Surgery for Complex Disorders
of the Upper Digestive Tract

E.J.B. Furnée

Surgery for Complex Disorders of the Upper Digestive Tract

Chirurgische Interventies voor Complexe Aandoeningen van de Bovenste Tractus Digestivus

(met een samenvatting in het Nederlands)

Proefschrift

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1

General Introduction

Hiatal Hernia

The gastro-oesophageal junction is fixed in the subdiaphragmatic position by the phreno-oesophageal membrane that attaches the serosa of the distal oesophagus to the crural fibers, the median arcuate ligament, and the pre-aortic fascia[1] (*Figure 1*). Most hiatal hernias are a type I or sliding hernia of the gastro-oesophageal junction, whereas large hiatal hernias (type II-IV) only comprise 5%[2,3]. In patients with a type I hiatal hernia, there is circumferential laxity of the phreno-oesophageal membrane allowing the gastro-oesophageal junction to migrate to the posterior mediastinum (*Figure 2A*), while a more focal weakening in the ventral part of this membrane is present in patients with a type II hiatal hernia. This allows the fundus of the stomach, facilitated by the intra-abdominal and intrathoracic pressure gradient, to slide along the anterior side of the oesophagus to the posterior mediastinum. Herein, the gastro-oesophageal junction is positioned in its normal anatomical place[4] (*Figure 2B*). This type II hiatal hernia is also called the rolling or true para-oesophageal hiatal hernia. In the type III or mixed hiatal hernia, a combination of a type I and II hiatal hernia is present, with both the gastro-oesophageal junction and the fundus of the stomach herniated to the thorax (*Figure 2C*). One theory claims that this type III hiatal hernia develops from a growing type II hiatal hernia[5], whereas others hypothesize that this may be the end-stage of a type I hiatal hernia[6].

Figure 1   *Anatomy at the gastro-oesophageal junction*

Lower oesophageal sphincter
Intrinsic
Extrinsic
Diaphragm
Phreno-oesophageal membrane
Stomach
Squamocolumnar junction
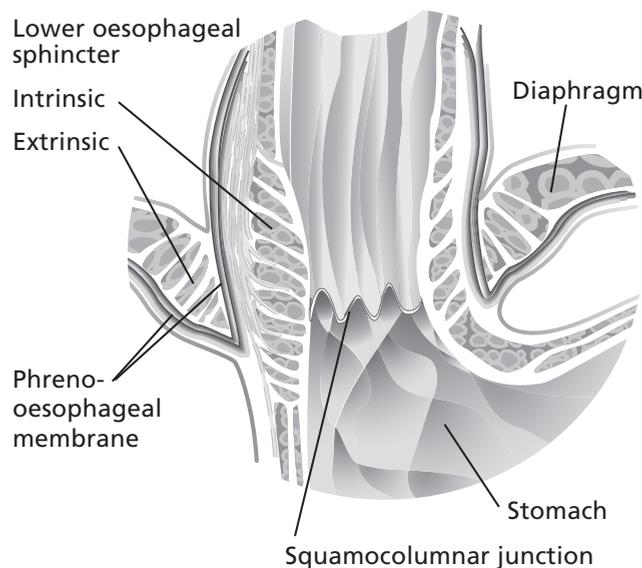
The gastro-oesophageal junction is fixed in the subdiaphragmatic position by the phreno-oesophageal membrane.

The type III hiatal hernia is the most frequently encountered large hiatal hernia[3,5,7,8]. In type IV or giant hiatal hernias, the stomach is completely migrated through the oesophageal hiatus combined with other intra-abdominal organs, like the omentum, transverse colon, the spleen or even the liver and pancreas[2] (*Figure 2D*).

Figure 2   *Type of hiatal hernia*
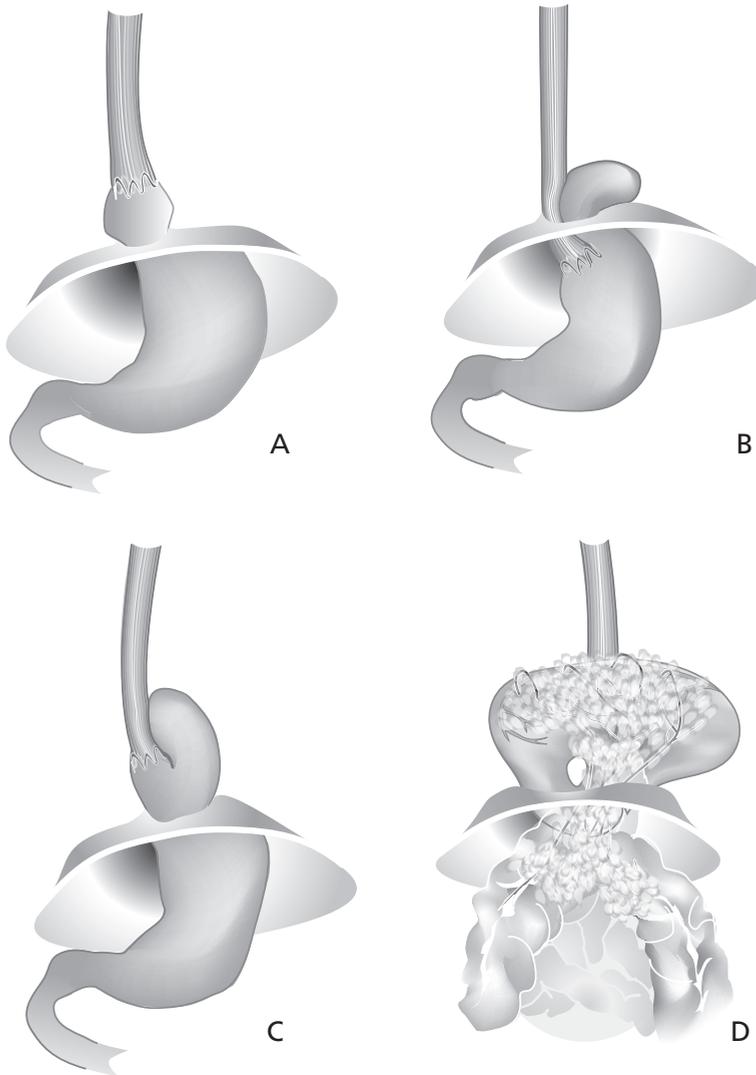
A: type I or sliding hiatal hernia; B: type II, rolling, or true para-oesophageal hiatal hernia; C: type III or mixed hiatal hernia; D: type IV or giant hiatal hernia.

Gastro-oesophageal reflux disease

Type I hiatal hernia is associated with gastro-oesophageal reflux disease (GORD). In patients with GORD, the oesophageal mucosa is excessively exposed to hydrochloric acid produced by the parietal cells in the gastric mucosa. Although the stomach has several defending mechanisms, the oesophageal mucosa is not resistant to such an acidic environment. This causes mucosal injury of the oesophagus and upper abdominal complaints[9]. In 20% of the population in North America and in 10-18% in Europe, symptoms related to GORD are experienced at least once a week[10]. Although the pathophysiology is not completely clarified, three main mechanisms have been identified to promote GORD[11]. First, a substantial number of patients with GORD has a hypotensive, and therefore incompetent intrinsic lower oesophageal sphincter (LOS). Secondly, an increase in the number of inappropriate transient relaxations of the LOS takes place in patients with GORD. These relaxations normally occur only during belching in response to gastric distension[12]. Finally, a type I hiatal hernia is present in 63-84% of the patients with GORD[13], which disturbs the natural synergy of the intrinsic and extrinsic LOS, and hereby its function to prevent gastro-oesophageal reflux[14].

Clinical presentation, diagnosis and conservative treatment

The two most common symptoms associated with GORD are heartburn and regurgitation of acid fluid possibly blended with some food, also known as "volume reflux"[15]. Although dysphagia is less frequently reported in association with GORD, it may be present in the case of reflux oesophagitis or GORD induced oesophageal dysmotility[16]. Other non-specific symptoms that may occur are non-cardiac chest pain, odynophagia, nausea, globus sensation, hoarseness, nocturnal cough, and pulmonary symptoms due to aspiration of gastric acid[15].

The first diagnostic step in patients with symptoms related to gastro-oesophageal reflux is oesophagogastroduodenoscopy. Reflux oesophagitis is detected in only one third of the patients with typical GORD symptoms, and in 48-79% of patients with abnormal oesophageal acid exposure[13]. Therefore, the absence of oesophagitis is not a sufficient indication to exclude GORD. Additionally, the presence and extent of a type I hiatal hernia, and complications of reflux oesophagitis (ie, peptic stricture, Barrett's oesophagus and oesophageal adenocarcinoma) may be identified during endoscopy[9]. Especially in patients refractory to antisecretory drugs, oesophageal 24-hour pH monitoring should be performed to establish the relation between reflux and symptoms. In order to exclude other diagnoses, like achalasia, ambulatory oesophageal manometry should be carried out as well, especially when these patients are considered candidates for antireflux surgery[9].

The first step in the conservative treatment of GORD is lifestyle modification including cessation of smoking, dietary modifications, decrease of weight, and head of bed elevation. These changes alone, however, are unlikely to control symptoms in the majority of patients[9]. The next option is medical treatment with acid suppression therapy (ie, antacids, histamine-2-receptor antagonists, or proton pump inhibitors). Proton pump inhibitors are by far the most effective medical treatment option[17-19].

Surgical treatment

Surgery is indicated in patients with objectively established GORD refractory to conservative treatment, and in those unwilling to take lifelong medication. This latter group of patients, however, should be even more extensively informed about morbidity of surgical treatment[20]. The goal of antireflux surgery is to reinforce the barrier for reflux. During surgery, the hiatal hernia is reduced, tensionless intra-abdominal length of the distal oesophagus is obtained by oesophageal dissection from the posterior mediastinum, and the LOS is supported by adding a fundoplication. The 360° Nissen fundoplication, introduced by Rudolf Nissen in 1956[21], is currently by far the most frequently used antireflux procedure. The fundoplication may induce a pressure zone, but it certainly sharpens the Angle of His to re-establish the flap-valve mechanism of the gastro-oesophageal junction. Another possible mechanism to prevent gastro-oesophageal reflux by a fundoplication is the reduction of the number of gastric distension induced transient LOS relaxations based on anatomical gastric alterations[22,23]. In 85-90% of patients, the long-term symptomatic and objective outcome of both the laparoscopic and open Nissen fundoplication is successful[24]. Failure of primary antireflux surgery in 10-15% of patients is due to recurrence or persistence of GORD, or development of postoperative troublesome dysphagia. This may be accompanied with one or more anatomical abnormalities that may develop after primary surgery; disruption of the wrap, telescoping (ie, cephalad migration of the gastro-oesophageal junction through the wrap), para-oesophageal hiatal herniation (ie, intrathoracic migration of a part of the stomach with the wrap in its normal subdiaphragmatic position), and intrathoracic wrap migration (*Figure 3*).

Although conservative treatment (ie, with antisecretory drugs in patients with recurrent GORD, and prokinetics or endoscopic dilatations in patients with persistent troublesome dysphagia) is sufficient in most of these patients, a new surgical intervention is required in a proportion that ranges between 3-6%[25-30]. During surgical reintervention, a partial or total fundoplication by an abdominal or thoracic approach is performed, depending on the indication of reoperation and the anatomical status of the primary repair. Several studies on redo antireflux surgery have been performed, however, most studies only report on the feasibility and symptomatic outcome, and constitute a small patient population. Objective and functional outcome after these reinterventions are essentially lacking.

Figure 3   *Anatomical abnormalities after primary antireflux surgery*
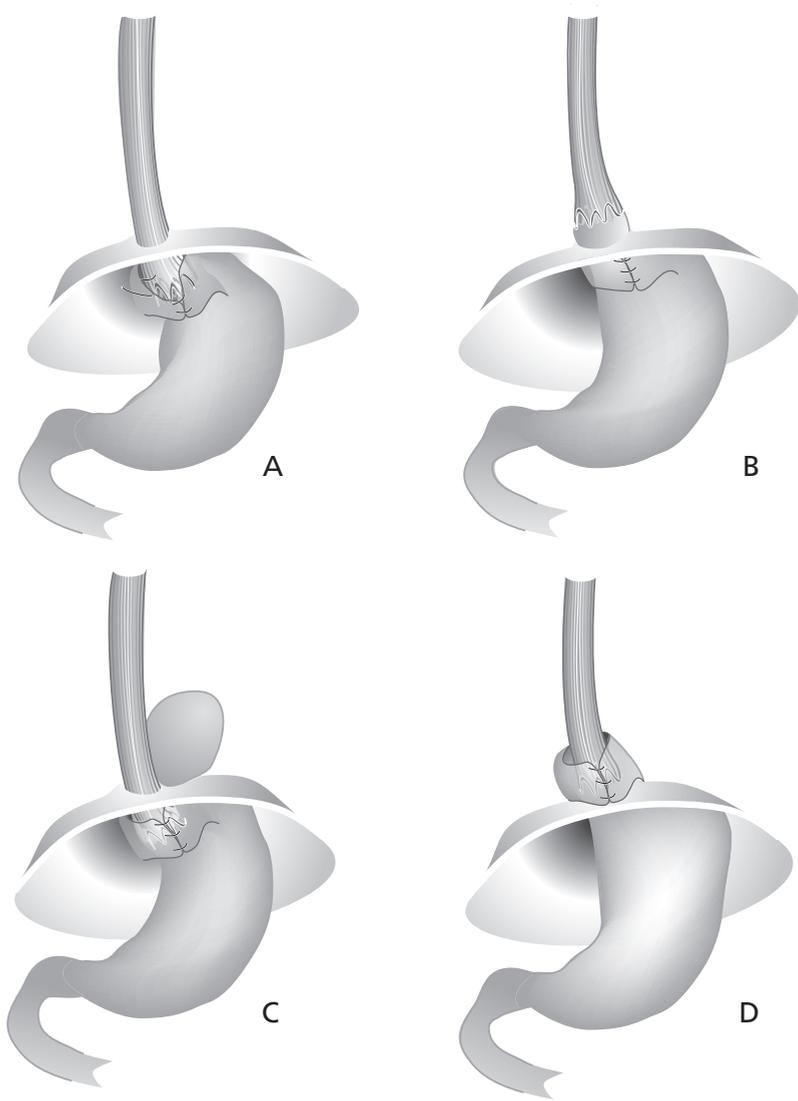
A: wrap disruption; B: telescoping; C: para-oesophageal hiatal herniation; D: intrathoracic wrap migration.

Endoscopic treatment

In essence, endoscopic antireflux procedures have been introduced on the same indications as antireflux surgery. These were considered an alternative to antireflux surgery to prevent morbidity like troublesome dysphagia and gas bloating[31]. In the past, several endoscopic procedures, such as radio frequency ablation of the LOS (Stretta procedure), the bulking implantation therapies (ie, the Enteryx and Gatekeeper procedures), and EndoCinch gastroplications have been introduced[11]. The most recently introduced type of endoscopic antireflux therapy is the endoluminal EsophyX fundoplication. Although improvement of symptoms and reduction of the use of antisecretory drugs have been demonstrated in most patients, the effect on oesophageal acid exposure appears to have been disappointing[32]. After an endoluminal EsophyX fundoplication, a substantial number of patients requires a surgical antireflux procedure because of inadequate symptom control and objectified recurrent or persistent GORD. It is therefore essential to analyse how a previous endoluminal EsophyX fundoplication may influence the outcome of antireflux surgery. The outcome of antireflux surgery after previous EsophyX fundoplication, however, is unknown so far.

Large hiatal hernias

Clinical presentation and diagnosis

Large hiatal hernias may be asymptomatic and diagnosed "by accident" on a routine chest X-ray. In other cases, patients seek medical help because of (intermittent) chest and upper abdominal complaints. In type II hiatal hernias, obstructive symptoms like (postprandial) epigastric/ substernal discomfort or pain, oesophageal dysphagia, nausea, postprandial satiation and vomiting are most prominent[33]. Reflux-related symptoms can also be expressed if the LOS is incompetent, probably as a result of its abnormal anatomical position in type III and IV hiatal hernias[28].
Barium oesophagogram is the most useful diagnostic test to differentiate the four types hiatal hernias (*Figure 4*). To evaluate the presence of oesophagitis and to exclude other causes of symptoms, oesophagogastroduodenoscopy should be performed additionally[33]. Oesophageal pH monitoring may be carried out to evaluate the relation between symptoms and reflux[26].

