British Journal of Surgery 1995, 82, 938–942

Laparoscopic Nissen fundoplication is a satisfactory alternative to long-term omeprazole therapy

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A total of 168 patients with proven gastro-oesophageal reflux disease (GORD) receiving long-term medical therapy underwent laparoscopic Nissen fundoplication. The operation was converted to open fundoplication in four patients. All patients reported complete (92·3 per cent) or partial (7·7 per cent) relief of reflux symptoms 1 month after surgery. There were no associated deaths and the perioperative complication rate was 8·9 per cent. The mean(s.e.m.) length of operating time was 69·9(2·4) min and mean(s.e.m.) hospital stay 2·7(0·1) days. Symptom score assessment, 24-h oesophageal pH recording and lower oesophageal sphincter pressure showed significant ($P < 0·0001$) improvement 6 months after surgery in 85 evaluable patients. Before operation 37·5 per cent of the patients were considered symptomatically controlled on omeprazole and had excellent symptom control after surgery. This initial experience suggests that laparoscopic Nissen fundoplication is a safe and effective treatment for patients with GORD requiring long-term medication.

Gastro-oesophageal reflux disease (GORD) is a chronic disorder affecting a significant proportion of the population. Surveys of the general population selected at random have shown that 25–30 per cent of people questioned complained of regular heartburn and/or acid regurgitation[1–3].

Surgery has traditionally been reserved for patients who do not respond to maximum medical therapy or for those with repeated chest infection and severe respiratory symptoms attributed to reflux and aspiration[4–6]. Omeprazole has been shown to be the most effective medical therapy for oesophagitis unresponsive to H_2 antagonists[7]. Between 71 and 90 per cent of patients with moderate or severe oesophagitis were healed after 8 weeks of omeprazole therapy[8–12], but if the drug was then stopped 82 per cent relapsed over the next 6 months[13]. These patients may then require therapy with omeprazole on a long-term basis. After 1 year of omeprazole 67–89 per cent remained in remission[13], but by 4 years this value had fallen to 47 per cent[14]. Omeprazole has been used for up to 9 years in patients with Zollinger–Ellison syndrome[15] but concerns remain about its long-term use in patients with GORD. Maintenance therapy with omeprazole is associated with a persistent rise in serum gastrin level, an increase in micronodular argyrophil cell hyperplasia, and subacute or chronic atrophic gastritis[14]. Case reports indicate that there may be other potential side-effects with omeprazole, including haemolytic anaemia[16], hepatic failure[17], interstitial nephritis[18,19], malabsorption[20,21], angio-oedema[22,23] and interaction with drugs including diazepam, warfarin and phenytoin[24].

Laparoscopic Nissen fundoplication was first described by Dallemagne *et al.*[25]. Laparoscopic fundoplication has been found to be associated with low morbidity and mortality rates, short hospital stay and early return to full activity[26–28]. These benefits make it more attractive than open operation. Laparoscopic Nissen fundoplication thus has the potential to become an alternative therapy for patients with GORD who require long-term continuous omeprazole therapy for control of daily symptoms.

Paper accepted 14 February 1995

A report is made of the initial experience with 168 patients with GORD receiving long-term medication who underwent laparoscopic Nissen fundoplication at the authors' institution, and of the 6-month follow-up results in 85 of these patients.

Patients and methods

Patients

A total of 168 patients (66 men) of mean(s.e.m.) age 46·8(1·1) (range 15–80) years underwent laparoscopic Nissen fundoplication between August 1992 and November 1994 by a single surgeon. The only exclusion criterion was a history of previous gastric surgery. All patients underwent endoscopic examination, 24-h oesophageal pH testing, oesophageal manometry and symptom score evaluation of antireflux medication before operation. In addition videofluoroscopic examination of the oesophagus, gastric emptying studies, and a double-blind randomized Bernstein test were performed for better evaluation of symptoms, when clinically indicated.

All patients referred had already had the diagnosis of GORD confirmed by other specialists and were taking long-term antireflux therapy. In all, 159 (95 per cent) patients were receiving continuous omeprazole therapy; the other nine had been given a trial of the drug without success but were receiving other maintenance therapy.

