal impact on recovery, and minimizes the risk of later more difficult revision surgery[14].

There are several factors that might impact on recurrence rate following laparoscopic repair of a very large hiatus hernia, including surgeon experience and technique. Our trial was commenced in 2006, and the surgeons contributing patients all had substantial prior experience with the techniques used in the trial. In addition, care was taken to preserve the fascial coverings over the

edges of the hiatus as these provide support for hiatal repair sutures[2]. If not protected, the hiatal muscle can be exposed and the hiatal defect enlarged by the process of hiatal dissection until it cannot be closed without mesh. In our trial, the hiatus was closed adequately by sutures in all patients.

Strengths of our trial include a very high rate of clinical and objective follow-up, blinding of the patients and the follow-up process, and few exclusions. The trial was run across multiple sites in the public and private sectors in Australia and the results should be generalizable, at least in the Australian context where repair of very large hiatus hernias is usually undertaken by experienced upper gastrointestinal surgeons. Limiting the generalizability of the results, however, is the testing of only one mesh configuration. However, the configuration was similar to that used in 2 of the 3 previous randomized trials. When establishing the protocol for the trial there was no enthusiasm in Australia for encircling the esophagus with mesh as some surgeons had encountered problems with mesh erosion and hiatal fibrosis in patients in whom the technique described by Frantzides et al[6] had been used. For this reason, posteriorly placed mesh reinforcement of a sutured hiatal repair was the most acceptable approach for the participating surgeons. However, care should be taken before trying to extrapolate the results of our trial to mesh repair using different mesh shapes and different mesh placement techniques.

The follow-up in our trial is currently limited to 12 months, and the outcomes from Oelschlager et al's trial do suggest that results can change with more extended follow-up[8], so longer term follow-up to confirm our initial findings is also needed. This is underway. Further barium meal radiology and endoscopy examinations are scheduled for 3-4 years after surgery and the outcomes will be reported when they becomes available. Another potential weakness is that a large number of clinical outcomes were evaluated, and there is a risk of false positive P values with multiple data analyses. However, the trend data and positive P values consistently pointed to a somewhat poorer clinical outcome in the group who underwent repair with Surgisis, although the magnitude of these differences are unlikely to be clinically significant. With a larger trial, however, the trend towards a higher hernia recurrence rate following Surgisis repair, might have become statistically significant.

The outcomes of our trial have shown no significant differences for the assessed primary outcome - recurrent hiatus hernia at radiology or endoscopy, and in general, the clinical

outcome differences between the 3 techniques were small and unlikely to be clinically significant. The rate of recurrent hiatus hernia measuring 2cm or greater in size was low across all groups. The results of this randomized trial do not add support for the routine use of mesh repair of very large hiatus hernias.

Acknowledgements

This randomized trial was supported by Research Project Grants from the National Health and Medical Research Council (NHMRC) of Australia - Grant numbers 375111 and 1022722. We are grateful for the assistance of Tanya Irvine, Nicky Carney and Lorraine Sheehan-Hennessy who contributed to data collection.

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TABLES

Table 1: Preoperative parameters

Variable	*Randomization* *Suture repair*	*Surgisis*	*Timesh*	*p value*
Age (yrs)	67.8 (64.7 to 70.9)	68.0 (65.1 to 70.9)	68.1 (64.7 to 71.5)	0.991
Gender (M:F)	14:29	10:31	16:26	0.403
Height (cm)	1.65 (1.63 to 1.70)	1.64 (1.61 to 1.68)	1.66 (1.63 to 1.70)	0.556
Weight (kg)	82.5 (77.3 to 87.7)	78.7 (74.0 to 83.4)	79.4 (73.7 to 85.0)	0.516
BMI	29.6 (28.0 to 31.2)	29.4 (27.8 to 31.0)	28.5 (26.6 to 30.5)	0.663
Duration of symptoms (yrs)	9.7 (6.2 to 13.1)	10.2 (5.9 to 14.2)	7.3 (4.6 to 10.0)	0.496

All data are expressed as mean (95% CIs) or n (%). ANOVA used to compare continuous data sets, Chi-squared test used to assess categorical variables.