Figure 4   *Type III hiatal hernia on barium oesophagogram*

Complications

The most feared complication of large hiatal hernias is longitudinal rotation of the intrathoracic herniated organs, the organo-axial volvulus, leading to vascular decompression, incarceration, strangulation and perforation if the volvulus is not recognised in time. Chronic anaemia is another complication of a large hiatal hernia due to intermittent blood loss from linear mucosal erosions (Cameron lesions) which is caused by friction of the herniated gastric pouch at the level of the oesophageal hiatus[26]. Furthermore, pulmonary complications may develop due to mechanical compression of the lower lobes of the lungs by herniated intra-abdominal organs, inducing (postprandial) dyspnoea[34].

Treatment

Surgery is the only curative treatment option for patients with a large hiatal hernia. As the risk of developing the aforementioned life-threatening complications was considered high in the past, all patients were offered surgical repair, regardless of the type and symptoms[35]. More recent studies, however, have shown that the complication rate is much lower than previously thought[36,37]. Therefore, watchful waiting is the current strategy, and surgery is only offered to symptomatic patients.

The principles of surgical repair are straightforward and consist of reposition of the hernia, excision of the peritoneal hernia sac, and posterior crural repair[38,39]. Controversy on the approach (ie, open or laparoscopic), the use of mesh for reinforcement of the crural repair, and the routine addition of an antireflux procedure persists[40].

Laparoscopic repair of large hiatal hernias was first described in 1992[41]. Several studies have shown its advantages over the open abdominal approach, namely fewer complications, less postoperative pain, and shorter hospital stay[31,32,42,43]. Proper comparison between the open and laparoscopic approach in a randomised controlled trial, however, is not available. Anatomical failure of laparoscopic large hiatal hernia repair at short and mid-term follow-up ranges between 0% and 44%[44-47]. Some authors therefore have questioned the symptomatic and objective durability of the laparoscopic repair[31,42,43,48-50]. Studies on the long-term durability are still hardly available in the current literature. The use of mesh in the crural repair of large hiatal hernias is gaining popularity, but consequential complications (ie, oesophageal erosions and troublesome dysphagia) are described[51-53]. The true long-term recurrence rate after laparoscopic repair of large hiatal hernias, however, has to be established before routine use of a mesh can be proposed.

A third important controversy in the repair of large hiatal hernias is the tailored or routine addition of an antireflux procedure. Some authors recommend to routinely add a fundoplication to treat or prevent concomitant gastro-oesophageal reflux disease[54-56], and even to "buttress" the repair under the diaphragm[47,57], whereas others advise to selectively add a fundoplication in patients with concomitant gastro-oesophageal reflux disease, hereby avoiding the risk of post-fundoplication dysphagia[58]. As studies reporting well-documented pre- and postoperative symptomatic and objective data are currently not available, these recommendations are not evidence-based.

Aims and outlines of this thesis

Part 1   Surgical reintervention after failed antireflux procedures for gastro-oesophageal reflux disease

The aim of the first part of this thesis is to analyse the morbidity, and the symptomatic and objective outcome of antireflux surgery after previous endoluminal or surgical antireflux fundoplications. To tailor the procedure and thus optimising the outcome, factors which influence the outcome of these surgical interventions were explored. These aims were pursued in the studies as described in the next four chapters.

In *chapter 2*, the symptomatic and objective outcomes of surgical reintervention after failed primary antireflux surgery in a prospective cohort of 130 patients are described. Furthermore, the morbidity of these reinterventions and the causes of failure of the primary operations are discussed.

In *chapter 3*, in order to tailor the reintervention to the individual problem, predictors of the symptomatic and objective outcome of surgical reinterventions after primary antireflux surgery are identified by logistic regression analysis. Furthermore, identification of these predictors may be used to counsel patients preoperatively with regard to morbidity and chances of success.

In *chapter 4*, the individual studies currently available in the literature reporting on redo antireflux surgery are critically appraised and operative, symptomatic and objective results are summarised in order to offer a complete overview of the results of this kind of surgery.

In *chapter 5*, to identify in which way endoluminal EsophyX fundoplications may influence the results of antireflux surgery, the morbidity and symptomatic and objective outcomes after laparoscopic Nissen fundoplication are described in a cohort of patients who previously underwent EsophyX fundoplication.

Part 2   Surgical repair of large hiatal hernias

In this part, the aim is to elucidate two main controversies regarding the surgical treatment of large hiatal hernias; the long-term symptomatic and anatomical outcome of laparoscopic repair, and the routine or tailored addition of an antireflux fundoplication. An additional aim was to analyse symptomatic outcome of laparoscopic large hiatal hernia repair with regard to dyspeptic symptoms.

In *chapter 6*, the long-term symptomatic and anatomical outcome of laparoscopic repair of large hiatal hernias is described in a prospective cohort of 70 patients. Furthermore, possible predictors of both outcome parameters were explored by logistic regression analysis. Additionally, the suggested "buttress" function of an antireflux fundoplication to prevent recurrent hiatal herniation is discussed.

In *chapter 7*, to determine if a tailored or routine addition of an antireflux procedure should be recommended, the symptomatic and objective outcomes with regard to gastro-oesophageal reflux disease are described in a comparative cohort of patients who, based on the preoperative presence of gastro-oesophageal reflux disease, underwent large hiatal hernia repair either with or without an added antireflux fundoplication.

In *chapter 8*, the presence of dyspeptic symptoms after the laparoscopic repair of large hiatal hernias, in comparison to a cohort of patients who underwent laparoscopic Nissen fundoplication primarily performed for refractory gastro-oesophageal reflux disease, is evaluated.

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Part 1
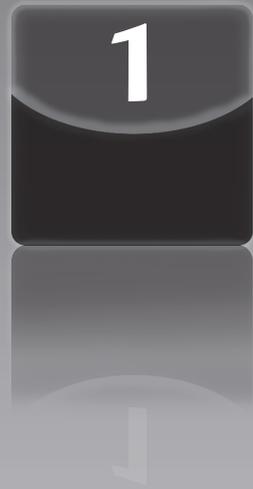
Surgical Reintervention after Failed
Antireflux Procedures for
Gastro-oesophageal Reflux Disease

2

Surgical Reintervention after Antireflux Surgery for Gastro-oesophageal Reflux Disease; *A Prospective Cohort Study in 130 Patients*

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Abstract

Background

Surgical reintervention after antireflux surgery for gastro-oesophageal reflux disease is required in 3-6% of patients. The subjective outcome after reintervention has been reported in several studies, but objective results after these subsequent operations have rarely been published. The aim of this study was to assess the symptomatic and objective outcomes in patients who underwent subsequent operation because of recurrent reflux symptoms or troublesome dysphagia after primary antireflux surgery.

Methods

Between January 1, 1994, and March 31, 2005, 130 patients (mean age ± SD, 48.4 ± 14.1 years) undergoing surgical reintervention after antireflux surgery for gastro-oesophageal reflux disease were prospectively studied. Symptomatic outcome was determined by questionnaires. Oesophageal manometry and 24-hour pH monitoring were performed to assess the objective outcome.

Results

A total of 144 reinterventions were performed in 130 patients, for recurrent reflux in 94 patients (65.3%) and for troublesome dysphagia in 50 patients (34.7%). Belsey Mark IV fundoplication through a left-sided thoracotomy was performed in 78 (54.2%) and a subsequent Nissen or partial fundoplication during 66 reinterventions (45.8%), including 16 laparoscopic procedures. After a mean follow-up of 60.1 ± 37.2 months, symptoms were absent or significantly improved in 70.3% of patients and oesophageal acid exposure was normalised in 70.2% of patients after surgery. Postoperative complications occurred after 14 subsequent operations (9.7%).

Conclusion

Surgical reintervention after antireflux surgery for gastro-oesophageal reflux disease yielded good symptomatic and objective results in 70% of patients in this prospective cohort study. Since the morbidity of this type of surgery is far from negligible, the expectations should be discussed in detail before additional operation.

Introduction

Antireflux surgery is an effective surgical intervention for gastro-oesophageal reflux disease (GORD). Satisfactory results have been reported in 85-90% of patients up to 5 years after surgery[1-4]. Revisional surgery is necessary in 3-6% of patients[5-10]. Indications for surgical reintervention can be subdivided into recurrent reflux symptoms and troublesome dysphagia[11]. The cause of failure may be technical errors, wrap migration or telescoping, an incorrect primary diagnosis, or selection of a wrong procedure in patients with severe oesophageal motility disorders[5]. Frequently, however, no cause of failure can be demonstrated and surgical reintervention after failed fundoplication is known to be technically demanding. Several studies have been published on the outcome of additional operation[10,12-27]. Because of the relative scarcity of these procedures, most of these studies are small. Furthermore, most studies have been directed toward the feasibility of and the subjective outcome after reintervention, whereas objective data on postoperative results are rarely available. Therefore, the effect of revisional antireflux surgery on functional outcome remains unclear.

This prospective study aimed to assess the subjective and objective outcomes in patients who underwent subsequent operation for either recurrent reflux symptoms or troublesome dysphagia in a tertiary care referral centre.

Methods

Patients

A total of 130 patients who underwent surgical reintervention for recurrent reflux symptoms or troublesome dysphagia after one or more failed previous antireflux procedures between January 1, 1994 and March 31, 2005, were included in this prospective cohort study. Patients with a para-oesophageal hernia without documented GORD as the indication for primary surgery and patients with achalasia were excluded.

The indication for the initial procedure and subsequent operation, the type of procedures and treatment with proton pump inhibitors, and the use of histamine-2-receptor antagonists and prokinetic drugs before subsequent operation were assessed. Intraoperative anatomical findings that suggested a possible cause of failure for the previous antireflux procedure and intraoperative and postoperative complications were documented.

Effect of surgery on outcome

Symptomatic assessment
Information on symptomatic outcome was obtained by sending a standardised symptom questionnaire that included the Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) score to all patients. This questionnaire contains nine GORD-specific items that have to be scored according to a system combining severity and frequency, eventually yielding a score between 0 and 45[28]. Furthermore, a Visick score (symptoms resolved, improved, changed, or worsened) and preoperative and postoperative general quality of life using a visual analogue scale were assessed.

Objective assessment
Stationary oesophageal manometry and ambulatory 24-hour oesophageal pH monitoring were performed before and after subsequent operative antireflux procedures. Written informed consent was obtained from all patients who agreed with both investigations.
Use of all medication that could affect the results was stopped before oesophageal manometry and 24-hour pH monitoring were performed. Manometry was performed using a water-perfused system with a multiple-lumen catheter that had an incorporated sleeve sensor (Dentsleeve Pty Ltd, Adelaide, Australia). The sleeve sensor was positioned at the level of the lower oesophageal sphincter (LOS). Mean end-expiratory LOS pressure was determined in response to ten wet swallows (5-mL water bolus). The end-expiratory gastric baseline pressure served as the zero-reference point. A LOS pressure of 0.6-3.5 kPa was defined as normal. Thereafter, oesophageal pH monitoring was performed by positioning a pH glass electrode (model LOT 440 M3; Medical Instruments Corporation, Solothurn, Switzerland) 5 cm above the manometrically determined proximal margin of the LOS. The pH signals were recorded with a digital portable data recorder using a sample frequency of 1 Hz (Orion; Medical Measurements Systems BV, Enschede, the Netherlands). During 24-hour recording of intraluminal pH, patients registered the episodes of reflux-related symptoms and the periods of supine and upright positions. Reflux parameters were calculated with an analysis program (Medical Measurements Systems BV). Reflux was defined as abnormal if the pH was lower than 4 during for more than 5.8% of the total time of pH recording and with the patient in the upright and supine positions during more than 8.2% and more than 3.5% of the time, respectively[29]. Moreover, the symptom index and the symptom association probability were calculated. Symptoms were considered to be reflux related if the symptom index was larger than 50% or the symptom association probability was more than 95%[30,31].

Surgical approach

The surgical approach depended on the localisation of the wrap. An abdominal approach was performed if (the remnants of) the fundoplication were below the diaphragm. In the case of recurrent GORD, Nissen fundoplication was performed. In patients who underwent a subsequent operation for dysphagia, additional Nissen fundoplication was performed if other causes than a too-tight wrap could be held responsible for the dysphagia. In all other circumstances, the 360° Nissen fundoplication was transformed into a partial posterior fundoplication. Left-sided thoracotomy was chosen in case of migration of the wrap to the posterior mediastinum, and a 270° wrap according to Belsey Mark IV was performed independent of the indication for subsequent operation. All abdominal additional operations were performed by two surgeons (H.G.G. and I.A.M.J.B.) with adequate experience in upper gastrointestinal tract procedures, and all thoracic approaches were performed by one surgeon (H.G.G.).

Interpretation of data

Patients were analysed and compared according to the indication of subsequent operation (ie, recurrent reflux symptoms or troublesome dysphagia) and accordingly assigned to the reflux group (RG) or dysphagia group (DG). Patients who underwent more than one additional operation were analysed depending on the indication of their last additional operation. Furthermore, intraoperative and postoperative complications, quantity of blood loss, and duration of operation and hospital stay were compared between abdominal (conventional and laparoscopic) and thoracic subsequent operations.

Symptomatic outcome was defined as successful if postoperative Visick score on symptoms were marked as resolved or improved. Successful objective outcome was defined as the absence of abnormal oesophageal acid exposure.

Statistical analysis

Values were expressed as mean ± SD. Data were analysed using SPSS for Windows version 12.0.2 (SPSS Inc., Chicago, Illinois, USA). The paired samples *t* test was used for statistical analysis of continuous preoperative and present values and the *t* test for independent samples for statistical analysis of continuous values between groups. Statistical analysis of categorical values between groups was performed with the Pearson χ^2 test and statistical analysis of categorical preoperative and present values by the McNemar test. The Spearman coefficient was used to determine correlations. Preoperative and present differences and differences between groups were considered statistically significant at $P < .050$.

Results

A total of 130 patients (65 men and 65 women; mean age 48.4 ± 14.1 years) participated in the study. Nissen fundoplication was the most performed primary antireflux operation (110 patients, 84.6%). Of these, 44 patients (40.0%) were operated on laparoscopically. In eight patients (6.2%), partial fundoplication served as the primary antireflux operation. Two of these operations were performed laparoscopically, three through a left-sided thoracotomy, and three through an upper abdominal midline incision. The other primary interventions were gastropexy (5.4%), implantation of an Angelchik prosthesis (2.3%), and two other procedures (1.5%), all performed through an upper abdominal midline incision. Forty-seven of the primary interventions (36.2%) were performed in our centre, the remaining ones in other hospitals in the Netherlands. Reflux-related symptoms were the indication for primary intervention in all but one patient, who was primarily operated on for dysphagia. Before referral, 16 patients (12.3%) had undergone another antireflux procedure because of failure of the primary antireflux operation.

Overall, a total of 144 reinterventions were performed in 130 patients. Fourteen patients underwent two reinterventions. The mean interval between the first antireflux procedure and the subsequent operation was 52.9 ± 70.6 months. The indication for subsequent operation was recurrent reflux symptoms in 94 operations (65.3%) and troublesome dysphagia in 50 (34.7%). The indication for the first additional operation in those patients who underwent two reinterventions was recurrent reflux symptoms in 11 and dysphagia in three patients. In the RG, 94 subsequent operations were performed: 55 thoracic and 39 abdominal. In the DG, 50 subsequent operations were performed: 23 thoracic and 27 abdominal. An abdominal approach was used in 66 subsequent operations (45.8%): 54 Nissen fundoplications (43 open, 29.9%, and 11 laparoscopic fundoplications, 7.6%) and 12 partial wraps (seven open, 4.9%, and five laparoscopic, 3.5%). The other 78 additional operations (54.2%) were Belsey Mark IV fundoplications. Collis gastroplasty was added in nine patients; seven in addition to a Belsey Mark IV procedure and two during open Nissen fundoplication.