The patients were divided into two categories: group 1 included those who were unresponsive to omeprazole therapy up to 40 mg daily, or who were unable to tolerate omeprazole and were unresponsive to other antireflux measures (105 patients); group 2 comprised 63 patients controlled on omeprazole therapy who chose to have laparoscopic Nissen fundoplication in preference to long-term medication.

There were 11 patients who had previously been advised against open fundoplication because of severe respiratory disorder.

Technique of laparoscopic Nissen fundoplication

The technique used is similar to that described by Jamieson *et al.*[27]. In brief, the procedure is performed through five cannulas (2×10 mm and 3×5 mm). The oesophagus is mobilized for a distance of 4–5 cm, partially through the hiatus. The vagi are identified and protected. Dissection behind the oesophagus is minimized to the opening of a window large enough for the fundus to be pulled through. Short gastric vessels are divided only if necessary for creating a loose wrap without pulling the

spleen over. The superior pole of the fundus is pulled behind the oesophagus through the window created, and three interrupted 2-0 silk sutures are used to fashion a standard Nissen fundoplication by approximating the two folds of fundus and the oesophagus. The sutures are positioned 1–1·25 cm apart, creating a 2–2·5-cm wrap. The fundoplication wrap is constructed over a 42–52 Fr intraoesophageal bougie. The oesophageal hiatus is repaired only if the defect is large enough to allow herniation of intraperitoneal structures into the chest.

Postoperative care

A water-soluble contrast swallow was performed on the first morning after surgery to rule out any leakage and to check the profile of the wrap and assess oesophageal clearance. The patients were then started on fluid diet and discharged home on the second postoperative day if they were tolerating the diet. Patients were given instructions slowly to change their food to soft followed by normal food over the ensuing 3 weeks. They were allowed to resume full activity on discharge. Omeprazole therapy was stopped after operation.

Follow-up investigations

All patients were invited to undergo 24-h pH testing, oesophageal manometry and symptom score evaluation 6 months after operation. Endoscopy, gastric emptying and barium studies were performed only when clinically indicated.

Oesophageal manometry and 24-h pH testing

Oesophageal manometry was carried out with a seven-lumen sleeve–sidehole catheter. The basal pressure at the lower oesophageal sphincter region was measured by the sleeve sensor (Dent Sleeve; Adelaide, Australia) in relation to the gastric pressure.

An ambulatory digitrapper (light Proxima, Bologna, Italy) was used to perform 24-h pH testing. The pH probe was positioned 5 cm above the position of the lower oesophageal sphincter, as determined earlier by manometry. Gastro-oesophageal reflux was considered as a drop in oesophageal pH below 4, and the percentage reflux in 24 h was calculated for each patient. All patients were asked to stop omeprazole or other antireflux medication for 5 days before 24-h pH testing.

Symptom score evaluation

Symptom score evaluation was carried out by an independent observer on all patients before laparoscopic Nissen fundoplication and 6 months after operation. No patient was taking antireflux medication at the time of the preoperative questionnaire. Six specific symptoms of GORD, namely heartburn, regurgitation, epigastric or chest pain, epigastric fullness, dysphagia and cough (after meals or lying down), were scored as a product of severity (0–3) and frequency (0–4)[29]. A further four non-specific symptoms of nausea, constipation, diarrhoea and anorexia were scored.

Subsequently, 30 patients were studied before operation, both while taking and while not taking omeprazole therapy. These patients were also divided into those with poor symptom control (18 patients) and good control (12).

Statistical analysis

All values are expressed as mean(s.e.m.). Paired values were compared with Student's t test. $P<0·05$ was considered statistically significant.

Results

Operative data

Laparoscopic Nissen fundoplication was successfully completed in 164 patients (97·6 per cent). Conversion to open fundoplication in four patients was because of difficulty with adequate visualization of the oesophageal hiatus to allow safe mobilization of the oesophagus. Thirty-one patients had a hiatus hernia greater than 3 cm in size. In three patients more than half the stomach was in the chest cavity, but in all three cases the stomach was reduced into the abdominal cavity without any difficulty and the wrap was completed laparoscopically.

The mean(s.e.m.) operating time was 69·9(2·4) (range 30–195) min, which included eight patients who had laparoscopic cholecystectomy and two who underwent excision of Zenker's diverticulum and cricopharyngeal myotomy in addition to laparoscopic Nissen fundoplication. There were no intraoperative complications.