Table 2: Assessment of Heartburn using 0-10 Visual Analog Scale

	Sutures	*Surgisis*	*Timesh*	*p value*
Preoperative	2.24 (1.29 to 3.20)	2.05 (1.18 to 2.92)	1.65 (0.86 to 2.44)	0.614
Postoperative				
1 month	0.58 (0.092 to 1.07)	0.69 (0.027 to 1.36)	0.73(0.098 to 1.35)	0.936
3 months	0.45 (0.062 to 0.84)	1.57 (0.60 to 2.54)	0.38 (-0.19 to 0.96)	**0.022**
6 months	1.49 (0.58 to 2.40)	1.44 (0.48 to 2.40)	0.17 (-0.092 to 0.44)	**0.024**
12 months	1.10 (0.45 to 1.76)	1.28 (0.37 to 2.20)	0.55 (0.059 to 1.04)	0.303

All data are expressed as mean (95% CI's)

Table 3: Assessment of Chest Pain using 0-10 Visual Analog Scale

	Sutures	*Surgisis*	*Timesh*	*p value*
Preoperative	2.88 (1.74 to 4.02)	4.35 (3.13 to 5.57)	1.45 (0.57 to 2.31)	**0.0013**
Postoperative				
1 month	1.34 (0.52 to 2.22)	1.36 (0.52 to 2.20)	1.13 (0.29 to 1.97)	0.903
3 months	1.19 (0.39 to 1.99)	1.60 (0.67 to 2.52)	0.74 (0.03 to 1.46)	0.343
6 months	0.83 (0.26 to 1.40)	1.20 (0.46 to 1.94)	0.54 (-0.05 to 1.12)	0.329
12 months	0.82 (0.14 to 1.51)	1.10 (0.37 to 1.83)	0.38 (-1.04 to 0.85)	0.261

All data are expressed as mean (95% CI's)

Table 4: Preoperative and Postoperative symptoms assessed using yes vs. no questions

	Preop			*1 mth*			*3 mths*			*6 mths*			*12 mths*		
Symptom	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*
Heartburn	**66.7%**	**63.4%**	**40.5%***	15.8%	10.3%	15.0%	14.3%	24.3%	5.1%	31.7%	20.0%	12.2%	25.0%	27.5%	14.6%
Chest pain	**45.2%**	**61.0%**	**31.0%**§	26.3%	25.6%	17.5%	19.0%	21.6%	12.8%	14.6%	22.5%	9.8%	15.0%	15.0%	4.9%
Epigastric pain	50.0%	53.7%	54.8%	21.1%	35.9%	35.0%	21.4%	37.8%	20.5%	31.7%	25.0%	29.3%	25.0%	27.5%	12.2%
Regurgitation	66.7%	51.2%	61.9%	2.6%	12.8%	12.5%	9.5%	21.6%	10.3%	26.8%	17.5%	12.2%	15.0%	25.0%	17.1%
Odynophagia	14.3%	9.8%	4.8%	**0%**	**7.7%**	**0%¶**	2.4%	5.4%	2.6%	4.9%	5.0%	2.4%	2.5%	2.5%	0%
Early Satiety	54.8%	54.8%	50.0%	52.6%	56.4%	60.0%	57.1%	37.8%	41.0%	46.3%	47.5%	39.0%	45.0%	50.0%	29.3%
Epigastric bloat	64.3%	70.7%	47.6%	39.5%	30.8%	32.5%	35.7%	40.5%	17.9%	39.0%	37.5%	19.5%	**42.5%**	**42.5%**	**19.5%**ξ
Anorexia	33.3%	24.4%	23.8%	31.6%	35.9%	30.0%	21.4%	18.9%	20.5%	12.2%	17.5%	14.6%	12.5%	20.0%	4.9%
Nausea	35.7%	24.4%	50.0%	26.3%	15.4%	15.0%	**4.8%**	**27.0%**	**10.3%θ**	12.2%	22.5%	17.1%	**15.0%**	**27.5%**	**4.9%**ψ
Vomiting	21.4%	31.7%	31.0%	2.6%	7.7%	5.0%	2.4%	5.4%	0%	9.8%	12.5%	4.9%	7.5%	15.0%	2.4%
Coughing	38.1%	41.5%	26.2%	8.3%	7.7%	7.5%	11.9%	5.4%	10.3%	14.6%	17.5%	17.1%	12.5%	17.5%	9.8%
Wheezing	28.6%	22.0%	11.9%	2.6%	5.1%	5.0%	7.1%	5.4%	7.7%	**0%**	**15.0%**	**7.3%**Φ	7.5%	17.5%	9.8%
Can relieve bloat	69.0%	47.5%	55.0%	73.7%	66.7%	60.0%	71.4%	54.1%	74.4%	73.2%	67.5%	75.6%	**92.5%**	**72.5%**	**97.5%¶**
Eats normal diet	59.5%	50.0%	65.0%	42.1%	30.8%	25.0%	83.3%	70.3%	82.1%	75.6%	77.5%	87.8%	92.5%	85.0%	95.0%
Diarrhea	NA	NA		28.9%	15.4%	27.5%	16.7%	13.5%	7.7%	19.5%	27.5%	12.2%	25.0%	17.5%	19.5%
Increased flatus	NA	NA		57.9%	64.1%	55.0%	66.7%	62.2%	56.4%	58.5%	62.5%	48.8%	57.5%	47.5%	41.5%