Intraoperative and postoperative results

Several causes of failure of the previous antireflux procedure were identified during subsequent operation (*Table 1*). At least one anatomical abnormality was found during 131 (91.0%) and two or more during 39 subsequent operations (27.1%). Complete or partial disruption of the wrap and cephalad slippage of the gastro-oesophageal junction and stomach through the wrap were the most common findings, followed by migration of the wrap into the chest and the presence of a para-oesophageal hernia. Disruption of the wrap was more frequently found during subsequent operation performed for recurrent reflux symptoms, whereas the absence of any intraoperative anatomical abnormality was more frequent during subsequent operation for dysphagia.

Table 1 *Anatomical abnormalities encountered during subsequent operation*

Abnormalities	Total (n = 144)	Reflux group (n = 94)	Dysphagia group (n = 50)	P-value*
	Thoracic operations			
Lower oesophageal sphincter in place				
wrap disruption	26 (33.3%)	22 (40.0%)	4 (17.4%)	.050
no anatomical failure	1 (1.3%)	0 (0%)	1 (4.3%)	.295
para-oesophageal hiatal hernia	23 (29.5%)	16 (29.1%)	7 (30.4%)	.906
Lower oesophageal sphincter migrated				
intrathoracic wrap migration	28 (35.9%)	20 (36.4%)	8 (34.8%)	.894
telescoping	23 (29.5%)	18 (32.7%)	5 (21.7%)	.368
other	3 (3.8%)	0 (0%)	3 (13.0%)	.020
	Abdominal operations			
Lower oesophageal sphincter in place				
wrap disruption	22 (33.3%)	17 (43.6%)	5 (18.5%)	.034
no anatomical failure	12 (18.2%)	3 (7.7%)	9 (33.3%)	.011
para-oesophageal hiatal hernia	6 (9.1%)	4 (10.3%)	2 (7.4%)	.999
Lower oesophageal sphincter migrated				
intrathoracic wrap migration	10 (15.2%)	6 (15.4%)	4 (14.8%)	.999
telescoping	19 (28.8%)	10 (25.6%)	9 (33.3%)	.979
other	1 (1.5%)	1 (2.6%)	0 (0%)	.999

*P-value represents the difference between the reflux and dysphagia group.

Intraoperative complications are listed in **Table 2**. Splenectomy for injury of the spleen was required during two subsequent abdominal operations (3.0%). Injury of the liver and (contralateral) pneumothorax occurred more frequently during subsequent thoracic operations (P = .036 and P = .001, respectively). Three subsequent laparoscopic operations (18.8%) were converted to laparotomy. Subsequent thoracic operations were associated with significantly greater blood loss (539 ± 357 vs. 221 ± 199 mL; P < .001) and longer operating times (161 ± 40 vs. 106 ± 37 minutes, P < .001).

Postoperative complications occurred after 14 subsequent operations (9.7%) (**Table 2**). Pulmonary complications were more frequent after thoracotomy (P = .031). Two patients (1.4%) died, both after a thoracotomy. One patient died of acute cardiac arrest, and postmortem evaluation did not reveal a cause directly related to the surgical procedure. The other patient had septic shock and postoperative bleeding from the thoracic aorta with a low-grade local sepsis and fistula to the oesophagus due to foreign material implanted during the first operation. Hospital stay was shorter after subsequent abdominal reoperations (7.9 ± 2.9 vs. 14.4 ± 14.0 days; P < .001).

Table 2   *Intraoperative and postoperative complications*

	Total (n = 144)
Intraoperative complications	
oesophageal or gastric perforation	22 (15.3%)
superficial injury of the oesophagus or stomach	16 (11.1%)
injury of vagus nerve	2 (1.4%)
contralateral pneumothorax	16 (11.1%)
injury of the liver	9 (6.3%)
injury of the spleen	7 (4.9%)
other	5 (3.5%)
Postoperative complications	
wound infection	1 (0.7%)
pulmonary complication	6 (4.2%)
haemorrhage	3 (2.1%)
other	4 (2.8%)
death	2 (1.4%)

Figure 1   *Study profile*
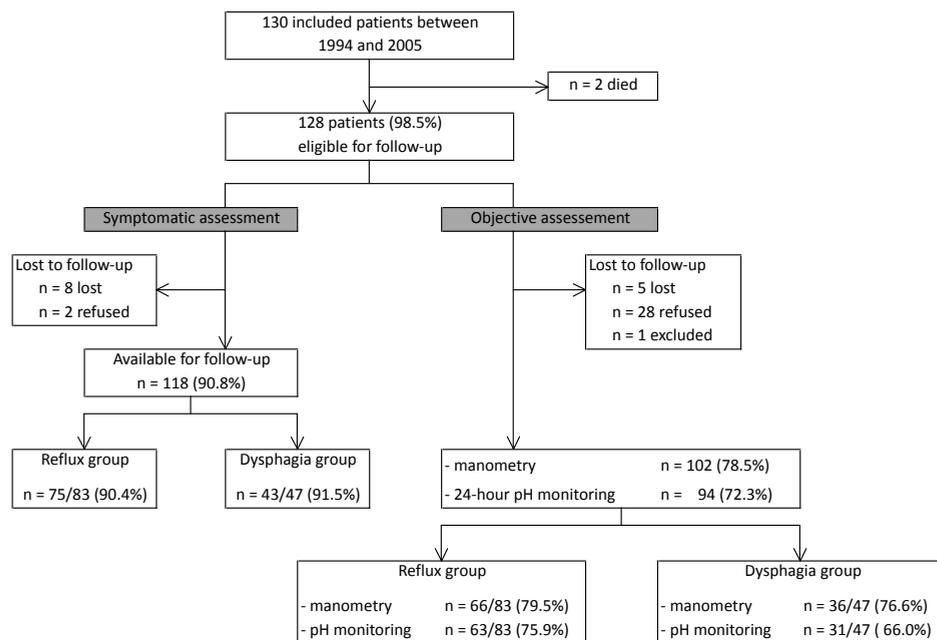
Effect of operation on outcome

Symptomatic assessment

A total of 118 patients (90.8%) were available for follow-up. Eight patients were lost to follow-up, two patients refused collaboration, and two patients died during follow-up (*Figure 1*). The mean time to follow-up for the subjective outcome was 60.1 ± 37.2 months. Daily heartburn was documented by 15 patients (20.0%) and daily symptoms of dysphagia by nine (12.0%) in the RG. Nine patients (20.9%) in the DG still experienced dysphagia every day at follow-up. Heartburn on a daily basis was present in 13 of these patients (30.2%). No significant differences were found between the RG and DG with regard to the presence of daily heartburn and dysphagia, GERD-HRQoL score, self-rated change in symptoms, and general quality of life (*Table 3*). Overall, 36 patients (30.5%) had heartburn and/ or dysphagia on a daily basis at follow-up. No significant correlation was found between heartburn and the presence of abnormal acid exposure (r = -0.011; P = .918). Use of antisecretory drugs decreased significantly in the RG (P = .001; *Table 3*).

Table 3   *Symptomatic outcomes*

	Total (n = 118)	Reflux group (n = 75)	Dysphagia group (n = 43)	P-value*
Self-rated change in symptoms compared with preoperative status (Visick grading system)				
resolved	24 (20.3%)	13 (17.3%)	11 (25.6%)	.284
improved	59 (50.0%)	42 (56.0%)	17 (39.5%)	.085
unchanged	15 (12.7%)	8 (10.7%)	7 (16.3%)	.378
worsened	20 (16.9%)	12 (16.0%)	8 (18.6%)	.717
GERD-HRQoL score	9.9 ± 9.0	9.4 ± 8.2	10.9 ± 10.1	.419
General quality of life score (VAS)				
preoperative	34.6 ± 25.0	34.2 ± 23.7	35.2 ± 27.5	.840
follow-up	52.5 ± 23.0	54.6 ± 22.5†	48.8 ± 23.7‡	.219
Use of antisecretory drugs				
preoperative	73 (61.9%)	60 (80.0%)	13 (30.2%)	<.001
follow-up	63 (53.4%)	40 (53.3%)†	23 (53.5%)	.987
Use of prokinetic drugs				
preoperative	23 (19.5%)	17 (22.7%)	6 (14.0%)	.280
follow-up	16 (13.6%)	11 (14.7%)	5 (11.6%)	.643

Values are given as mean ± SD, unless otherwise stated.
*P-value represents the difference between the reflux and dysphagia group.
P-value with regard to the difference between the preoperative and postoperative value was <.001†, and .009‡.
Abbreviations: GERD-HRQoL, Gastro-Esophageal Reflux Disease Health Related Quality of Life; VAS, visual analogue scale.

In the DG, 13 patients (30.2%) used antisecretory drugs but they had no reflux symptoms before subsequent surgery. This finding represents a trend toward increased use during follow-up (P = .077). The use of antisecretory drugs was significantly correlated with heartburn (r = 0.401; P = .001) and the presence of abnormal acid exposure (r = 0.307; P = .003) at follow-up.

Objective assessment

Sixty-three patients (75.9%) in the RG underwent oesophageal manometry and 66 patients (79.5%) underwent 24-hour pH monitoring as part of their preoperative workup before subsequent operation. Manometry was performed in 35 patients (74.5%) and 24-hour pH monitoring in 28 patients (59.6%) before surgery in the DG. Five patients were lost to follow-up, and one patient was excluded for objective assessment because measurement was unreliable owing to subtotal gastric resection after Belsey Mark IV fundoplication. Moreover, 29 patients refused manometry, pH monitoring or both. Eventually, 102 patients (78.5%) underwent stationary oesophageal manometry, and 94 (72.3%) underwent 24-hour pH monitoring during the follow-up period (*Figure 1*). No significant difference in frequency of daily heartburn and/or dysphagia was found between patients who refused both investigations and patients in whom objective data were obtained. The mean time to follow-up for the objective outcome was 18.6 ± 30.5 months. Mean preoperative end-expiratory LOS pressure was significantly higher in the DG than the RG (1.7 ± 1.0 kPa vs. 1.2 ± 0.8 kPa; P = .009). Oesophageal motility was preoperatively abnormal (hypertensive LOS pressure, incomplete relaxation of the LOS, and/ or low-amplitude peristaltic contractions of the distal part of the oesophagus) in 30 patients (63.8%) in the DG. At least one unsuccessful dilatation before surgery was performed in 22 patients (46.8%) in this group. Mean LOS pressure decreased significantly in the DG to 1.1 ± 0.8 kPa at follow-up (P = .030) but not in the RG (1.2 ± 0.7 kPa; P = .830). This difference in LOS pressure in the DG was not correlated with the incidence of postoperative symptoms of daily dysphagia in patients who had a subsequent operation through a left-sided thoracotomy. For patients with a subsequent abdominal reoperation for dysphagia, however, a significant correlation was detected between decrease in LOS pressure and postoperative dysphagia (r = 0.556; P = .030). In half of the patients who had daily symptoms of dysphagia at follow-up, oesophageal motility was abnormal.

Results of preoperative and postoperative 24-hour pH monitoring are presented in *Table 4*. Mean preoperative total oesophageal acid exposure was abnormal in patients in the RG only (*Figure 2*) and decreased significantly after surgery. Symptom indexes (ie, symptom index and symptom association probability) also decreased significantly after surgery. No differences were detected between preoperative and postoperative 24-hour pH profiles in patients in the DG. Furthermore, no differences in acid exposure times and symptom indexes existed between the RG and DG at follow-up. Excessive oesophageal acid exposure at follow-up was still present in 21 patients (33.3%) in the RG and in seven patients (22.6%) in the DG (P = .280).

Table 4   *Outcome of 24-hour oesophageal pH monitoring*

	Total	Reflux group		Dysphagia group		P-value*
		Thoracic	Abdominal	Thoracic	Abdominal	
Number of reflux episodes						
preoperative	49.7 ± 90.2	54.2 ± 102.8	69.7 ± 85.0	56.0 ± 129.8	5.4 ± 8.6	.170
follow-up	17.0 ± 26.1	14.6 ± 19.5†	24.4 ± 39.1†	30.3 ± 26.5	6.3 ± 5.2	.642
Total acid exposure time with pH < 4 (%)						
preoperative	8.7 ± 11.8	9.7 ± 10.7	13.7 ± 15.4	4.0 ± 5.6	1.4 ± 2.0	<.001
follow-up	3.6 ± 6.0†	3.8 ± 5.5†	4.8 ± 8.4†	4.4 ± 5.5	1.0 ± 1.3	.442
SI > 50%						
preoperative	21 / 94 (22.3%)	8 / 38 (21.1%)	10 / 28 (35.7%)	2 / 14 (14.3%)	1 / 14 (7.1%)	.062
follow-up	5 / 94 (5.3%)	3 / 38 (7.9%)	0 / 25 (0%)†	2 / 14 (14.3%)	0 / 17 (0%)	.731
SAP > 95%						
preoperative	25 / 94 (26.6%)	10 / 38 (26.3%)	13 / 28 (46.4%)	1 / 14 (7.1%)	1 / 14 (7.1%)	.002
follow-up	11 / 94 (11.7%)	7 / 38 (18.4%)	1 / 25 (4.0%) †	2 / 14 (14.3%)	1 / 17 (5.9%)	.668

Values are given as mean ± SD, unless otherwise stated.
*P-value represents the difference between the total reflux and total dysphagia group.
†P-value with regard to the difference between the preoperative and postoperative value was <.050.
Abbreviations: SI, symptoms index; SAP, symptom association probability.

Figure 2   *Preoperative and postoperative oesophageal acid exposure in the reflux and dysphagia group*
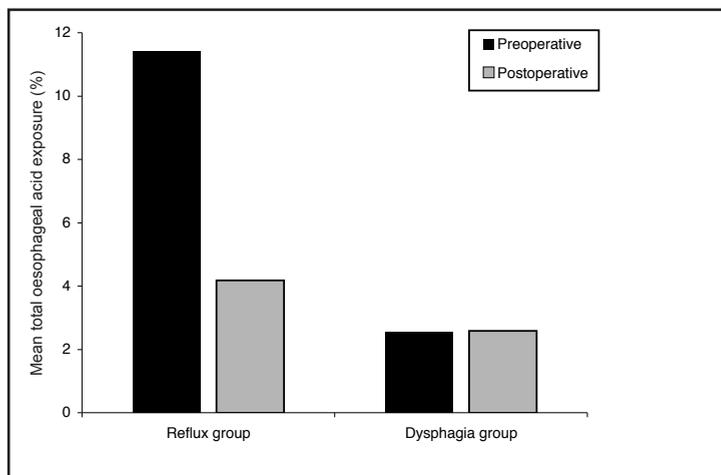
P-value with regard to the difference between the preoperative and postoperative values
in the reflux group was <.001.

Overall outcome of subsequent operation

Overall, 70.3% of the patients had a successful symptomatic outcome and 70.2% had a successful objective outcome at follow-up without significant differences between the RG and DG. Subtotal gastric resection after subsequent operation was performed in three patients. Indications were persistent reflux symptoms refractory to medication in one and intractable symptomatic gastroparesis due to vagal nerve damage in two other patients.

Discussion

To our knowledge, this is the largest prospective study to date on subjective and objective outcomes of surgery for recurrent GORD and troublesome dysphagia after failed antireflux surgery. An overall successful symptomatic and objective outcome was demonstrated in 70% of patients, regardless of the surgical strategy, laparotomy, laparoscopy, or thoracotomy used.

Intraoperative and postoperative complications, including the incidence of splenectomy, were comparable to those reported in other studies[5,7,20,22], although higher after subsequent operation through a left-sided thoracotomy. The thoracic approach is prone to causing more pulmonary complications. Nevertheless, we prefer this approach in case of intrathoracically herniated wrap because it is usually fixed to the surrounding tissue, and with this approach the oesophagus can be dissected free from the mediastinum to gain length. Morbidity, including postthoracotomy pain, however, is discussed in detail before subsequent operation. Pathophysiologic figures, analysis of results, and anticipated outcome for subsequent operations performed because of recurrent GORD and troublesome dysphagia are different. In the first group of patients, the wrap has subsided in the abdomen or in the thorax, resulting in an insufficient gastro-oesophageal antireflux barrier and subsequent recurrent symptoms and/or oesophagitis. In case of dysphagia, the pathophysiologic defect is far less clear. Different mechanisms can be a factor in unsatisfactory outcome, such as a narrow wrap, tight crural repair, para-oesophageal hernia through the wrap, or migration of fundoplication into the mediastinum, isolated or in combination[5]. Although the surgical treatment of these complications is less straightforward, it has been consistent for years in this cohort.

