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Randomized Controlled Trial of Laparoscopic Anterior 180° Partial vs. Posterior 270° Partial Fundoplication

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Abstract

***Background*:** Previous trials show good outcomes following anterior and posterior partial vs. Nissen fundoplication for gastro-oesophageal reflux. However, it is unclear which partial fundoplication performs best. This study compared anterior 180^0 vs. posterior 270^0 fundoplication.

***Methods*:** At three hospitals patients were randomized to anterior 180° vs. posterior 270^0 partial fundoplication, and clinical outcomes were determined using a structured questionnaire at 3, 6 and 12 months. Heartburn, dysphagia and satisfaction were assessed using 0-10 analog scales, and adverse outcomes and side effects were determined. Endoscopy, manometry and pH monitoring were performed 6 months after surgery.

***Results*:** Forty-seven patients were randomized to anterior (n=23) vs. posterior (n=24) fundoplication. Clinical outcomes for 93-98% of patients were available at each follow-up point. At 12 months, the mean heartburn score was higher following anterior fundoplication (2.7 vs. 0.8, p=0.045), although differences were not significant at earlier follow-up. Conversely, following posterior fundoplication, patients were less able to belch at 3 (56% vs. 16%, p=0.013) and 6 months (43% vs. 9%, p=0.017). No significant differences were demonstrated for dysphagia. Both groups had high rates of satisfaction with the outcome - 85% vs. 86% satisfied at 12 months follow-up.

***Conclusion*:** Both partial fundoplications are effective treatments for gastro-oesophageal reflux. Posterior partial fundoplication is associated with less reflux symptoms offset by more side effects.

Key Words

Randomized controlled trial, Fundoplication, Laparoscopy, Gastro-oesophageal reflux disease

Trial registration – This trial is registered with the Australia and New Zealand Clinical Trials Registry ACTRN12605000035628

INTRODUCTION

Whilst medication is effective treatment for gastro-oesophageal reflux disease, some individuals respond poorly and require antireflux surgery. Previous randomized trials have shown good outcomes following both anterior and posterior partial vs. Nissen fundoplication for the treatment of reflux[1-9]. However, it is not clear which type of partial fundoplication performs best. Two comparative trials have been reported. A comparison of anterior 120^0 vs. posterior fundoplication showed equivalent satisfaction, but trade-offs between recurrent reflux vs. side effects[10]. The other study compared anterior 180^0 vs. posterior fundoplication and found similar outcomes[11]. However, different types of anterior fundoplication were used in these trials, and follow-up in the second study was 58% at 12 months. As the type of partial fundoplication which yields the best outcome remains uncertain, we undertook a prospective randomized trial of anterior 180^0 vs. posterior 270^0 partial fundoplication to compare the best performing anterior fundoplication variant[1] with a posterior fundoplication.

METHODS

Two techniques for laparoscopic partial fundoplication (anterior 180^0 vs. posterior 270^0) were compared. Five consultant surgeons from three teaching hospitals participated. The trial was approved by each hospital's research ethics committee, and consent was obtained from all participants. Initial outcomes at up to 12 months follow-up are reported.

All patients had objective evidence of gastro-oesophageal reflux, and symptoms that were not controlled by medication. Patients were randomized in the operating theatre to either anterior 180^0 or posterior 270^0 partial fundoplication by opening a sealed envelope. All patients undergoing laparoscopic fundoplication were considered for entry. Exclusion criteria were previous gastric surgery, large hiatus hernia, and a preference for Nissen fundoplication. Patients underwent preoperative investigation with oesophageal manometry and endoscopy. pH monitoring was performed selectively to confirm reflux in those without erosive oesophagitis, or with atypical symptoms.

Operative techniques were standardized. The lower oesophagus was dissected, with preservation of the hepatic branch of the vagus nerve and short gastric blood vessels, followed by posterior hiatal repair. Posterior partial fundoplication entailed placement of the gastric fundus behind the intra-abdominal oesophagus, with anchorage to the oesophagus on the right and left sides at the 10 and 2 o'clock positions, and also to the hiatal rim postero-laterally on the right side, leaving the anterior oesophagus uncovered. Details of the anterior 180^0 fundoplication have been described elsewhere[12]. The fundoplication was constructed by suturing the anterior wall of the fundus across the front of the oesophagus to attach it to the

postero-lateral wall of the oesophagus and the right hiatal pillar, and apical sutures were added to close the anterior hiatus.