All data is % patients interviewed at each time point.
No statistically significant differences were demonstrated between the three groups (p=>0.05 at all follow up intervals) except where indicated
* p=0.031, § p=0.023, ¶ p=0.046, θ p=0.0119, Φ p=0.0328, ξ p=0.0424, ψ p=0.0197, ¶ p=0.0017

Table 5: Dysphagia Assessment

	Preop			*1 mth*			*3 mths*			*6 mths*			*12 mths*		
	Sutures	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*
Dysphagia															
Lumpy solids	42.9%	41.5%	31.0%	18.4%	30.8%	12.5%	23.8%	24.3%	15.4%	19.5%	15.0%	9.8%	15.0%	17.5%	19.5%
Soft solids	14.3%	19.5%	11.9%	5.3%	7.7%	5.0%	7.1%	5.4%	5.1%	0%	5.0%	4.9%	2.5%	5.0%	2.4%
Liquids	11.9%	19.5%	14.3%	7.9%	7.7%	7.5%	7.1%	0%	2.6%	0%	10.0%	0%	2.5%	5.0%	0%
Visual analog scale															
Solids	2.7 (1.6-3.8)	3.2 (2.1-4.4)	2.2 (1.1-3.3)	1.4 (0.5-2.2)	2.3 (1.2-3.5)	1.3 (0.4-2.2)	1.8 (0.9-2.6)	1.6 (0.7-2.5)	1.4 (0.3-2.4)	1.3 (0.15-2.2)	1.2 (0.5-1.9)	1.1 (0.3-1.8)	1.1 (0.4-1.9)	1.5 (0.7-2.2)	1.1 (0.3-1.8)
Liquids	0.9 (0.1-1.6)	1.4 (0.6-2.2)	1.0 (0.2-1.8)	0.3 (-0.2-0.8)	0.7 (0.2-1.3)	0.4 (-0.1-0.9)	0.3 (-0.1-0.7)	0.5 (-0.1-1.2)	0.3 (-0.1-0.7)	0.2 (-0.04-0.5)	0.5 (0.04-0.9)	0.07 (-0.1-0.2)	0.3 (-0.1-0.7)	0.5 (0.1-0.9)	0.0 (0.0-0.0)
Dysphagia score (0-45)															
Overall score	6.9 (3.9-10.0)	8.8 (5.3-12.4)	8.7 (4.5-13.0)	11.7 (7.8-15.6)	18.7 (14.9-22.5)	17.6 (14.2-20.9)	5.1 (2.7-7.5)	7.2 (3.5-11.0)	4.2 (1.3-7.1)	4.8 (2.3-7.4)	4.9 (1.9-7.8)	4.2 (1.5-6.9)	2.9 (1.0-4.8)	4.8 (1.9-7.8)	2.4 (0.8-4.0)
Scored 0 only	52.4%	47.5%	62.5%	44.7%	20.5%	20.0%	54.8%	56.8%	74.4%	61.0%	67.5%	70.7%	75.0%	62.5%	75.0%

All data given as percentages or mean (95% CIs).
No statistically significant differences were demonstrated between groups (p=>0.05 at all follow up intervals)