An anatomical explanation for failure of antireflux surgery was found in 90.3% of subsequent operations in the present study. Other studies[7,15,16,21,26] report figures ranging from 69-100%. Abnormalities at the gastro-oesophageal junction responsible for dysphagia are frequently lacking during subsequent operation, which was also recognised in this study. Intrathoracic wrap migration was the standard indication for a thoracotomy, however, it was also found during ten subsequent abdominal operations. This finding can partially be explained by the inaccuracy of the preoperative oesophagogram. During the last three years of the study

period, the procedure was started with diagnostic laparoscopy, and if the migrated wrap could be freed, a new laparoscopic Nissen fundoplication procedure was performed. If the wrap was fixed or not enough length could be gained, the procedure was converted to a left-sided thoracotomy. Symptomatic and objective outcome after subsequent laparoscopic operations was comparable to the conventionally operated-on group. Several other larger studies[12,21,27,32,33] have been published showing the feasibility of this approach, with successful outcome in 65-93% of patients. However, the conversion rate was high in this study (19%), which might be explained, as mentioned herein, by the fact that we prefer to start laparoscopically in patients with an intrathoracic wrap after primary laparoscopic Nissen fundoplication. Going forward, we will consider the possibility of conversion to a left-sided thoracotomy if the wrap cannot be freed from the posterior mediastinum.

Absence of daily reflux or dysphagia symptoms correlated well with Visick scores, and this was attained in approximately 70% of patients in both groups. As for documentation of symptomatic results, we have abandoned separate scoring of heartburn, regurgitation and dysphagia and have now returned to the Visick grading as probably the most useful instrument to document the overall subjective outcome of antireflux surgery. At follow-up, the use of antisecretory drugs significantly decreased in patients subsequently operated on for recurrent reflux symptoms, whereas this did not differ in patients operated on for dysphagia. Nevertheless, figures at follow-up were high compared with other studies[19,20,23,32,33] that reported percentages varying from 7-46%. Although the use of antisecretory drugs was not based on abnormal acid exposure in all patients, a significant correlation between the use of proton pump inhibitors and the presence of abnormal oesophageal acid exposure after surgery was found in this study. This stands in contrast to earlier observations by our group[34]. We did not identify the reason for this treatment in patients with physiologic acid exposure.

In the RG, preoperative pH monitoring was not performed in 20.5% of patients, as was the case for oesophageal manometry in 25.5% in the DG. Patients in the RG, however, had typical symptoms and oesophagitis on endoscopy, whereas the patients who were subsequently operated on for dysphagia without manometry had severe dysphagia (ie, they lost weight despite maximal use of a high-calorie liquid oral food supply) and abnormal position of the wrap, a combination that justified additional operation. It has become the standard of care to perform additional operations for such anatomical abnormalities as demonstrated during endoscopy and barium swallow with either recurrent reflux symptoms and/ or dysphagia.

With regard to objective outcome, there were some unexpected findings. The decrease in gastro-oesophageal reflux in patients operated on for reflux was significant, but normalization was not attained in all patients. This finding has been observed in a previous study as well, and full normalisation is apparently not an absolute prerequisite for a subjectively successful outcome[35]. In two of these patients, preoperative acid exposure was not measured, and in nine patients acid exposure did not normalise but decreased at follow-up. Further analysis of objective failure of subsequent operation was not performed.

Outcome of pH monitoring was different between patients who underwent additional operations by an abdominal and thoracic approach in both the RG and DG; however, this finding is probably not directly influenced by the surgical approach but by the indication the approach was based on. By separately analysing either group, a decrease in the number of reflux episodes in the thoracic group was found and no change was found in the patients operated on with laparotomy or laparoscopy in the DG. This finding probably means that the mechanism of recurrent reflux is not only caused by an insufficient LOS complex but also by the anatomical position of the wrap. In case of the combination of dysphagia and reflux, with telescoping of the wrap and the LOS migrated to the posterior mediastinum, the part of the stomach above the wrap continues to secrete acid, which "easily" refluxes through the LOS because of the obstruction at the position of the wrap (*Figure* 3). Subsequent operation in this subgroup was found to reduce the number of reflux episodes but not the total percentage of oesophageal reflux time.

In conclusion, our study demonstrated satisfactory symptomatic and objective results in 70% of patients who underwent subsequent thoracic or abdominal surgery for recurrent reflux symptoms or troublesome dysphagia. These subsequent operations, however, are accompanied by higher morbidity and mortality than primary intervention. Patients should be informed about the outcome of additional operation, and the results of this study help to tailor this preoperative counselling to the type and anatomy of the failure of the first operation.

Figure 3   *Intrathoracic migrated fundoplication and telescoping in a patient with recurrent gastrooesophageal reflux disease after conventional Nissen fundoplication*

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3

Predictors of Symptomatic and Objective Outcomes after Surgical Reintervention for Failed Antireflux Surgery

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Abstract

Background

Recurrent gastro-oesophageal reflux disease (GORD) and troublesome dysphagia after primary antireflux surgery are treated successfully by reoperation in 70% of patients. Identifying predictors of outcome could allow selection of patients likely to benefit from further surgery. The aim was to identify such predictors in patients reoperated on for recurrent GORD or troublesome dysphagia.

Methods

Between 1994 and 2005, 83 patients (mean age ± SD, 47.2 ± 14.4 years; 47 men) with recurrent GORD and 47 (aged 50.7 ± 13.4 years; 18 men) with troublesome dysphagia had further surgery. The predictive values of demographic, anatomical and manometric variables, and 24-hour pH-monitoring were analysed with respect to symptomatic and objective outcomes in each group.

Results

None of the factors included in a multivariable analysis predicted outcome after surgery for recurrent GORD. Independent predictors of symptomatic outcome after reoperation for dysphagia were amplitude of distal oesophageal contractions (odds ratio (OR) 1.613 (95% confidence interval (c.i.) 1.087-2.393), P = .017), intrathoracic wrap migration (OR 0.077 (0.003-1.755); P = .108) and an abdominal approach (OR 0.012 (0.001-0.337); P = .009).

Conclusion

Low-amplitude distal oesophageal contractions, intrathoracic wrap migration and an abdominal approach were significant predictors of an unsuccessful symptomatic outcome after reoperation for troublesome dysphagia.

Introduction

Outcomes following reoperation for recurrent gastro-oesophageal reflux disease (GORD) or troublesome dysphagia after primary antireflux surgery have been reported recently by the present authors[1]. Successful symptomatic and objective outcomes were achieved in about 70% of patients, comparable to results in other studies[2-5]. The reasons for failure after surgical reintervention remain unclear. Identification of factors that predict outcome may help in selecting and tailoring the intervention as well as informing patients about the expected outcome of reoperation.

Several studies have shown that the success rate of surgery for GORD decreases with the number of surgical reinterventions performed[6,7]. In one recent study, the presence of intrathoracic wrap migration was the only significant predictor of the need for further intervention[8]. In another, a preoperative diagnosis of Barrett's oesophagus, alone or in combination with oesophagitis, was a significant predictor of reducing regurgitation and controlling dysphagia. The need for Collis gastroplasty for a short esophagus was a significant predictor of increased regurgitation[9]. In both studies, however, the number of predictive variables analysed was restricted and did not include objective factors established before reoperation, such as results of oesophageal manometry and 24-hour pH monitoring.

The aim of the present study was to identify preoperative and intraoperative predictors of symptomatic and objective outcome in patients having reoperation for recurrent GORD or troublesome dysphagia.

Methods

Between 1994 and 2005, 130 patients underwent surgical reintervention for recurrent GORD or troublesome dysphagia after previous antireflux surgery. Primary antireflux procedures were Nissen fundoplications in 110 patients (84.6%), partial fundoplications in eight (6.2%) and other procedures in 12 patients (9.2%). After this primary intervention, 29 patients (22.3%) had another surgical antireflux procedure before the reintervention analysed in the present study. The indication for reintervention was recurrent reflux in 83 patients (63.8%) (reflux group) and troublesome dysphagia in 47 (36.2%) (dysphagia group). Of patients reoperated on for recurrent reflux, 30 patients (36.1%) had a 360º Nissen fundoplication and one patient (1.2%) a partial posterior fundoplication, all performed via an abdominal approach. The remaining 52 patients (62.7%) had a Belsey mark IV 270º fundoplication via a left-sided thoracotomy. Reoperations for troublesome dysphagia included Belsey mark IV fundoplication in 23 patients (48.9%),

Nissen fundoplication in 13 (27.7%) and partial posterior fundoplication by an abdominal approach in 11 (23.4%). All patients underwent objective evaluation before reoperation comprising stationary oesophageal manometry and ambulatory 24-hour pH monitoring[1].

A set of preoperative and intraoperative variables hypothesized to be of predictive value for symptomatic outcome was assessed separately in patients reoperated on for recurrent GORD and those who had surgery for troublesome dysphagia. The predictive value of these variables was determined in each group for improvement or resolution of preoperative symptoms, scored by the Visick grading system. In addition, their predictive value was determined for the development of new-onset dysphagia after reoperation for GORD, and for the recurrence of primary reflux symptoms after reoperation for dysphagia. Data on both postoperative symptoms were obtained using the Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) score[10].

In the reflux group, the predictive value of the variables was also analysed with respect to successful objective outcome, defined as the absence of pathological reflux (pH < 4 in the distal oesophagus for at most 5.8% of total time, 8.2% of time in the upright position and/ or 3.5% of time in the supine position) assessed by postoperative 24-hour pH monitoring.

Patient-specific characteristics (sex and age), number of previous antireflux procedures before reintervention (one or more than one), and surgical approach (abdominal or thoracic) were analysed for all outcome measures in both groups. Additionally, the predictive value of preoperative use of antisecretory drugs was determined for the effect on reflux symptoms and for objective outcome in the reflux group.

The impact of anatomical abnormalities that might have led to failure of the previous antireflux procedure was determined. Intrathoracic wrap migration, wrap disruption, telescoping of the lower oesophageal sphincter (LOS) and para-oesophageal hiatal herniation were assessed as prognostic factors for all outcome measures in both groups.

A series of objective variables, determined by oesophageal manometry and 24-hour pH monitoring before reoperation, were evaluated. The manometric variables mean end-expiratory pressure of the LOS, hypotensive (mean LOS pressure below 0.6 kPa) or hypertensive (more than 3.5 kPa) LOS, incomplete relaxation of the LOS during swallowing (nadir LOS pressure at least 1.4 kPa), mean peak contraction amplitude in the distal part of the oesophagus, presence of low-amplitude (less than 8.5 kPa) and peristaltic wave contractions in the body of the oesophagus (peristaltic contractions during more than 70% of swallowing) were analysed for their predictive value with respect to all outcome measures in both groups. The predictive value of the percentages of total, upright and supine time with pH < 4 in the distal oesophagus during preoperative 24-hour pH monitoring, presence of pathological reflux during total time (more than 5.8%), time in the upright position (more than 8.2%) and in the supine position (more than 3.5%)[11], presence of isolated upright and supine

pathological reflux, bipositional pathological reflux, number of reflux episodes, symptom index[12] and symptom association probability[13] was assessed with respect to reflux symptoms and objective outcome in patients reoperated on for recurrent reflux.

Statistical analysis

Values were expressed as mean ± SD. Analysis was performed using SPSS for Windows version 12.0.1 (SPSS Inc., Chicago, Illinois, USA). For univariable analysis, all continuous and categorical variables were analysed separately by binary logistic regression analysis. Variables with P < .200 in univariable analysis were entered together into a multivariable analysis performed by binary logistic regression, using backward stepwise selection of variables. Variables with P < .100 in multivariable analysis were considered to be significant predictors of outcome. The odds ratio (OR), 95% confidence interval (c.i.) and P-value are presented for each variable.

Receiver-operator characteristic (ROC) curves were constructed for outcome measures identified as significant predictors in multivariable analysis. The area under the curve (AUC) was calculated to determine the discriminative ability of the predictive model. The AUC was calculated with and without borderline significant predictors (variables with a P-value between .100 and .150 in the multivariable analysis) and the predictive model with the best discriminative ability was chosen.

To establish a score for predicting clinical outcome after reoperation in individual patients, points were assigned to independent predictive variables by dividing the logistic regression coefficients of all variables by the smallest coefficient and rounding each quotient to the nearest integer. Different cut-off points for the clinical prediction score were examined to find the score with the highest positive predictive value (fewest false positives).

Results

Patient characteristics and outcomes at follow-up information are presented in *Table 1*. Overall, 118 of 130 patients (90.8%) were available for symptomatic follow-up and 63 of 83 (75.9%) for objective follow-up after surgery for recurrent reflux. Of 43 patients in the dysphagia group, troublesome dysphagia was improved or resolved in 28 patients (65.1%) and daily symptoms of reflux were absent in 30 (69.8%). Among 75 patients reoperated on for recurrent reflux, preoperative symptoms were improved or resolved in 55 (73.3%) and daily symptoms of dysphagia were absent in 66 (88.0%). Pathological reflux was absent at follow-up in 42 of 63 patients (66.7%).

Table 1   *Baseline characteristics*

	Reflux group (n = 83)	Dysphagia group (n = 47)
Age (years)	47.2 ± 14.4	50.7 ± 13.4
Sex (male / female)	47 (56.6%) / 36 (43.4%)	18 (38.3%) / 29 (61.7%)
Mean time to follow-up		
subjective (months)	61.7 ± 37.3	57.2 ± 37.1
objective (months)	20.3 ± 32.8	-
Number of patients at follow-up		
subjective	75 (90.4%)	43 (91.5%)
objective	63 (75.9%)	-

Values are given as means ± SD, unless otherwise stated.

Univariable analysis

Univariable analysis of all potential predictive factors was performed with respect to outcome measures outlined above in each group. In patients reoperated on for recurrent reflux, none of the variables predicted the development of dysphagia after reoperation. Variables that significantly predicted the effect of reoperation on preoperative symptoms or objective outcome are shown in *Table 2*.

Significant predictors of the effect of reoperation for troublesome dysphagia on preoperative symptoms are presented in *Table 3*. Age was the only variable with predictive value regarding recurrent reflux symptoms after reoperation in this group.

Multivariable analysis

In patients reoperated on for recurrent reflux, none of the predictive factors identified by univariable analysis was shown by multivariable analysis to be an independent predictor of either the effect of reoperation on reflux symptoms or objective outcome.

In patients reoperated on for troublesome dysphagia, age was the only significant predictor of recurrent reflux symptoms after reoperation identified by univariable analysis, and so a predictive model could not be constructed for this outcome. With regard to the effect of reoperation on preoperative symptoms, two variables with significant predictive value by univariable analysis remained significant independent predictors of outcome in the multivariable analysis (*Table 4*). The odds of improvement or resolution of symptoms after reoperation significantly increased with higher preoperative amplitudes of distal oesophageal contractions, whereas an abdominal approach to revisional surgery was a significant predictor

Table 2   *Results of univariable analysis in patients reoperated on for recurrent reflux*

	Odds ratio	95% confidence interval	P-value*
Improvement or resolution of preoperative symptoms			
female	3.346	1.068 - 10.486	.029
abdominal approach during reoperation	2.323	0.740 - 7.290	.135
intrathoracic wrap migration	0.417	0.143 - 1.216	.111
preoperative hypotensive lower oesophageal sphincter pressure	0.356	0.092 - 1.378	.141
preoperative contraction amplitude of distal oesophagus (kPa)	1.136	0.960 - 1.344	.114
preoperative upright pathological reflux	0.400	0.122 - 1.311	.130
preoperative symptom association probability > 95%	2.368	0.628 - 8.926	.190
Absence of pathological reflux at follow-up			
intrathoracic wrap migration	0.443	0.141 - 1.397	.166
preoperative use of antisecretory drugs	6.882	0.667 - 71.003	.077
preoperative symptom association probability > 95%	1.010	0.997 - 1.023	.146
preoperative isolated supine pathological reflux	0.370	0.108 -1.273	.113

*Binary logistic regression analysis.