Follow-up data was collected by a nurse who was blinded to the randomization, and patients were blinded to the type of partial fundoplication. Clinical follow-up used a standardized questionnaire (described elsewhere[13]). Patients were interviewed preoperatively, 3, 6 and 12 months after surgery by telephone. The presence of various symptoms was sought: heartburn, epigastric pain, regurgitation, dysphagia for lumpy solids, soft solids, fluids, odynophagia, inability to belch, post prandial fullness, epigastric bloating, anorexia, nausea, vomiting, nocturnal coughing, wheezing, diarrhea and increased flatulence, ability to relieve bloating and consumption of a normal diet. The severity of heartburn, dysphagia for solids and dysphagia for liquids was determined using analog scores (0 = no symptoms, 10 = severe symptoms). A validated dysphagia score (0 = no dysphagia, 45 = severe dysphagia) which integrated dysphagia for various liquids and solids was also applied[14].

Overall outcome was determined by asking whether patients thought that their decision to have surgery was correct, and by grading the outcome using a previously described Visick grade[13], an outcome grade[13] - excellent, good, fair vs. poor, and analog satisfaction score (0 = dissatisfied, 10 = satisfied). Objective investigation was undertaken approximately 6 months after surgery using endoscopy, oesophageal manometry and 24 hour pH monitoring.

A power calculation determined that 100 patients would be needed to demonstrate a 20% difference in measures of reflux or dysphagia at $p<0.05$ and power = 80%. Analyses were performed on intention to treat basis. Data were analyzed using SPSS version 19.0. Fisher's

exact test was used to assess contingency tables, and the Mann Whitney test to assess continuous data sets. Significance was accepted at $p<0.05$.

RESULTS

Forty-seven patients (12 men, 35 women) underwent surgery from September 2005 to February 2012. Twenty-three were randomized to anterior and 24 to posterior fundoplication. Groups were well matched (Tables 1-5). Twenty-four hour pH monitoring was performed before surgery in 85%, with mean % pH<4 in 13.8% in the anterior group vs. 11.2% in the posterior group (p=0.081).

All but one patient had a fundoplication constructed as randomised. In one an attempt was made to perform a posterior fundoplication, but as a satisfactory posterior fundoplication could not be fashioned an anterior fundoplication was constructed. Operating time ranged from 30-147 minutes (mean 87.2) in the anterior group vs. 32-146 (mean 90.4; p=0.767) in the posterior group.

Both groups recommenced oral intake at a similar time (0.7 vs. 0.8 days), and the hospital stay was also similar (1.8 vs. 1.7 days). Two complications occurred in each group; anterior group - umbilical wound infection and severe shoulder pain; posterior group - cardiac arrhythmia requiring anticoagulation, and unsuccessful re-exploration 2 days after surgery for a lost suture needle.

Completeness of clinical follow-up was 95.7% at 3 months, 95.7% at 6 months, and 93.6% at 12 months. Two patients were not contactable during early follow-up. One was not willing to be interviewed using the questionnaire, but did indicate he was happy with his outcome. Another patient withdrew due to communication problems associated with a previous laryngectomy. One patient did not contribute data at 12 months as her husband had just died.

Tables 2, 3, 4 and 6 summarize the clinical outcomes. Significant differences were seen for nausea, belching, and heartburn. All other outcomes were similar. In the posterior group more patients reported nausea at 12 months, and more reported they were unable to belch at 3 and 6 months. Heartburn outcomes are summarized in Tables 2 and 3. For most questions the outcomes were similar at 3 and 6 months. However, the heartburn score was higher in the anterior group at 12 months (Table 2). There were no significant differences for dysphagia (Table 4). Satisfaction with the outcome was similar for the 2 groups (Table 6). No patients underwent revision surgery during the follow-up period.