Hospital stay and perioperative morbidity

The mean(s.e.m.) hospital stay was 2·5(0·1) (range 2–16) days for the laparoscopic group, 7·0(1·0) (range 5–10) days for the converted group and 2·7(0·1) for the total group. There were no deaths and only three significant postoperative complications, which included two patients with transhiatal herniation of the stomach (rolling type) on the second postoperative day, and one with delayed oesophageal perforation on day 4. One of the two transhiatal herniations was reduced laparoscopically and the other required open reduction and wedge excision of a necrotic segment of the fundus. The oesophageal perforation occurred after a normal water-soluble contrast swallow on the first postoperative day, after the patient had been discharged home. It was treated by thoracotomy and drainage, and the small oesophageal leak 3 cm above the wrap closed spontaneously. Twelve patients developed minor perioperative complications (*Table 1*). The five cases of postoperative 'gastritis' symptoms were observed in the first 60 patients when the practice was to stop long-term omeprazole therapy without a short course of other antisecretory medication. Four of the five patients were taking oral or inhaled corticosteroids. All five patients presented 5–7 days after surgery with symptoms of epigastric discomfort and increasing dysphagia, and all responded to the reintroduction of antisecretory medication. Three of these patients were readmitted for a 2–4-day hospital stay. Since then all patients on omeprazole therapy have received a 2-week course of ranitidine after operation, and there has been no further incidence of symptoms of gastritis following operation.

Long-term complications

Four patients (2·4 per cent) experienced significant dysphagia with every meal 3 months after operation; they

Table 1 Perioperative complications in 168 patients after laparoscopic Nissen fundoplication

Complication	No. of patients
Symptoms of 'gastritis'	5
Respiratory infection	3
Pneumothorax	1
Wound infection	1
Incisional hernia	1
Supraventricular tachycardia	1
Delayed oesophageal perforation	1
Transhiatal herniation	2

had had moderate to severe oesophageal dysmotility with dysphagia before operation and had been warned about worsening of this condition after surgery. In one patient the symptoms necessitated reoperation 4 months after the initial surgery: the fundoplication wrap was taken down laparoscopically and converted to a partial 180° wrap. Five other patients experienced occasional dysphagia for solid meals but without any significant effect on oral intake.

Gas–bloat syndrome occurred in four patients (2·4 per cent), but none has required further treatment except for diet modification and prokinetic drugs.

One patient (0·6 per cent) experienced recurrence of reflux symptoms and has restarted omeprazole therapy. Two other patients with primary respiratory complaints developed partial recurrence of cough, but have not required antireflux therapy to date.

Follow-up study at 6 months

Of 104 eligible patients four had moved away and 15 refused follow-up studies. Eighty-five patients completed symptom score assessment before and after operation, 74 oesophageal manometry before and after operation, and 67 preoperative and postoperative 24-h pH monitoring.

Symptom score assessment. All 85 patients reported an improvement in both reflux- and non-reflux-related symptoms. The reflux symptom score fell significantly ($P<0·0001$) from a mean(s.e.m.) of 42·3(1·6) before operation to 10·5(1·1) after operation (*Table 2*). The score for the non-specific symptoms also fell significantly (*Table 2*). A single patient has experienced recurrence of reflux symptoms, but nevertheless reported an improvement (reflux symptom score from 42 to 1; non-specific symptoms from 10 to 0) and has been well controlled on 20 mg omeprazole daily.

The preoperative and postoperative symptom scores for dysphagia showed that 28 patients (33 per cent) had no dysphagia either before or after operation, 45 (53 per cent) had the same or less dysphagia after operation, and 12 (14 per cent) reported increased dysphagia 6 months after operation. Of the 12 patients with an increased dysphagia score, the difference was minor in six; 14 of 18 patients with moderate or severe oesophageal dysmotility reported either no change or an improvement in the dysphagia score after operation.