Table 3   *Results of univariable analysis in patients reoperated on for troublesome dysphagia*

	Odds ratio	95% confidence interval	P-value*
Improvement or resolution of preoperative symptoms			
preoperative contraction amplitude of distal oesophagus (kPa)	1.228	0.977 - 1.543	.049
abdominal approach during reoperation	0.273	0.069 - 1.070	.052
intrathoracic wrap migration	0.326	0.079 - 1.342	.119
Recurrence of primary daily reflux symptoms after reoperation			
age (years)	0.958	0.905 - 1.014	.125

*Binary logistic regression analysis.

of persisting dysphagia. As intrathoracic wrap migration was identified as a borderline significant predictor of persistent dysphagia, predictive models were tested with inclusion and exclusion of this variable. AUC values were 0.917 (95% c.i. 0.814 to 1.019; P < .001) and 0.886 (95% c.i. 0.764 to 1.008; P < .001), respectively, indicating that the first model had the best discriminative ability. Herniation of the wrap disappeared as a significant predictor when analysis excluded the 29 patients who had undergone at least one previous revisional operation.

Points were assigned to the significant independent predictors, based on the logistic regression coefficients, to establish a clinical prediction score for each patient. One point was assigned to contraction amplitude of the distal oesophagus because this variable had the smallest coefficient (*Table 4*); the number of points equalled the amplitude (one point equivalent to one kPa). Based on the logistic regression coefficient of the other two predictors, five points were subtracted if the wrap had migrated intrathoracically and nine if an abdominal approach had been used. The mean clinical prediction score was 1.6 ± 5.3. Different cut-off points were examined and a clinical prediction score of two was chosen for the final predictive model, because this cut-off point yielded a positive predictive value of 93% (13 of 14 patients) and a negative predictive value of 65% (11 of 17) for outcome after reoperation for troublesome dysphagia (*Table 5*).

Table 4   *Results of multivariable analysis in patients reoperated on for troublesome dysphagia with respect to improvement or resolution of symptoms*

	Coefficient (SE)	Odds ratio (95% c.i.)	P-value*	Points†
Preoperative contraction amplitude of distal oesophagus (kPa)	0.478 (0.201)	1.613 (1.087 - 2.393)	.017	1‡
Abdominal route of reoperation	-4.444 (1.713)	0.012 (0.001 - 0.337)	.009	-9
Intrathoracic wrap migration§	-2.559 (1.593)	0.077 (0.003 - 1.755)	.108	-5

*Binary logistic regression analysis, with backward stepwise selection of variables.
†Points were assigned by dividing the coefficient of each variable by 0.478 (the smallest coefficient), rounding each value to the nearest integer.
‡Preoperative amplitude of the distal oesophagus equals the number of points assigned for this continuous variable.
§A borderline significant predictor in multivariable analysis.
Abbreviations: SE, standard error; c.i., confidence interval.

Table 5   *Symptomatic outcome prediction in patients reoperated on for troublesome dysphagia according to clinical prediction score*

	Successful outcome	Unsuccessful outcome
Clinical prediction score ≥ 2	13 / 14 (92.9%)	1 / 14 (7.1%)
Clinical prediction score < 2	6 / 17 (35.3%)	11 / 17 (64.7%)

Discussion

None of the anatomical and physiological factors analysed in this study proved to be of predictive value for symptomatic and objective outcome in patients reoperated on for recurrent reflux. Only three factors – preoperative amplitude of distal oesophageal contractions, operative approach and intrathoracic wrap migration – were significant predictors of the effect of reoperation on dysphagia.

Smith et al.[8] also identified intrathoracic wrap migration as a significant predictor of outcome after reoperation. For primary antireflux surgery, others found that complete or partial response to acid suppression therapy and abnormal score on 24-hour oesophageal pH monitoring significantly predicted successful symptomatic outcome[14,15]. Winslow and co-workers[16] noted that patients with isolated upright reflux had a worse symptomatic outcome after primary antireflux surgery than those with isolated supine or bipositional reflux. These factors were also analysed in the present study, but none was identified as a predictor of outcome after reoperation for recurrent GORD.

Several studies of primary Nissen fundoplication have shown that impaired motility, defined as inadequate peristalsis and/ or low-amplitude contractions of the distal part of the oesophagus, is not associated with higher rates of dysphagia at follow-up, even if a total fundoplication is created[17-19]. This contrasts with the present finding that the contraction amplitude of the distal oesophagus was an independent predictor of the effect of reoperation on dysphagia. Apparently, there is a subgroup of patients who cannot be identified before primary surgery, but are probably at risk of developing dysphagia from the start if construction of the wrap was not optimal (too long or not "floppy" enough) or the hiatal repair was (a little) too tight. Therefore, surgeons should be aware that the outcome of reoperation may be disappointing in terms of postoperative dysphagia in patients with low-amplitude contractions of the distal oesophagus established before reoperation.

Herniation of the wrap and an abdominal approach appeared to be independent predictors of an unsuccessful symptomatic outcome in patients reoperated on for dysphagia. Wrap migration was analysed because it had previously been described as a negative predictor of outcome[8], although there is no obvious explanation for its predictive value. The predictive value of the abdominal approach might be because attention is directed particularly at the wrap as a possible cause of troublesome dysphagia during abdominal reoperation, where inspection of the hiatus may be restricted. With a thoracic approach, the posterior crural closure sutures have to be removed to mobilize the (remnants of) the primary wrap into the thorax and create a new wrap, which is subsequently replaced under the diaphragm. Afterwards, the hiatus is closed again, with potentially better exposure than during abdominal reoperation. It cannot be inferred from the present results that the thoracic approach is superior. It should

be acknowledged, however, that control of the hiatus is a crucial part of revisional operation. Another factor potentially contributing to the predictive value of the abdominal approach could be that thoracic reoperations were performed by the senior author, who has extensive experience in and a preference for this approach. Based on the scoring system described in the present study, an abdominal approach is likely to be avoided in patients with intrathoracic wrap migration. Indeed, the policy in this hospital is to select a thoracic approach if preoperative endoscopy and barium swallow indicate that intrathoracic wrap migration has occurred. Preoperative investigations, however, cannot reliably assess the anatomical situation at the level of the hiatus. Therefore, laparoscopy is used as the first step in deciding whether to continue the procedure laparoscopically, through a laparotomy or by conversion to thoracotomy.

The model developed in this study was based on a relatively small number of patients and the results should be interpreted with caution as there may have been a risk of overestimation of the identified significant predictors of outcome. In contrast, the lack of significance of the other variables may also be explained by the limited sample size. The present findings require validation in a larger population.

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4

Surgical Reintervention after Failed Antireflux Surgery;
A Systematic Review of the Literature

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Abstract

Background

Outcome and morbidity of redo antireflux surgery are suggested to be less satisfactory than those of primary surgery. Studies reporting on redo surgery, however, are usually much smaller than those of primary surgery. The aim of this study was to summarise the currently available literature on redo antireflux surgery.

Methods

A structured literature search was performed in the electronic databases of MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials.

Results

A total of 81 studies met the inclusion criteria. The study design was prospective in 29, retrospective in 15, and not reported in 37 studies. In these studies, 4 584 reoperations in 4 509 patients are reported. Recurrent reflux and dysphagia were the most frequent indications. Intraoperative complications occurred in 21.4% and postoperative complications in 15.6%, with an overall mortality rate of 0.9%. The conversion rate in laparoscopic surgery was 8.7%. Mean ± SEM duration of surgery was 177.4 ± 10.3 min and mean hospital stay was 5.5 ± 0.5 days. Symptomatic outcome was successful in 81.1% and was equal in the laparoscopic and conventional approach. Objective outcome was obtained in 24 studies (29.6%) and success was reported in 78.3%, with a slightly higher success rate in case of laparoscopy than with open surgery (85.8% vs. 78.0%).

Conclusion

This systematic review on redo antireflux surgery has confirmed that morbidity and mortality after redo surgery is higher than after primary surgery and symptomatic and objective outcome are less satisfactory. Data on objective results were scarce and consistency with regard to reporting outcome is necessary.

Introduction

Antireflux surgery for refractory gastro-oesophageal reflux disease (GORD) has satisfactory outcome in 85-90% of patients[1-6]. In the remaining 10-15%, reflux symptoms persist, recur or complications occur. Dysphagia is a frequent complication of fundoplication[7]. The indications for reoperation are far from straightforward, varying from severe recurrent symptoms with a more than adequate anatomical result to recurrent abnormal anatomy without any symptoms at all. Studies on reoperations also show similar wide variations with a full range of abnormal anatomy, symptoms and objective failure documented by oesophageal manometry, and pH monitoring.

In our recently published study on redo antireflux surgery, morbidity and mortality were higher than after primary antireflux surgery, with a symptomatic and objective success rate of 70% which is obviously inferior to the outcome of primary surgery[4,8]. Several other studies have been published describing causes of failure of conventional and laparoscopic antireflux surgery. Most studies have included only a small group of patients, so an adequate impression on the outcome of reoperation is hard to extract from such studies.

This study aimed to summarize the currently available literature on surgical reintervention after primary antireflux surgery focusing on morbidity, mortality, and outcome in order to get a more complete overview of the results of redo antireflux surgery and to give guidelines about how patients should be informed on their chances of success.

Methods

Search strategy

A literature search was performed in three electronic databases, MEDLINE using the Pubmed search engine, EMBASE, and the Cochrane Central Register of Controlled Trials. The databases were searched for all years, up to November 2008. Search terms were entered to identify the relevant studies. Separate search terms were entered for the intervention (ie, surgical reintervention) and the disease (ie, GORD). For the disease, dysphagia was also used, because this is a frequent indication for reoperation. For both the intervention and the disease, headwords in the thesaurus of the three databases (Medical Subject Heading (MeSH) Thesaurus in Pubmed and the Cochrane library and the Emtree Thesaurus in EMBASE) and free text words in title and abstract were used as search terms. The headwords from the thesaurus and the different synonyms for free text words were coupled by the Boolean operator "OR". The combination of search terms for the intervention and disease were subsequently coupled by the Boolean operator "AND". The free text words and headwords identified in the thesauruses are listed in *Table 1*.

Table 1 *Search terms*

Intervention	Disease
Free text words in title and abstract of MEDLINE, EMBASE, and the Cochrane library	
Refundoplication(s)	Gastro esophageal reflux
Redo	Gastro esophageal reflux disease(s)
Redo surgery	Gastro esophageal reflux disorder(s)
Redo surgical procedure	Gastro oesophageal reflux
Redo Nissen (fundoplication)	Gastro oesophageal reflux disease(s)
Redo antireflux procedure	Gastro oesophageal reflux disorder(s)
Redo antireflux surgery	Gastroesophageal reflux
Reoperative antireflux surgery	Gastroesophageal reflux disease(s)
Revisional surgery	Gastroesophageal reflux disorder(s)
Reoperation(s)	GERD
Reintervention(s)	GORD
Surgical revision(s)	Reflux disease(s)
Second look surgery	Esophagitis
	Oesophagitis
	Dysphagia
Headwords in the Medical Subject Head (MeSH) Thesaurus of Pubmed and the Cochrane library	
Reoperation	Deglutition Disorders
Second-Look Surgery	Esophagitis
Headwords in the Emtree Thesaurus of EMBASE	
Reoperation	Stomach function disorder
Second look surgery	Dysphagia
	Esophagitis

Selection of studies

The studies identified by the search strategy were independently selected by two reviewers (E.J.B.F. and W.A.D.) based on title, abstract, and full-text. The literature was searched for randomised controlled trials, cohort studies, and case-control studies on the feasibility and/ or outcome of surgical reinterventions. Studies in children, on other indications for primary surgery than GORD, conservative treatment of symptoms following primary antireflux surgery, surgical reintervention within 30 days after primary surgery, and patients cohorts with less than ten patients were not included. Only articles in English were included. Additionally, references of all selected publications were reviewed for other relevant studies. In case of a difference in opinion between the two reviewers about in- or exclusion of a study, the opinion of a third reviewer was decisive.

Analysis of data from selected studies

Data of the selected studies were independently acquired by two reviewers (E.J.B.F. and W.A.D.). Study design, time period, number of patients, sex ratio, and mean age were retrieved from the studies. Based on the study design, each study was qualified by a level of evidence according to the Oxford Centre for Evidence Based Medicine Levels of Evidence[9]. Type and approach of primary antireflux interventions and reoperations, mean period between both interventions, causes of failure of primary surgery and perioperative information (ie, intra- and postoperative complications, mortality, number and causes of conversions in case of laparoscopic reoperations, and mean intraoperative blood loss, duration of reoperations, and hospital stay) were also extracted from the included studies. Completeness of follow-up, number of patients available, mean duration of follow-up, method of obtaining outcome at follow-up, and the definition and percentage of patients with successful symptomatic and objective outcome were extracted from all studies.

Data analysis

Data were analysed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA). Values were expressed as mean ± SEM. Statistical analysis was not performed owing to the lack of statistically appropriate data from the included studies.

Results

One thousand six hundred twenty-five articles were eligible for further selection after removing duplicate hits, and finally 73 articles met the inclusion criteria (*Figure 1*). The references of these articles yielded eight more articles for inclusion. These articles had not been identified with the initial search strategy because of absence of abstracts in the databases or atypical description for the intervention or disease. Eventually, 81 articles were eligible for inclusion in this study. According to the Oxford Centre for Evidence Based Medicine Levels of Evidence, 27 studies had a level of evidence IIb (33.3%)[8,10-35], two level of evidence IIIb (2.5%)[36,37], and 15 level of evidence IV (18.5%)[38-52]. The remaining 37 studies (45.7%) were cohort studies, but a level of evidence could not be adjudged owing to unknown study design[53-89]. Baseline characteristics extracted from the individual studies are shown in *Table 2*.

Figure 1   *Results of search strategy and selection of studies*
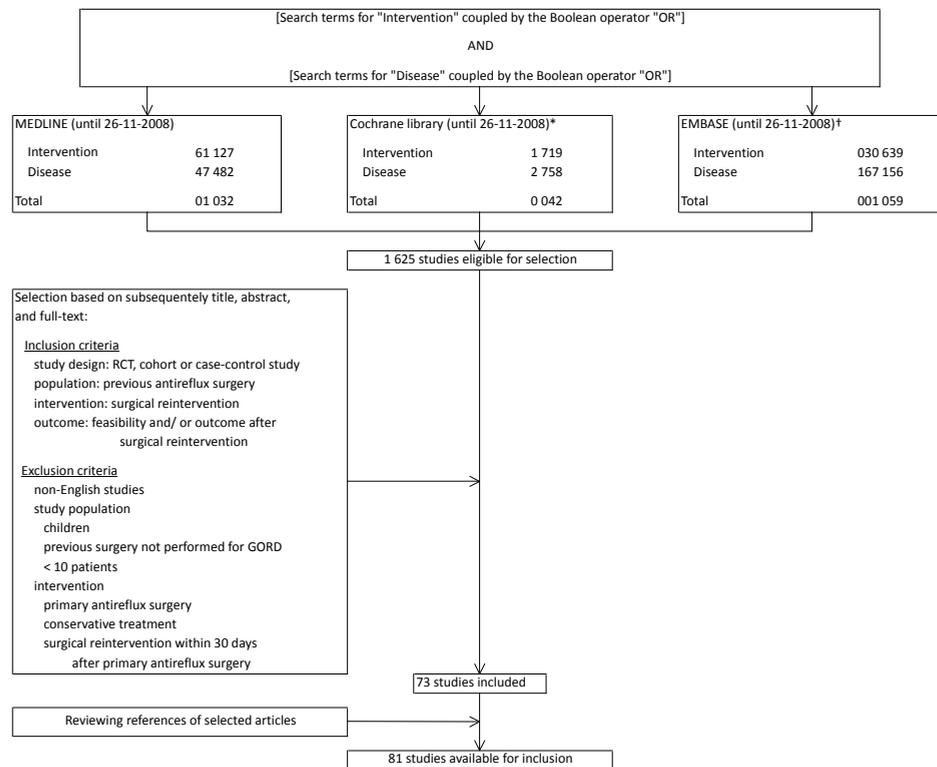
*The Cochrane Central Register of Controlled Trials.
†EMBASE only.
Abbreviations: RCT, randomised controlled trial; GORD, gastro-oesophageal reflux disease.