Endoscopy was undertaken at 6 months in 32 (68%) patients, oesophageal manometry in 27 (57%), and pH monitoring in 26 (55%). At endoscopy, 2 patients in the anterior group had a "loose" fundoplication. One of these also had a small sliding hiatus hernia. The fundoplication appeared intact in all patients in the posterior group. No significant differences were seen for manometry outcomes (Table 5). Of the patients who underwent pH studies, 3 had abnormal acid exposure; posterior group - 1, anterior group - 2. Only one (anterior group) reported reflux symptoms, and all 3 reported high satisfaction scores (8, 9, and 10). The median percentage time for pH<4 was 0.05% in the anterior group vs. 0.30% in the posterior group ($p=0.668$).

DISCUSSION

Despite the good control of reflux achieved by Nissen fundoplication, the occurrence of undesirable side effects in some patients has led to the procedure being modified. Partial fundoplications probably offer the best opportunity to reduce side effects without compromising reflux control. Level 1 evidence from meta-analyses of randomized trials supports the use of posterior and anterior partial fundoplications as alternatives to the Nissen procedure[6,8], but comparisons between the different partial fundoplications are limited.

Thirteen randomized trials have compared posterior vs. Nissen fundoplication[4-7].. In general, these have shown equivalent reflux control, with the larger trials showing less wind-related side effects after posterior fundoplication. However, only 2 trials demonstrate less dysphagia following posterior partial fundoplication[5,7], both at relatively short term follow-up. Five randomized trials have compared anterior 180^0 partial vs. Nissen fundoplication[1,2,8], These trials also report similar control of reflux for anterior 180^0 partial vs. Nissen fundoplication, but less dysphagia and wind related side effects. Two other trials have compared anterior 90^0 partial with Nissen fundoplication[3,9], and shown similar overall satisfaction, but a trade-off between better reflux control following Nissen vs. less side effects following anterior 90^0 fundoplication.

As the trials of partial vs. Nissen fundoplication suggest good outcomes for both partial fundoplication variants, the next step is to compare anterior vs. posterior partial fundoplication. Two trials have done this[10, 11]. A trial from Sweden enrolled 95 patients to anterior 120^0 vs. posterior fundoplication[10], and the results at 5 years showed similar satisfaction, but better reflux control following posterior offset against less side effects

following anterior fundoplication[10]. The anterior 120° partial fundoplication was different to the anterior 180^0 variant performed in the current study in which the fundus was sutured to the right hiatal pillar. A second trial from Sheffield, UK, compared anterior 180° vs. posterior partial fundoplication[11], and showed less dysphagia following anterior 180° fundoplication at 3 months, offset by a higher proportion of patients in the anterior fundoplication group reporting early heartburn symptoms. A weakness of that trial was the incomplete follow-up at 12 months.

Our findings support the observations from these two studies. At up to 12 months we identified similar levels of satisfaction, but a trade-off between reflux vs. side effects. Inability to belch was more common after posterior fundoplication, but the heartburn scores were higher after anterior 180^0 partial fundoplication at 12 months, consistent with the trend towards higher pH scores. Dysphagia rates were similar between the two groups at all time points.

A weakness of our study was the failure to recruit 100 patients. Hence, some analyses might be underpowered. The reasons for this were complex. We originally established a protocol to randomize to Nissen vs. anterior vs. posterior fundoplication. Consensus was sought from across Australia, and enthusiasm was expressed for the original protocol. However, most surgeons had difficulty achieving equipoise for all 3 procedures and were unwilling to randomize. To address this, the Nissen arm was dropped, and the trial was changed to the reported two-arm trial. Whilst it was hoped that recruitment would be easier, other factors led to slow recruitment, including a progressive shift from surgery for reflux to surgery for very large hiatus hernia[15]. Despite this, the results are consistent with the other trials, and the data should contribute to future metanalyses of trials of different partial fundoplication techniques.