Oesophageal pH recording. The percentage reflux time in 24 h dropped significantly ($P<0·0001$) from a mean(s.e.m.) preoperative value of 11·0(1·56) to 0·7(0·2) per cent (*Table 2*). One patient with continuing reflux symptoms had a fall from a preoperative value of 19·0 per cent to 9·5 per cent after operation and was the only subject who had a postoperative 24-h reflux time greater than 4·0 per cent. The two patients with partial recurrence of cough had postoperative 24-h reflux values of 2·7 and 3·0 per cent respectively.

Lower oesophageal sphincter pressure. The mean(s.e.m.) pressure recorded at the lower oesophageal region increased significantly ($P<0·0001$) from a preoperative value of 8·1(0·9) mmHg to 22·3(1·4) after operation (*Table 2*). The patient with continuing reflux had a rise in LOSP from 0 to 12 mmHg.

Indications for surgery

There was no significant difference in the mean age between the two groups, but there were proportionately

Table 2 Results of follow-up at 6 months

	Before operation	After operation	Significance
Symptom score for reflux symptoms off medication ($n=85$)	42·3(1·6) (8–72)	10·5(1·1) (0–36)	$t=17·29$, 84 d.f., $P<0·0001$
Symptom score for non-specific symptoms off medication ($n=85$)	7·4(0·8) (0–33)	3·8(0·6) (0–24)	$t=4·03$, 84 d.f., $P=0·0001$
pH monitoring (percentage reflux in 24 h) ($n=67$)	11·0(1·6) (0–66·4)	0·7(0·2) (0–9·5)	$t=6·50$, 66 d.f., $P<0·0001$
Lower oesophageal sphincter pressure (mmHg) ($n=74$)	8·1(0·9) (0–36)	22·3(1·4) (10–57)	$t=9·32$, 73 d.f. $P<0·0001$

Values are mean(s.e.m.) with range in parentheses

Table 3 Results of 6-month follow-up of patients whose symptoms were controlled on omeprazole before operation

	Before operation	After operation	Significance
Symptom score for reflux symptoms ($n=32$)	42·7(2·3) (11–60)	9·5(2·0) (0–36)	$t=11·01$, 31 d.f., $P<0·0001$
Symptom score for non-specific symptoms ($n=32$)	7·0(1·3) (0–33)	3·5(1·2) (0–24)	$t=2·42$, 31 d.f., $P=0·022$
pH monitoring (percentage reflux in 24 h) ($n=28$)	10·3(2·7) (0–66·4)	1·1(0·4) (0–9·5)	$t=3·48$, 24 d.f., $P=0·002$
Lower oesophageal sphincter pressure (mmHg) ($n=29$)	7·9(1·1) (0–31)	21·7(2·0) (10–57)	$t=7·01$, 28 d.f., $P<0·0001$

Values are mean(s.e.m.) with range in parentheses

Table 4 Symptom scores in 30 patients assessed before operation while taking or not taking omeprazole therapy which had failed or succeeded in controlling symptoms

	Reflux score*		
	With omeprazole	Without omeprazole	Significance
Failure of omeprazole to control symptoms ($n = 18$)	27·9(3·5)	44·5(3·1)	$t = 5·92$, 17 d.f., $P < 0·0001$
Good control with omeprazole ($n = 12$)	21·2(4·7)	38·7(3·6)	$t = 6·57$, 11 d.f., $P < 0·0001$

*Values are mean(s.e.m.)

more men in group 2 (controlled by omeprazole; 52 *versus* 31 per cent in group 1).

In group 1 the reasons for failure of response to omeprazole therapy were poor control of typical symptoms in 39 patients, inadequate control of reflux-related respiratory complaints such as persistent cough and repeated aspiration in 57, and intolerance to the drug in nine.

In group 2 32 patients were available for 6-month evaluation. They showed a significant improvement in reflux-related symptom scores, 24-h pH monitoring results and LOSP (*Table 3*).

The subsequent assessment of symptoms in 30 patients with and without omeprazole therapy showed significantly lower scores in both groups of patients while taking medication, but the scores on treatment were considerably higher than those seen in patients who had had fundoplication (*Table 4*).

Discussion

Laparoscopic Nissen fundoplication combines the efficacy of the well established Nissen procedure with the advantages of a minimally invasive technique in the treatment of patients with severe GORD. This study demonstrates that, when performed by a trained surgeon the technique is extremely safe and associated with a low morbidity rate and a high success rate, and may be justly considered as a possible alternative to long-term omeprazole therapy.