Primary antireflux procedures

Total fundoplication performed by laparoscopy, laparotomy, or thoracotomy was the most frequently reported primary antireflux procedure followed by partial fundoplication (*Table 3*). The type of primary antireflux procedure was not reported in almost one third, and 241 patients (5.3%) underwent more than one previous operation before inclusion in the original studies.

Table 2   *Baseline characteristics extracted from the included studies*

Number of patients	4 509
male	1 524 (33.8%)
female	1 762 (39.1%)
sex not reported	1 223 (27.1%)
Age (years)	51.3 ± 0.8
Number of reoperations	4 584
Study period (months)	10.8 ± 0.7
Duration between primary surgery and reoperation (months)	38.3 ± 4.1
Study design of the individual studies	
prospective cohort study	27 (33.3%)
retrospective cohort study	14 (17.3%)
prospective case-control study	2 (2.5%)
retrospective case-control study	1 (1.2%)
not reported	37 (45.7%)
Values are given as mean ± SEM, unless otherwise stated.	

Table 3   *Type and indication of primary antireflux procedures and reoperations*

	Primary procedures (n = 4 750)	Reoperations (n = 4 584)
Indication of operation		
recurrent reflux	-	1 912 (41.7%)
dysphagia	-	760 (16.6%)
recurrent reflux and dysphagia	-	184 (4.0%)
anatomical abnormality	-	114 (2.5%)
gasbloat syndrome	-	31 (0.7%)
miscellaneous	-	148 (3.2%)
not reported	-	1 435 (31.3%)
Type of operations		
total fundoplication	2 162 (45.5%)	2 397 (52.3%)
partial fundoplication	471 (9.9%)	999 (21.8%)
resection surgery	-	327 (7.1%)
miscellaneous procedures	657 (13.8%)	737 (16.1%)
not reported	1 460 (30.7%)	124 (2.7%)

Causes of failure of primary antireflux surgery

Causes of failure of the previous antireflux procedure were reported on 3 175 reoperations in total. Intrathoracic wrap migration, total or partial disruption of the wrap, and telescoping were the most common anatomical abnormalities encountered (*Table 4*). Oesophageal motility disorder or erroneous diagnosis (ie, another primary disease than GORD) were the causes of failure of the previous operation in 62 patients (2.0%). In 194 reoperations (6.1%), no cause of failure could be identified.

Table 4   *Causes of failure of previous antireflux procedure*

	Total (n = 3 175)
Anatomical abnormalities	
intrathoracic wrap migration	885 (27.9%)
wrap disruption	722 (22.7%)
telescoping	448 (14.1%)
para-oesophageal hiatal herniation	195 (6.1%)
hiatal disruption	167 (5.3%)
tight wrap	168 (5.3%)
stricture	60 (1.9%)
Wrong primary diagnosis	
achalasia	37 (1.2%)
oesophageal spasms	7 (0.2%)
sclerodermia	4 (0.1%)
oesophageal carcinoma	1 (0.03%)
Disturbed oesophageal motility	13 (0.4%)
No cause for failure identified	194 (6.1%)
Miscellaneous	347 (10.9%)
Not reported	120 (3.8%)

Percentages exceed 100% since more than one cause of failure was found during several reoperations.

From six studies, it was shown that wrap disruption and telescoping were more frequent after conventional primary surgery, whereas disruption of hiatal repair and a tight wrap were more frequent after laparoscopic primary repair (*Table 5*)[18,49,61,67,84,85]. Intrathoracic wrap migration was reported by Serafina et al.[85] to be more frequent after conventional primary procedures (13 / 17, 76.5% vs. 5 / 11, 45.5%), whereas Heniford et al.[67] showed that this was more frequent after laparoscopic primary repair (16 / 22, 72.7% vs. 13 / 33, 39.4%). In the study by Salminen et al.[84], intrathoracic wrap migration was equal after conventional and laparoscopic primary surgery. In five other studies[8,11,12,31,72], it was shown that intrathoracic wrap migration and wrap disruption were more frequent in the case of recurrent reflux, whereas in the case of dysphagia, no cause of failure could be demonstrated more frequently (*Table 5*).

Table 5   *Anatomical abnormalities depending on the approach of primary surgery and the indication of reoperation*

Anatomical abnormalities depending on the approach of primary surgery	Conventional (abdominal) approach (n = 120)	Laparoscopic approach (n = 132)
wrap disruption	48 (40.0%)	24 (18.2%)
telescoping	32 (26.6%)	10 (7.6%)
hiatal disruption	23 (19.2%)	42 (31.8%)
tight wrap	2 (1.7%)	24 (18.2%)
miscellaneous	36 (30.0%)	42 (31.8%)
Anatomical abnormalities depending on the indication of reoperation	**Recurrent reflux (n = 234)**	**Dysphagia (n = 118)**
intrathoracic wrap migration	104 (44.4%)	18 (15.3%)
wrap disruption	109 (46.6%)	12 (10.2%)
no cause of failure	34 (14.5%)	51 (43.2%)
miscellaneous	64 (27.4%)	54 (45.8%)

Percentages exceed 100% since more than one cause of failure was found during several reoperations.

Indications for reoperations

Recurrent reflux and dysphagia were the most frequent indications for reoperations (***Table 3***). In 1 435 reoperations (31.3%), the indication for reoperation was not reported. Preoperative symptoms were assessed by questionnaire in 26 studies (32.1%)[10,14,17,18,23-25,28,30,33,36,45,53,54,56,61-66,71,74,76,87,88]. In most studies (93.8%), preoperative workup consisted of oesophagogastroduodenoscopy, barium swallow and/ or oesophageal pH monitoring[10-28,30-41,43-46,48-76,78,79,81-89].

Type and route of reoperations

Total or partial fundoplication was the most frequently performed reoperation (***Table 3***), whereas the type of reoperation was not reported in 124 patients (2.7%). The laparoscopic approach was used in 1 666 reoperations (36.3%), 1 589 reoperations (34.7%) were performed by the conventional (open) abdominal route and 1 041 (22.7%) by thoracotomy. The approach of reoperation was not reported in the remaining 288 reoperations (6.3%). More than one reintervention was performed in 75 patients (1.7%).

The oesophagus was totally or partially resected during 125 reoperations (2.7%). The reasons to perform oesophageal resection were severe oesophagitis with or without Barrett metaplasia[15,25,59], peptic stricture of the oesophagus[10,33,51,57,72,81], severely disturbed oesophageal motility[26,44,57,81] or short oesophagus[70,82]. In 202 reoperations (4.4%), gastric resection was performed. Indications for this were alkaline reflux[10], dense adhesions on attempted refundoplication[33,59,86], or severe gastric paresis[25,81].

Intraoperative and postoperative results

The different intra- and postoperative parameters were only reported in a subset of the original studies. Intraoperative complications were reported in 454 of 2 123 reoperations (21.4%) and were more frequent during laparoscopic than during open abdominal reoperations (150 / 770, 19.5% vs. 5 / 92, 5.4%). Laceration or perforation of the oesophagus and/ or stomach were the most common (*Table 6*). Postoperative complications were present after 546 of 3 491 reoperations (15.6%). Infectious, pulmonary, and cardiac complications were the most common postoperative complications (*Table 6*). Open abdominal reoperations were accompanied with more complications than laparoscopic reoperations (55 / 317, 17.4% vs. 98 / 642, 15.3%). Thirty-seven of 4 329 patients (0.9%) died intra- or postoperatively (*Table 6*). No mortality occurred in studies only reporting on laparoscopic reoperations, while the mortality rate was 1.3% in studies in which all reoperations were performed by a conventional abdominal approach.

Table 6   *Intraoperative and postoperative results of reoperations*

Intraoperative complications	**n = 2 123***
injury of oesophagus and stomach	278 (13.1%)
pneumothorax	73 (3.4%)
haemorrhage	41 (1.9%)
splenectomy	7 (0.3%)
other	49 (2.3%)
not reported	6 (0.3%)
Postoperative complications	**n = 3 491***
pulmonary complication	125 (3.6%)
wound infection	64 (1.8%)
leakage from alimentary tract	52 (1.5%)
urinary tract infection	12 (0.3%)
other infectious complications	48 (1.4%)
cardiac complication	31 (0.9%)
haemorrhage	22 (0.6%)
other	136 (3.9%)
not reported	56 (1.6%)
Causes of mortality	**n = 4 329***
infectious	11 (0.3%)
pulmonary	7 (0.2%)
cardiac	4 (0.1%)
miscellaneous	10 (0.2%)
not reported	5 (0.1%)

*Total number of reoperations in which the intra- and postoperative complications and mortality rate were reported.

Mean duration of reoperation was 177 ± 10 minutes, mean intraoperative blood loss 205 ± 35 mL, and mean hospital stay 5.5 ± 0.5 days. Comparing results of laparoscopic reoperations with laparotomy regarding the preceding three parameters was not possible due to the small number of well-documented studies in the laparotomy group.

Reoperation was performed laparoscopically in 36.3% of all cases with a conversion rate of 8.7%. Causes of conversion were dense adhesions (n = 57, 39.3%), severe intraoperative bleeding (n = 11, 7.6%), poor visualisation (n = 3, 2.1%) and other (n = 15, 10.3%). In the remaining 59 cases (40.7%), the reason for conversion was not reported.

Symptomatic outcome after reoperations

Symptomatic outcome after reoperation was determined in 79 studies (97.5%)[8,10-18,20-28,30-89] and reported as successful in 81% of patients, although with different definitions of success (*Table 7*). Data were obtained by questionnaires in 29 studies (36.7%)[8,10,11,16-18,20,22-24,27,28,30,34-37,42,45,46,48,49,54,55,61,69,71,80,84], by interview in 21 (26.6%)[13,25,31,38,41,47,52,53,57,60,62,65-68,73,74,78,82,83,85] and this was not reported in the remaining 29 studies (36.7%) [12,14,15,21,26,32,33,39,40,43,44,50,51,56,58,59,63,64,70,72,75-77,79,81,86-89]. The mean success rate in studies only reporting on laparoscopic reoperations (17 studies)[11-13,23-25,28,31,35,39,41,48,50,53,61,70,85] was 84.2 ± 2.5% and 84.6 ± 3.4% in studies in which all reoperations were performed by a conventional abdominal approach (ten studies)[10,22,33,44,58,68,69,75,76,86].

Table 7   *Symptomatic and objective outcome after reoperation*

	Symptomatic outcome	Objective outcome
Definition of successful symptomatic outcome in the individual studies	(n = 79)	
degree of symptoms at follow-up	25 (31.6%)	-
patient satisfaction	22 (27.8%)	-
satisfaction defined	6 (27.3%)	-
satisfaction not defined	16 (72.7%)	-
visick grading system	7 (8.9%)	-
visick grading system combined with patient satisfaction	1 (1.3%)	-
scores calculated from specific quality of life questionnaires	5 (6.3%)	-
miscellaneous	5 (6.3%)	-
not reported	14 (17.7%)	-
Patients available at follow-up	3 338 (74.0%)	581 (12.9%)
Duration of follow-up (months)	34.2 ± 2.7	21.8 ± 4.7
Patients with successful outcome	2 706 (81.1%)	455 (78.3%)

Values are given as mean ± SEM, unless otherwise stated.

In patients in whom the reoperation was performed for symptoms only, 82.0 ± 10.7% had successful symptomatic outcome[47,79], and the success rate was 81.0 ± 12.1% in patients with recurrent reflux documented by pH monitoring[10,12,56,89]. Comparing the outcome of total and partial refundoplication, Awad et al.[53] reported symptomatic success in 68% and 60% of patients, respectively. In two other studies[11,45], however, no relationship between the type of fundoplication and the symptomatic outcome was found.

Objective outcome after reoperations

Objective outcome was reported in 696 patients (15.4%) in 24 studies (29.6%), without a definition of success[17,18,20] or the number of successful cases[14,17,18,20,28,49,87], however, in seven studies. In the remaining 17 studies, successful objective outcome was defined as normal acid exposure during pH monitoring in 11[8,15,19,23,25,36,38,51,57,58,88], absence of oesophagitis in four [10,54,59,76], combination of these both in one[75], and the absence of reflux during radiologic imaging in another one[65]. In these 17 studies, 78% had a successful objective outcome (*Table 7*). The mean success rate of laparoscopic reoperation (four studies[19,23,25,88]) seemed higher than in the case of a conventional abdominal approach (four other studies[10,58,75,76]), 85.8 ± 5.6% and 78.0 ± 10.1%, respectively.

Discussion

The often reported observations that morbidity and mortality are higher after redo antireflux surgery and symptomatic outcome is inferior to primary antireflux surgery have been confirmed in this systematic review on all studies currently available. Very few had a prospective study design, and in almost half of all, the type of analysis was not even reported. Moreover, most studies only presented symptomatic outcome, and data on anatomy and function of the oesophagogastric junction were scarce.

Morbidity was most frequently caused by direct injury of the oesophagus and stomach during reoperation in the current review, and this was confirmed in our own data on redo surgery[8], mainly as a result of increased complexity due to adhesions after the primary operation. Most primary interventions in the studies reviewed were performed by the conventional approach. Nowadays, with laparoscopy as the golden standard, less adhesions may be encountered if redo surgery is required. This might improve the outlook for these patients with a lower chance of iatrogenic organ damage, but this has to be proven in future studies. Although postoperative morbidity and mortality appeared to be lower after laparoscopic reoperations compared to the open abdominal approach, intraoperative complications occurred more frequently during laparoscopic surgery. These data, however, are not based on

comparison between both approaches within individual studies, and therefore, this should, in our opinion, be interpreted with caution.

The cause of failure was recognised in 93.8% and mainly consisted of anatomical abnormalities or an erroneous indication for primary surgery. Disruption of hiatal repair and a too tight wrap were more frequently observed after laparoscopic than after the open approach. This again underlines the difficulty of doing an adequate hiatal repair and creating a "floppy" wrap by laparoscopy. Achalasia was the most frequently reported incorrect diagnosis as the cause of failure, and this supports the inclusion of oesophageal manometry and 24-hour pH monitoring in the preoperative workup. It has also been suggested that a too tight fundoplication can cause an achalasia-like clinical picture[90]. Oesophageal manometry shows, in those circumstances, a non-relaxing lower oesophageal sphincter, but not an aperistaltic oesophagus[91].

Preoperative workup before reoperation is, apparently, not standardised but tailored to the cause of failure and the indication for reoperation. In the case of dysphagia, this consists of barium swallow to evaluate the oesophageal and gastric anatomy and oesophageal manometry to detect whether or not a motility disorder may be an (additional) cause of failure. In patients with reflux symptoms, extensive re-evaluation is essential. Symptoms have been shown, however, to be bad predictors of pathological reflux after primary antireflux surgery[92] and unrelated to anatomical wrap position[93]. Therefore, objective preoperative workup is equal to patients evaluated for primary antireflux surgery and consists of oesophagogastroduodenoscopy, oesophageal manometry and 24-hour pH monitoring, completed with barium swallow to evaluate the anatomy in addition to endoscopy.

Symptomatic outcome was described in most studies in this review with a success rate ranging from 56-100%. The definitions for success showed considerable variation and focus either on a more general or overall system or on specific symptoms with or without mentioning data on quality of life and the effect of surgery on quality of life aspects, compromising comparison between the individual studies. Patient satisfaction was a frequently used method for scoring symptomatic outcome. Patient satisfaction is important and clinically highly relevant, but it does not directly refer to the specific symptoms of the disease, and consequently, this type of scoring does not provide insight in which aspects of the disease have improved and whether or not reflux symptoms have been exchanged by, for example, dysphagia. The Visick grading system, indicating that the disease was cured or improved with Visick grades I and II or unchanged or worsened in grades III and IV considered a symptomatic failure[94], correlated well with postoperative daily reflux-related symptoms and daily complaints of dysphagia in our patient group on redo antireflux surgery[8].

Objective outcome was only reported in less than one third of the included studies in this review, with a mean success rate of 78%, which is slightly worse than after primary surgery.