We have shown similar high satisfaction with both types of partial fundoplication, but a trade-off between reflux symptoms vs. side effects. When considered alongside other trials of Nissen vs. the various forms of partial fundoplication there is probably a spectrum of outcomes ranging from Nissen to posterior to anterior partial fundoplication, and a progressive trade-off between reflux control vs. side effects across this spectrum. All trials show good rates of satisfaction no matter what the fundoplication type, and this lends support to the concept of a tailored approach to antireflux surgery, in which each individual patient preferences can be balanced against the risk of reflux vs possible side-effects.

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TABLES

Table 1: Preoperative parameters

Variable	*Type of fundoplication* *Anterior (n= 23)*	*Posterior (n=24)*	*p value*
Age (yrs)	57.8 (53.8to 61.8)	57.3(52.5 to 62.0)	0.860
Gender (M:F)	6:17	6:18	0.932
Height (cm)	1.64 (1.6 to 1.70)	1.65 (1.6 to 1.7)	0.824
Weight (kg)	79.3 (72.8 to 85.9)	81.2 (75.8 to 86.5)	0.656
BMI	29.3 (27.8 to 30.8)	29.9 (28.0 to 31.8)	0.607
Duration of symptoms (yrs)	14.5 (8.2 to 20.8)	9.9 (6.1 to 13.6)	0.109

All data are expressed as mean (95% CIs) or n (%)

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

Status	*Type of fundoplication* *Anterior (n=23)*	*Posterior (n=24)*	*p value*
Preoperative	5.35 (4.11 to 6.59)	6.58 (5.77 to 7.40)	0.124
Postoperative			
3 months	2.3 (0.8 to 3.8)	1.4 (0.2 to 2.7)	0.285
6 months	2.1 (0.9 to 3.4)	0.5 (0 to 1.0)	0.200
12 months	2.7 (1.1 to 4.2)	0.8 (0.1 to 1.4)	**0.045**

All data are expressed as mean (95% CIs) or n (%)

Table 3: Preoperative and Postoperative symptoms assessed using yes vs no questions

Symptom	*Preoperative*		*Post operative*					
			At 3 months		*At 6 months*		*At 12 months*	
	AP (n=23)	*PP (n=24)*	*AP (n=22)*	*PP (n=23)*	*AP (n=21)*	*PP (n=23)*	*AP (n=22)*	*PP (n=22)*
Heartburn	95%	100%	23%	9%	24%	4%	19%	10%
Epigastric pain	78%	79%	59%	39%	43%	35%	43%	30%
Regurgitation	74%	88%	4%	0%	9%	13%	2%	15%
Odynophagia	22%	29%	9%	17%	9%	9%	19%	10%
Post prandial fullness	52%	54%	82%	69%	62%	65%	67%	75%
Epigastric bloat	69%	88%	63%	56%	52%	61%	71%	60%
Anorexia	30%	25%	23%	17%	14%	9%	19%	15%
Nausea	30%	42%	18%	17%	24%	22%	**9%#**	**45%#**
Vomiting	22%	38%	4%	9%	0%	4%	5%	0%
Coughing	56%	50%	23%	26%	29%	26%	19%	20%
Wheezing	26%	33%	23%	17%	14%	13%	14%	15%
Can relieve bloat	56%	50%	59%	65%	52%	61%	57%	65%
Eats normal diet	69%	71%	41%	39%	38%	39%	33%	30%
Diarrhea	NA	NA	14%	26%	19%	26%	24%	30%
Unable to belch	NA	NA	**18%§**	**56%§**	**9%¶**	**43%¶**	14%	30%
Increased flatus	NA	NA	77%	83%	76%	83%	86%	85%

All data is % patients interviewed at each time point.
Abbreviations: AP = anterior partial fundoplication; PP=posterior partial fundoplication; NA= not applicable
No statistically significant differences were demonstrated between the two groups (p=>0.05 at all follow up intervals) except where indicated
p=0.015, § p=0.013, ¶ p=0.017