Nissen fundoplication has been shown to be an effective therapy for GORD[6,30–32]. The high incidence of dysphagia and recurrence reported by some surgeons, coupled with the morbidity and mortality associated with upper abdominal or transthoracic surgery, had led to the wide use of long-term medication in preference to surgery for patients with severe GORD[5]. However, the low morbidity, short hospital stay and early return to full activity reported with laparoscopic Nissen fundoplication[26–28] is leading to a change in the attitude of patients and referring physicians, who are now considering laparoscopic fundoplication as a serious alternative to long-term continuous omeprazole therapy[33]. All patients in the present study were given a trial of maximal medical therapy, including omeprazole, before surgery was advised. In the majority of patients the indication for surgery was inadequate control of GORD-related symptoms or complications, but a significant number of patients who were well controlled symptomatically chose to have laparoscopic Nissen fundoplication in preference to remaining on long-term omeprazole therapy. The observation of excellent symptom relief in these patients (*Table 3*), and the smaller difference in preoperative symptoms on and off therapy (*Table 4*), suggest that even patients who are well controlled on omeprazole therapy will experience excellent symptom relief from laparoscopic Nissen fundoplication. The authors recognize that these data are not strictly comparable, and that they need to be confirmed prospectively in a larger number of patients and preferably by randomized trial.

Another small but important group of patients who are helped by this technique are those with severe respiratory limitation suffering from GORD and repeated aspiration pneumonia, who require an antireflux operation, but in whom open fundoplication would carry a high perioperative morbidity rate. In the authors' experience this group of patients fare well with laparoscopic Nissen fundoplication without experiencing any significant morbidity from the surgery.

There are always arguments as to whether short gastric vessels should be divided routinely[26,28] or only when necessary to achieve a loose wrap[27], and whether the oesophageal hiatus should be repaired in every case. These often reflect the surgeon's preference rather than any clearly demonstrated benefit to the patient. We disagree with Collard *et al.*[34] that the presence or size of a hiatus hernia is a contraindication to performing fundoplication laparoscopically. We also do not believe that a patient should be denied surgery because of poor oesophageal motor function; rather these patients must be carefully evaluated and advised. Preoperative oesophageal manometry allows for better assessment of the risk of postoperative dysphagia, which is taken into consideration when deciding on the merits of an antireflux operation. Many patients with severe oesophageal dysmotility have in fact reported improved dysphagia scores after operation, which is unexpected and needs more detailed evaluation. The size of the bougie used to assess the tightness of the wrap during operation varies in different series. In the present authors' experience, use of a smaller bougie (42 Fr) in patients with normal oesophageal motility and a larger bougie (up to 52 Fr) in those with oesophageal motor abnormality allows the wrap to be 'tailored' to the patient to some extent. In addition, there may be no need for a routine postoperative water soluble contrast swallow, which can be performed selectively for assessment of oesophageal clearance or evaluation of anatomical integrity of the oesophagus and fundoplication wrap.

Considerable laparoscopic skill is required to perform these procedures and a sharp learning curve exists[34]. The morbidity and success of the procedure is related to the skill and experience of the surgeon[26,34]. Jamieson and colleagues[27] reported the collective early experience of four surgeons with a complication rate of 15 per cent and a conversion rate of 12 per cent, while Weerts *et al.*[26]

recently reported their experience of 132 patients with a 7·5 per cent morbidity rate and 3·3 per cent conversion rate. The present paper gives the results of a single surgeon with previous training in this procedure[27]. The low incidence of major complications and no deaths in this series reflects the surgeon's experience with the procedure, which he performs regularly. There is, however, concern that the early success may encourage surgeons with inadequate experience of the technique to attempt laparoscopic Nissen fundoplication, with less encouraging results.

Until follow-up studies have confirmed the long-term effectiveness of laparoscopic Nissen fundoplication, open fundoplication will remain an important established technique in the treatment of GORD. The authors have no doubt that laparoscopic Nissen fundoplication will be shown to be as effective as the open technique but, until then, close follow-up of patients is necessary.

Acknowledgements

This study was supported by a grant from Johnson and Johnson, Canada. The authors thank Miss J. Myers and Miss L. DiLuca for technical help with the study.

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