In our unit, all patients are encouraged to undergo stationary oesophageal manometry and ambulatory 24-hour oesophageal pH monitoring before and after primary as well as redo antireflux surgery primarily for quality control, but also to be able to correlate the functional results with symptoms and to understand possible future symptoms. Although previous studies have shown that for a good symptomatic outcome after primary surgery optimal anatomical and functional results are not a prerequisite[92,93], more studies reporting the anatomical and functional status of the oesophagus and stomach after redo surgery are required to outline a more complete overall picture of the outcome of redo antireflux surgery. In conclusion, redo antireflux surgery has a higher morbidity and mortality rate than primary antireflux surgery and symptomatic outcome is less satisfactory. Consistency with regard to reporting on symptomatic and objective outcome is necessary. Data on objective results after redo antireflux surgery are scarce and a plea can be made to subject all primary cases to full-scale evaluation, before and after antireflux surgery. Data to support this suggestion with evidence, like adequate cost-effectiveness studies, are lacking. The relative disappointing results of redo antireflux surgery with regard to morbidity, mortality, and symptomatic outcome support the opinion that redo surgery is tertiary referral centre surgery and these centres should continue their efforts to collect prospective subjective and objective data.

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5

Laparoscopic Nissen Fundoplication
after Failed EsophyX Fundoplication

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Abstract

Background

After endoluminal EsophyX fundoplication for gastro-oesophageal reflux disease, reflux control has shown to be ineffective in a substantial number of patients. Subsequent laparoscopic Nissen fundoplication (LNF) might be required to reach treatment goals. The aim of this study was to evaluate the outcome of LNF after previous EsophyX fundoplication.

Methods

Eleven consecutive patients who underwent LNF after failed EsophyX were included. Symptomatic outcome was obtained by standardised questionnaires, and objective outcome by endoscopy, oesophageal manometry and pH monitoring.

Results

During LNF, intraoperative gastric perforation occurred in two patients (18.2%), and one patient (9.1%) developed a subphrenic abscess postoperatively. After LNF, daily heartburn was present in one patient (9.1%) and three patients (27.3%) had daily troublesome dysphagia. General quality of life did not increase significantly. Oesophageal acid exposure was normalised in all patients after surgery. Oesophagitis was absent after LNF in all, except one patient (9.1%) who had persisting grade A oesophagitis.

Conclusion

This study has shown that symptomatic and objective reflux control are satisfactory after LNF for failed EsophyX fundoplication. Previous EsophyX, however, is associated with a risk of gastric injury during LNF. Although the number of included patients was small, a relatively high frequency of refractory troublesome dysphagia was found after surgery.

Introduction

To offer patients an alternative to lifelong use of antisecretory drugs and to avoid prolonged recuperation of antireflux surgery, endoscopic treatment modalities for gastro-oesophageal reflux disease (GORD) have been introduced[1,2]. In addition, treatment on outpatient basis has been claimed as an advantage[3,4]. These techniques have been developed with the objective to provide reflux control comparable to Nissen fundoplication without causing adverse events, such as dysphagia and gas bloating[5,6]. The EsophyX plications system is an endoscopic suturing technique which has been applied at larger scale.

One large prospective study concerning the symptomatic and objective outcome of endoluminal plication using the EsophyX device reported a significant reduction in reflux symptoms with cessation of PPI usage in approximately 70% of patients[7]. However, oesophageal acid exposure was normalised in only 37% at 12 months follow-up. After endoluminal EsophyX fundoplication, a subset of patients has recurrent or persistent GORD and may be a candidate for subsequent surgery. The outcome of laparoscopic Nissen fundoplication (LNF) after previous EsophyX fundoplication is unknown.

The aim of this study was to evaluate the influence of previous endoluminal EsophyX fundoplication on symptomatic and objective outcome of subsequent LNF.

Methods

Patients

Between 2006 and 2008, 88 patients underwent an EsophyX fundoplication (EsophyX, EndoGastric Solutions, Redmond, WA, USA). Because of persistent or recurrent GORD, a subset of eleven patients (12.5%) subsequently underwent LNF. For all patients, data of preoperative workup and intra- and postoperative course of the initial endoluminal procedure and subsequent LNF were prospectively documented.

Endoluminal and surgical techniques

EsophyX procedure

During the EsophyX procedure, a full-thickness plication of the stomach wall was created. The EsophyX device was advanced into the stomach over a standard endoscope with visualisation of the gastro-oesophageal junction using retroversion of the scope. To create a full-thickness fold at the level of the gastro-oesophageal junction over 180-300° of the circumference, the angle of His was retracted by the EsophyX device. The fold was fixated with 14-20 polypropylene fasteners. The procedures were performed by a surgeon and a gastroenterologist under

general anaesthesia with the patients positioned on the left side. Patients with a type I hiatal hernia larger than 3 cm, oesophageal stricture, Barrett's oesophagus, reflux oesophagitis grade C or D, or previous oesophageal or gastric surgery were not considered candidates for the EsophyX procedure.

Laparoscopic Nissen fundoplication

Laparoscopic Nissen fundoplication was performed in one of the three participating hospitals by three experienced laparoscopic surgeons. First, all visible polypropylene fasteners of the EsophyX fundoplication were cut by sharp dissection, and the EsophyX wrap was fully mobilised. Subsequently, a Nissen fundoplication was created in all patients, as previously described[8]. Briefly summarised, the oesophagus was mobilised until at least 3 cm of the distal part was positioned intra-abdominally. Posterior crural repair was performed in all patients, and a floppy 360º Nissen fundoplication was constructed after division of the short gastric vessels.

Symptomatic assessment

To obtain symptomatic information before treatment and after LNF, standardised questionnaires were used. Reflux-related symptoms were evaluated by the validated Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) score[9,10]. In addition, patients were asked to rate their preoperative symptoms as resolved, improved, unchanged or worsened according to the Visick grading system[11], and to score their general quality of life using a visual analogue scale (VAS)[12].

Objective assessment

Before EsophyX, upper endoscopy, stationary oesophageal manometry, and ambulatory oesophageal 24-hour pH monitoring were performed in all patients, and upper endoscopy was repeated in all patients afterwards. Furthermore, all patients were requested to undergo these investigations, completed by an additional barium oesophagogram after LNF. Written informed consent was obtained from all participating patients.

During upper endoscopy, data about the presence of reflux oesophagitis (graded according to the Los Angeles classification[13]), oesophageal stricture, Barrett's oesophagus and a type I hiatal hernia (ie, the distance between the squamocolumnar junction and diaphragmatic impression) were obtained. In addition, the presence of (partial) disruption of the wrap was evaluated during endoscopy after EsophyX and LNF.

Oesophageal manometry and pH monitoring were performed as previously described[14]. Briefly summarised, manometry was carried out by transnasal positioning of a sleeve sensor (Dentsleeve Pty Ltd, Adelaide, Australia) at the level of the lower oesophageal sphincter

(LOS). In response to ten standardised wet swallows, mean end-expiratory LOS pressure and residual pressure of the LOS during relaxation were determined. LOS pressure ranging from 0.6-3.5 kPa and residual LOS pressure for at most 1.4 kPa was defined as normal. Subsequently, a pH glass electrode (model LOT 440 M3; Medical Instruments Corporation, Solothurn, Switzerland) was introduced to measure the intraluminal pH during 24 hours. Oesophageal acid exposure was defined as abnormal with pH < 4 in the distal oesophagus during more than 5.8% of total time, more than 8.2% of time in upright position and/ or more than 3.5% of time in supine position[15].

Barium oesophagogram series was performed after LNF to assess the presence of wrap disruption, cephalad slippage of the gastro-oesophageal junction through the wrap (telescoping), intrathoracic wrap migration, and hiatal herniation.

Statistical analysis

Values were expressed as mean ± SD. Data were analysed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA). The paired samples *t* test was used for statistical analysis of differences between continuous values before and after the endoluminal EsophyX fundoplication, and after LNF.

Results

Basic demographics are presented in *Table 1*. All eleven patients who underwent subsequent LNF, experienced symptoms of heartburn before the primary EsophyX procedure. Additionally, two patients had regurgitation and one dysphagia. All patients were treated with antisecretory drugs, and symptoms were refractory in seven. After the EsophyX, seven patients experienced persistence of their primary symptoms, and four had recurrent symptoms. In three patients, endoscopy after EsophyX showed disruption of all fasteners, and in five, the EsophyX wrap was partially disrupted. Three of these eight patients had oesophagitis. The other five had no oesophagitis. However, as the anatomical failure of the repair combined with recurrence of the primary symptoms was the indication for LNF, oesophageal pH monitoring was not performed in them. In the remaining three patients, the EsophyX wrap was intact, but pH monitoring after EsophyX showed abnormal oesophageal acid exposure in two patients, whilst the third patient had typical symptomatic recurrence. LNF was performed after a mean period of 8.1 ± 5.2 months.

Intraoperative and postoperative results

During LNF, gastric perforation occurred in two patients (18.2%). Conversion to laparotomy was necessary in one patient to control damage of the fundus. Mean duration of operation was 95.8 ± 25.6 minutes. During the postoperative course, a left-sided subphrenic abscess, requiring surgical exploration, developed in one patient (9.1%). Oesophageal or gastric perforation as cause for this complication, however, was not recognised during laparotomy. There were no other postoperative complications. The mean hospital stay was 3.4 ± 1.1 days.

Outcome after surgery

Number of patients available for follow-up after Nissen fundoplication and time to follow-up are presented in *Table 1*.

Table 1   *Baseline characteristics*

	Total (n = 11)
Male / female	6 (54.5%) / 5 (45.5%)
Age (years)	45.8 ± 14.5
Body mass index (kg/m²)	24.9 ± 2.8
Time to follow-up (months)	11.2 ± 8.7
Patients available at follow-up	
symptomatic follow-up	11 (100%)
24-hour pH monitoring	7 (63.6%)
upper endoscopy	11 (100%)
barium oesophagogram	9 (81.8%)

Values are given as mean ± SD, unless otherwise stated.

Symptomatic assessment

In seven patients (63.6%), preoperative symptoms were resolved or improved. Three patients who rated their symptoms as worsened, had new-onset daily dysphagia, and underwent endoscopic dilatation without satisfactory outcome. The fourth patient with worsened symptomatic outcome had daily heartburn after Nissen fundoplication, but pathological oesophageal acid exposure was not objectified during postoperative pH monitoring. General quality of life and the GERD-HRQoL score were improved, although this was only statistically significant for the latter one (*Table 2*).

Table 2   *Symptomatic variables*

	Total (n = 11)
Self-rated change in symptoms compared with	
preoperative status (Visick grading system)	
resolved	5 (45.5%)
improved	2 (18.2%)
unchanged	0 (0%)
worsened	4 (36.4%)
GERD-HRQoL score	
preoperative (before EsophyX fundoplication)	20.7 ± 6.0
follow-up	6.6 ± 7.5*
General quality of life score (VAS)	
preoperative (before EsophyX fundoplication)	44.1 ± 22.8
follow-up	54.5 ± 30.2†

Values are given as mean ± SD, unless otherwise stated.
P-value with regard to the difference between preoperative value and value at follow-up was .001*, and .179†.
Abbreviations: GERD-HRQoL, Gastro-Esophageal Reflux Disease Health Related Quality of Life score; VAS, visual analogue scale.

Objective assessment

After LNF, four patients refused pH monitoring and two barium oesophagogram. Three of these four patients rated their preoperative symptoms as resolved or improved, and one had worsened symptoms due to troublesome dysphagia.

Five patients (45.5%) had oesophagitis before the EsophyX procedure; this was resolved in three patients after this procedure, and progressed from grade A to grade B in two. Two other patients developed oesophagitis after the EsophyX procedure. After LNF, one patient (9.1%) had oesophagitis grade A (**Table 3**).

Table 3   *Grade of oesophagitis*

	Before EsophyX fundoplication (n = 11)	After EsophyX fundoplication (n = 11)	After Nissen fundoplication (n = 11)
Grade of oesophagitis*			
none	6 (54.5%)	7 (63.6%)	10 (90.9%)
grade A	4 (36.4%)	1 (9.1%)	1 (9.1%)
grade B	1 (9.1%)	3 (27.3%)	0 (0%)

*Oesophagitis classified according to the Los Angeles classification.

After EsophyX, oesophageal manometry showed a decrease in mean LOS pressure from 1.3 ± 0.8 kPa to 1.0 ± 0.9 kPa, and a rise to 1.8 ± 0.8 kPa after LNF. During pH monitoring, mean oesophageal acid exposure times were increased after the EsophyX procedure, but reduced after Nissen fundoplication (*Figure 1*). After LNF, oesophageal acid exposure was normalised in all patients.

Barium oesophagogram series showed normal anatomy in all, except one patient who had intrathoracic wrap migration. This patient rated symptomatic outcome as resolved.

Figure 1   *Mean oesophageal acid exposure times*
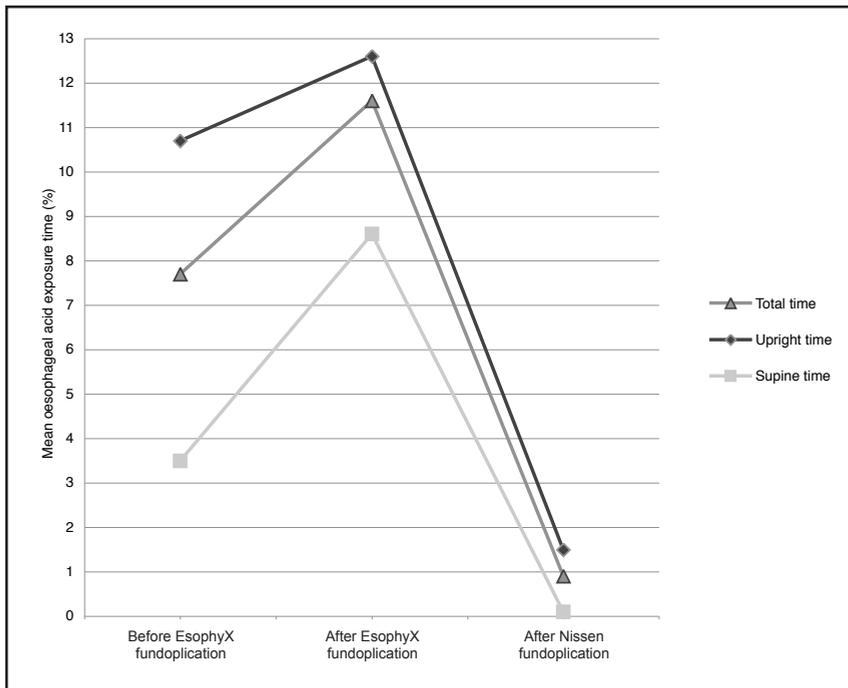
P-value with regard to the differences between before EsophyX fundoplication and after Nissen fundoplication was < .050 for the mean total and upright oesophageal acid exposure times.

Discussion

In this study, laparoscopic Nissen fundoplication after previous endoluminal EsophyX fundoplication was accompanied with a high incidence of gastric injury. Objective reflux control and reduction of reflux symptoms after LNF were satisfactory. However, daily complaints of dysphagia after Nissen fundoplication were encountered relative frequently, in 27% of patients. Additionally, general quality of life did not significantly improve after surgery. Compared to studies on patients with a Nissen fundoplication as primary treatment[16], postoperative scores according to the Visick grading system[11] were lower. The high incidence of dysphagia after LNF contributed mostly to this finding. All three patients with troublesome dysphagia after surgery had an endoscopic dilatation, but dysphagia persisted in all of them. As a result, recurrent heartburn after EsophyX may be easier to control by medical therapy than troublesome dysphagia after LNF. Therefore, patients should be warned against this possible poor symptomatic outcome before EsophyX is undertaken. In addition to the moderate objective reflux control of the primary EsophyX procedures as previously described[7], the presence of refractory dysphagia after LNF in a large subset of patients who underwent EsophyX prior to surgery supports the opinion that an EsophyX procedure may not be a desirable treatment modality for gastro-oesophageal reflux disease. However, due to the scarcity of patients who underwent a Nissen fundoplication after a previous endoluminal EsophyX fundoplication, the current study describes a relative small patient population. Therefore, this disappointing symptomatic outcome should be confirmed by future studies before definitive conclusions should be drawn from the results as were found in the current study.