Table 4: Dysphagia Assessment

Variable	*Preoperative*		*Postoperative*					
			At 3 months		*At 6 months*		*At 12 months*	
	AP (n=23)	*PP (n=24)*	*AP (n=22)*	*PP (n=23)*	*AP (n=21)*	*PP (n=23)*	*AP (n=22)*	*PP (n=22)*
Dysphagia								
Lumpy solids	35%	58%	41%	26%	33%	17%	33%	15%
Soft solids	13%	25%	14%	9%	9%	4%	5%	0%
Liquids	9%	21%	14%	13%	19%	13%	9%	5%
Visual analog scale								
Solids	2.0 (0.7-3.3)	3.8 (2.3-5.3)	3.9 (2.6-5.1)	2.9 (1.5-4.2)	2.2 (1.0-3.5)	2.0 (0.9-3.1)	3.3 (1.8-4.8)	2.2 (1.0-3.3)
Liquids	0.8 (0.1-1.8)	0.9 (0.1 -1.8)	1.2 (0.2-2.3)	1.0 (0.3-1.7)	1.0 (0.2-1.8)	0.9 (0.2-1.6)	1.2 (0.4-2.0)	0.4 (0-0.8)
Dysphagia score								
Overall result	6.5 (2.0-11.1)	11.2 (6.3-16.2)	10.9 (7.1-14.6)	10.3 (5.5-15.1)	10.7 (6.3-15.1)	7.0 (3.6-10.4)	10.6 (5.5-15.7)	5.7 (2.7-8.7)
Scored 0 only	65%	38%	23%	30%	33%	39%	29%	35%

All data given as percentages or mean (95% CIs).
Abbreviations: AP = anterior partial fundoplication; PP=posterior partial fundoplication; NA= not applicable
No statistically significant differences were demonstrated between the two groups (p=>0.05 at all follow up intervals) except where indicated

Table 5: Oesophageal Manometry Outcomes

Variable	*Type of fundoplication* *Anterior*	*Posterior*	*p value*
Preoperative			
LOS resting pressure (mmHg)	11.2 (6.2-16.1)	11.7 (6.5-16.9)	0.991
LOS residual relaxation Pressure (mmHg)	2.9(0.9-4.9)	2.6 (1.3-3.9)	0.737
% with resting LESP < 10mmHg	61%	61%	1.000
Post operative			
LOS resting pressure (mmHg)	25.2 (12.9-37.4)	19.8 (13.5-26.1)	0.742
LOS residual relaxation Pressure (mmHg)	8.2 (3.8-12.5)	7.0 (4.0-10.0)	0.936
% with resting LESP < 10mmHg	85%	71%	0.648

All data expressed as % or mean (95% CIs)
LOS = lower oesophageal sphincter

Table 6: Outcome scores, Satisfaction score and Visick Grading

Variable	*Preoperative*		*Post Operative*					
			3 months		*6 months*		*12 months*	
	AP (n=23)	*PP (n=24)*	*AP (n=22)*	*PP (n=23)*	*AP (n=21)*	*PP (n=23)*	*AP (n=22)*	*PP (n=22)*
Outcome								
Excellent	NA	NA	36%	48%	38%	56%	24%	45%
Good	NA	NA	55%	43%	48%	27%	57%	40%
Fair	NA	NA	4%	9%	5%	17%	14%	15%
Poor	NA	NA	4%	0%	9%	0%	5%	0%
Modified Visick grade								
1	4%	0%	14%	35%	14%	30%	14%	25%
2	9%	4%	68%	57%	72%	48%	57%	40%
3	44%	17%	5%	4%	0%	4%	10%	20%
4	43%	79%	9%	4%	14%	18%	14%	15%
5	NA	NA	5%	0%	0%	0	5%	0%
Satisfaction score								
Mean score	NA	NA	8.7	8.8	8.8	8.5	7.8	8.6
95% CI	NA	NA	(7.6 to 9.7)	(8.1 to 9.5)	(7.9 to 9.7)	(7.5 to 9.4)	(6.5 to 9.2)	(7.7 to 9.5)
Would have the operation again	NA	NA	91%	100%	90%	96%	86%	85%

All data expressed as %
Abbreviations: AP = anterior partial fundoplication; PP=posterior partial fundoplication; NA= not applicable
No statistically significant differences were demonstrated between the two groups (p=>0.05 at all follow up intervals) except where indicated