Table 6: Outcome scores, Satisfaction score and Visick Grading

	Preop			*1 mth*			*3 mths*			*6 mths*			*12 mths*		
	Sutures	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*	*Sutures*	*Surgisis*	*Timesh*
Outcome															
Excellent or Good	n/a	n/a	n/a	86.8%	79.5%	77.5%	95.2%	86.5%	89.7%	85.4%	87.5%	92.7%	90.0%	79.5%	95.0%
Fair or Poor	n/a	n/a	n/a	13.2%	20.5%	22.5%	4.8%	13.5%	10.3%	14.6%	12.5%	7.3%	10.0%	20.5%	5.0%
Modified Visick grade															
1&2	28.6%	15.0%	50.0%*	78.9%	79.5%	77.5%	92.9%	75.7%	87.2%	82.9%	85.0%	90.2%	87.5%	79.5%	95.0%
3, 4 & 5	71.4%	85.0%	50.0%*	21.1%	20.5%	22.5%	7.1%	24.3%	12.8%	17.1%	15.0%	9.8%	12.5%	20.5%	5.0%
Satisfaction score															
Mean score	n/a	n/a	n/a	8.6	8.3	8.5	9.4	8.6	9.2	8.3	8.4	9.5	8.8	8.2	9.4
95% CI	n/a	n/a	n/a	(8.0-9.3)	(7.5-9.1)	(7.7-9.2)	(9.1-9.7)	(7.7-9.5)	(8.6-9.8)	(7.5-9.1)	(7.6-9.2)	(9.1-9.9)	(8.3-9.4)	(7.3-9.2)	(9.0-9.8)
Correct decision to have operation	n/a	n/a	n/a	97.4%	97.3%	97.5%	97.6%	94.6%	100%	92.7%	97.5%	97.6%	97.5%	90.0%	97.5%

All data given as percentages or mean (95% CIs). n/a = not applicable
No statistically significant differences were demonstrated between groups (p=>0.05 at all follow up intervals), except * p=0.0030.

Table 7: Peri-operative outcomes

	Randomization			
	Suture repair	*Surgisis*	*Timesh*	*p value*
Operating time (mins)	111.8 (91.0-132.7)	110.3 (96.7-123.9)	111.8 (102.2-132.1)	0.831
Number of sutures used for hiatal repair	4.93 (4.37-5.49)	4.75 (4.41-5.36)	4.71 (4.06-5.36)	0.817
Fundoplication type	1 - Nissen 5 - Posterior partial 37 - Anterior partial	0 - Nissen 4 - Posterior partial 37 - Anterior partial	1 - Nissen 8 - Posterior partial 33- Anterior partial	

Data are expressed as mean (95% CIs).

Table 8 Complications and reoperations

	Randomization		
	Suture repair	*Surgisis*	*Timesh*
Intra-operative complications	2 - Pneumothorax 1 - Bleed from short gastric	1 - Pneumothorax 1 - Esophageal perforation	1 - Minor splenic injury
Major complications and revision operations (30 days)	1 - Tight hiatal repair (early reop) 3 - Acute hiatus hernia (laparoscopic reop) 1 - Death- day 7	1 - Esophageal perforation (stent on day 10)	2 - Tight hiatal repair (early reop) 1 - Acute hiatus hernia and gastric perforation (open reop)
Revision operations after 30 days	1 - Recurrent hiatus hernia (reop at 7 months)	nil	1 - Dysphagia (reop at 8 months)

Table 9: Radiology and Endoscopy outcomes at 6 months follow-up

	Sutures	*Surgisis*	*Timesh*	*p value*
Barium Meal Radiology				
Studied	n=31 (72.1%)	n=34 (82.9%)	n=35 (83.3%)	
Hiatus hernia -any size	7 (22.6%)	11 (32.4%)	4 (11.4%)	0.110
Hiatus hernia - 2cm+	1 (3.2%)	2 (5.9%)	0 (0.0%)	0.357
Endoscopy				
Studied	n=31 (72.1%)	n=34 (82.9%)	n=35 (83.3%)	
Hiatus hernia -any size	11 (35.5%)	13 (37.1%)	8 (22.9%)	0.346
Hiatus hernia - 2cm+	2 (6.5%)	3 (8.8%)	2 (5.6%)	0.858
Barium Meal and Endoscopy				
Underwent Barium meal or Endoscopy	n=39 (90.7%)	n=39 (95.1%)	n=39 (92.9%)	
Hiatus hernia -any size (Barium meal outcome prioritized)	9 (23.1%)	12 (30.8%)	5 (12.8%)	0.161
Hiatus hernia - 2cm+ (Barium meal outcome prioritized)	3 (7.9%)	2 (5.9%)	0 (0.0%)	0.223

All data expressed as n (%)

FIGURE LEGENDS

Figure 1 CONSORT diagram summarizing recruitment and follow-up compliance.

FIGURES

Figure 1