After EsophyX fundoplication, the (remnants of the) wrap had to be freed by cutting the polypropylene fasteners before a Nissen fundoplication could be applied. During all surgical interventions, part of the fasteners appeared to be fixated to the left and, to a less extent, to the right crus with firm adhesions between the stomach, oesophagus, and diaphragm. In our opinion, because of the presence of the fasteners and adhesions, the mobilisation and dissection of the stomach from the oesophagus and diaphragm is associated with an increased risk of injury to the gastric wall. A relatively high incidence of stomach perforations (27%) occurred in the current study compared to 0-2% during primary antireflux surgery[17,18], and 13% during redo antireflux surgery[19]. This is understandable in the perspective of the procedure. The fasteners perforate both the distal oesophagus and gastric fundus, but the line of fasteners is covered by the EsophyX fundoplication. During release, all fasteners are cut, and fastener channels that do not present as visible perforations are not covered by definition during subsequent Nissen fundoplication. As no oesophageal or gastric perforation could be detected during reoperation, this probably explains the development of an intra-abdominal abscess in one of the patients.

The macro- and micro-injuries of the gastric wall had major consequences in the current study; in one of the obvious intraoperative perforations, conversion to laparotomy was required, and the patient who developed a subphrenic abscess during the postoperative period, also required a laparotomy. Surgeons dealing with this kind of surgery should be thoroughly aware of the increased risk of gastric injury during LNF after EsophyX, and patients should be informed about this prior to EsophyX fundoplication.

In conclusion, this study has shown that LNF after previous EsophyX fundoplication entails a high risk of gastric injury. Complete mobilisation and thorough inspection of the gastric fundus is the key toward safe redo surgery. In addition, compared to primary LNF, the incidence of refractory troublesome dysphagia after surgery was relatively high. Consequently, general quality of life did not increase significantly. Although the number of included patients was small in the current study, surgery after previous failed EsophyX fundoplication seems not to be such a straightforward option as previously thought.

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Part

2

Surgical Repair of Large Hiatal Hernias

Long-term Symptomatic Outcome and Radiologic Assessment of Laparoscopic Large Hiatal Hernia Repair

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Abstract

Background

The long-term durability of laparoscopic repair of large hiatal hernias (type II-IV) is uncertain. This study focuses on the long-term symptomatic and radiologic outcome of laparoscopic large hiatal hernia repair.

Methods

Between 2000 and 2007, 70 patients (49 females, mean age ± SD, 60.6 ± 10.9 years) undergoing laparoscopic repair of a large hiatal hernia were studied prospectively. After a mean follow-up of 45.6 ± 23.8 months, symptomatic (65 patients, 92.9%) and radiologic follow-up (60 patients, 85.7%) was performed by standardised questionnaires and oesophagograms.

Results

The symptomatic outcome was successful in 58 patients (89.2%), and gastro-oesophageal anatomy was intact in 42 patients (70.0%). The addition of a fundoplication was the only significant predictor of unfavourable radiologic outcome in the univariable analysis (odds ratio 0.413 (95% confidence interval 0.130-1.308), P = .125).

Conclusion

The long-term symptomatic outcome of laparoscopic repair of large hiatal hernias was favourable in 89% of patients, and 70% had successful anatomical repair. The addition of a fundoplication did not prevent recurrent anatomical herniation.

Introduction

Type I hiatal hernias of the gastro-oesophageal junction comprise 95% of all hiatal herniations, whereas large hiatal herniation (type II-IV) is a relative uncommon disorder of the digestive tract[1,2]. Surgery was considered the treatment of choice and recommended in all patients with a large hiatal hernia for years regardless of the complaints experienced to avoid potentially life-threatening complications such as incarceration[3]. Most patients with a large hiatal hernia are symptomatic and therefore should be offered surgical repair[4], but for minimally symptomatic and asymptomatic patients a watchful waiting attitude is currently proposed. However, studies comparing operative correction and observation are scarce[5,6].

Less complications, less postoperative pain, and shorter hospital stay are the advantages for laparoscopic compared with open repair[7-10], and laparoscopy is therefore the preferred approach in the management of large hiatal hernias[10]. Despite the advantages of the laparoscopic repair, the durability of this approach regarding symptomatic and anatomical outcome is questioned by many authors[4,7-9,11,12]. Randomised trials comparing both approaches for large hiatal hernia repair are not available, but some case-control studies have been published[4,9,10]. These studies are mainly directed on feasibility and symptomatic outcome. The assessment of anatomical outcome is essential as well because symptomatic outcome may underestimate the true recurrence rate because of uncertain correlation between symptomatic and anatomical outcome[4,8,13]. In several cohort studies on the laparoscopic repair of large hiatal hernias, the anatomical outcome has been investigated, but most of these studies focus on short-term follow-up[7,8,14-25], whereas reports on long-term outcome are very scarce[11,26,27].

This study focuses on the long-term radiologic assessment after laparoscopic large hiatal hernia repair in a large prospective cohort and on the correlation of the radiologic findings to the symptomatic outcome.

Methods

Patients

Between January 2000 and December 2007, all patients over 18 years who had primary laparoscopic correction of a large hiatal hernia were included in this prospective cohort study. Patients who underwent surgical repair of recurrent hiatal herniation, surgery for gastro-oesophageal reflux disease without the presence of a large hiatal hernia, emergency surgery, or hiatal hernia repair after primary antireflux surgery were excluded.

Before surgery, the patient's presenting symptoms were assessed. Hiatal herniation was preoperatively diagnosed by a barium oesophagogram in all patients and defined

as protrusion of (a part of) the stomach into the thoracic cavity with or without the gastro-oesophageal junction. During the first part of the study period, upper endoscopy, stationary oesophageal manometry, and ambulatory oesophageal pH monitoring were only performed preoperatively if clinical history suggested gastro-oesophageal reflux disease. In more recent years, however, these investigations were part of the standard preoperative workup in our institution for patients with a large hiatal hernia, regardless of symptoms.

Surgical technique

All patients had repair of the large hiatal hernia by laparoscopy performed by two gastrointestinal surgeons with extensive experience in laparoscopic surgery (I.A.M.J.B. and R.K.J.S.). Repair consisted of dissection of the hernia sac from the mediastinum followed by reduction of the herniated stomach and oesophagus until at least 3 cm of the distal oesophagus was tension free in the abdomen. Subsequently, posterior crural repair was performed by approximating the right crus with non-absorbable stitches to narrow the oesophageal hiatus until approximately 1 cm between the oesophagus and crus remained. Herein, a bougie was not used to judge the extent of crural closure. Neither mesh nor pledgets were used in the repair of any patient. If gastro-oesophageal reflux disease was diagnosed based on preoperative symptoms and subsequent endoscopy and ambulatory 24-hour oesophageal pH monitoring, a fundoplication was added that was sutured to the crus posteriorly.

Follow-up after surgery

Symptomatic assessment
Symptomatic information was obtained by sending a standardised and validated symptom questionnaire to all patients. Preoperative symptoms were scored according to the Visick grading system (preoperative symptoms resolved, improved, changed, or worsened)[28], and general quality of life was assessed using a visual analogue scale. To evaluate reflux-related symptoms, the Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) questionnaire was used, containing nine gastro-oesophageal reflux disease-specific items that have to be scored according to a system combining severity and frequency (score from zero for no symptoms to five for symptoms incapacitating patients from performing daily activities), eventually yielding a score between zero and 45[29]. Furthermore, patients were also asked to report treatment with any antisecretory or prokinetic drug. Finally, the ability to belch and the extent of flatulence with respect to the preoperative status were scored for severity on a four-points scale and were compared between patients with and without an antireflux procedure. Symptomatic outcome at follow-up was defined as successful if patients scored preoperative symptoms according to the Visick grading system as resolved or improved.

Radiologic assessment

Patients were invited to undergo a barium oesophagogram to establish the anatomical status of the repair. Written informed consent was obtained from all patients who agreed to participate.

Oesophagograms were first judged by one of several independent radiologists and afterwards reviewed by a radiologist with extensive experience with oesophageal pathology (G.S.) to exclude misinterpretation. In patients without an antireflux procedure, the position of the stomach and the gastro-oesophageal junction in relation to the diaphragm was assessed to determine if any type of recurrent hiatal hernia had occurred. The following items were assessed on an oesophagogram if fundoplication was added to the repair: completeness of the wrap, telescoping (ie, cephalad slippage of the gastro-oesophageal junction through the wrap), intrathoracic wrap migration, and para-oesophageal hiatal herniation (herniation of a part of the stomach to the posterior mediastinum with the gastro-oesophageal junction and the wrap in its normal subdiaphragmatic position). Most patients (n = 44, 62.9%) had previous postoperative imaging showing intact oesophageal and gastric anatomy.

Radiologic outcome at follow-up was considered successful if herniation of the stomach, wrap, and gastro-oesophageal junction were absent on contrast oesophagogram.

Predictors of symptomatic and radiologic success during follow-up

Different variables were analysed to identify independent predictors of both successful symptomatic and radiologic outcome, as previously defined. The predictability of patient-specific characteristics including sex, age and body mass index (defined as body weight divided by the square of the height in metres), type of large hiatal hernia, addition of an antireflux procedure to the repair, and duration of follow-up was assessed for both successful symptomatic and successful radiologic outcome. Furthermore, the predictive value of successful symptomatic outcome was determined for successful radiologic outcome.

Statistical analysis

Values were expressed as mean ± SD. Data were analysed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA). The paired samples *t* test was used for statistical analysis of differences between continuous preoperative and follow-up values, and, for categorical values, the McNemar test was used. Statistical analysis of categorical values between groups was performed using the Pearson χ^2 test. Correlations between categorical values were determined using the Spearman coefficient. Differences between preoperative and follow-up values and differences between groups were considered statistically significant with P < .050. The predictive value of the aforementioned variables for successful symptomatic and radiologic outcome was separately determined in univariable analysis by binary logistic

regression analysis. Variables with P < .200 in the univariable analysis were entered together in the multivariable analysis performed by binary logistic regression analysis using backward stepwise selection of variables. Variables with P < .100 in the multivariable analysis were considered independent significant predictors of follow-up. The odds ratio, 95% confidence interval and P-value are presented for these variables.

Results

Baseline characteristics of the 70 patients are presented in *Table 1*. The preoperative presenting symptoms were heartburn in 39 patients (55.7%), regurgitation in 33 (47.1%), dysphagia in 27 (38.6%), chest pain in 13 (18.6%), and 12 patients (17.1%) had anaemia and were otherwise asymptomatic. Hiatal herniation was diagnosed by barium oesophagogram in all patients, and most patients had a type III hiatal hernia (*Table 1*). Upper endoscopy was performed in 31 patients (44.3%) before operation, and the mean intrathoracic herniation of the gastro-oesophageal junction was 6.6 ± 2.9 cm in these patients.

During repair, an antireflux procedure was added in 37 patients (52.9%; Nissen fundoplication in 32 and partial fundoplication in five patients) who had reflux-related symptoms and signs of gastro-oesophageal reflux disease on endoscopy and/ or pathological acid exposure during 24-hour oesophageal pH monitoring. Collis gastroplasty was added in one patient (1.4%) because of intraoperatively encountered short oesophagus.

Table 1   *Baseline characteristics*

	Total (n = 70)
Male / female	21 (30.0%) / 49 (70.0%)
Age (years)	60.6 ± 10.9
Body mass index (kg/m²)	28.6 ± 5.3
Type of large hiatal hernia	
type II	6 (8.6%)
type III	55 (78.6%)
type IV	9 (12.9%)

Values are given as mean ± SD, unless otherwise stated.

Follow-up after surgery

The mean duration of follow-up was 45.6 ± 23.8 months, and a total of 65 patients (92.9%) were available for symptomatic follow-up. There was one in-hospital death caused by cardiac failure, three patients were lost during the follow-up period, and one patient never returned the questionnaire despite repeated contact (*Figure 1*). In addition, five patients who participated at symptomatic follow-up refused barium oesophagogram, and, therefore, 60 patients (85.7%) were available for radiologic follow-up.

Figure 1 *Study profile*
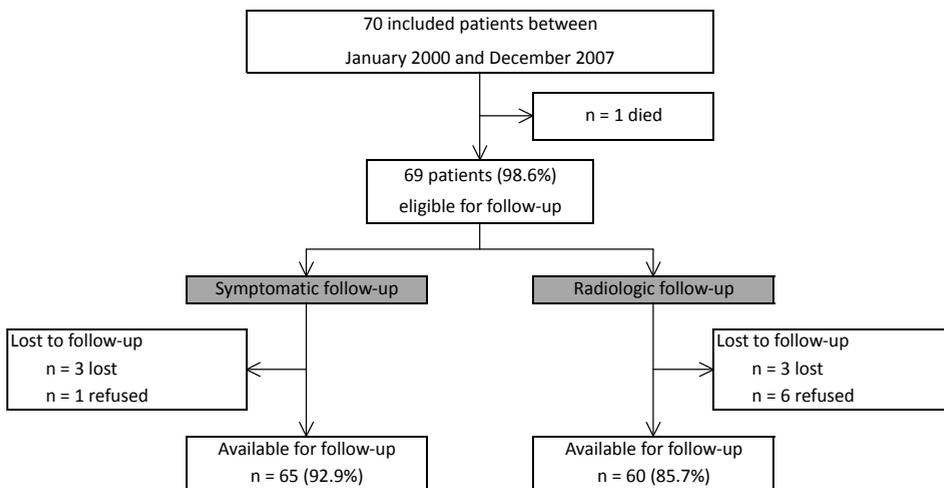
Symptomatic assessment

Fifty-eight patients (89.2%) rated their preoperative symptoms according to the Visick grading system as resolved or improved. Furthermore, there was a significant improvement of the Gastro-Esophageal Reflux Disease Health Related Quality of Life score as well as the general quality of life score at follow-up with respect to preoperative reference values (*Table 2*).

Eight patients (12.3%) experienced daily heartburn at follow-up. Five out of these eight patients had oesophageal pH monitoring during their postoperative course; three of them had normal oesophageal acid exposure, whereas pathological acid exposure was present in the other two patients. Daily dysphagia was also present in eight patients (12.3%) at follow-up. In four, this was new-onset dysphagia, and two of these patients had a Nissen fundoplication added during the repair. In the four patients with persistent dysphagia, two patients had a fundoplication added to the hiatal hernia repair. The presence of daily heartburn and

daily dysphagia at follow-up were both correlated to an unsuccessful symptomatic outcome according to the Visick grading system (r = 0.323; P = .009 and r = 0.474; P < .001, respectively). The ability to belch was not statistically significant different between patients with and without added antireflux procedure at follow-up (19 / 34, 55.9% vs. 18 / 31, 58.1%, respectively; P = .951) as was the postoperative increase of flatulence between both groups (21 / 34, 61.8% vs. 12 / 31, 38.7% , respectively; P = .065). Chest pain was present in 7 patients (10.8%) at follow-up.

Table 2   *Outcome of symptomatic follow-up*

	Total (n = 65)	P-value*
Self-rated change in symptoms compared with preoperative status (Visick grading system)		
resolved	23 (35.4%)	
improved	35 (53.8%)	Not applicable
unchanged	3 (4.6%)	
worsened	4 (6.2%)	
GERD-HRQoL score		
preoperative	11.7 ± 10.0	.006
follow-up	6.5 ± 7.3	
General quality of life score (VAS)		
preoperative	30.6 ± 23.0	<.001
follow-up	55.9 ± 24.4	
Use of antisecretory drugs		
preoperative	49 (75.4%)	.048
follow-up	22 (33.8%)	
Use of prokinetic drugs		
preoperative	9 (13.8%)	.493
follow-up	5 (7.7%)	

Values are given as mean ± SD, unless otherwise stated.
*P-value represents the difference between preoperative value and value at follow-up.
Abbreviations: GERD-HRQoL, Gastro-Esophageal Reflux Disease Health Related Quality of Life; VAS, visual analogue scale.

Radiologic assessment
Recurrent large hiatal herniation was shown on a barium oesophagogram in 11 patients (18.3%, type II in two and type III in nine), one patient (1.7%) had intrathoracic wrap migration, and in another six patients (10.0%) a limited type I hiatal hernia or telescoping in the case of an added antireflux procedure, with a mean extent of intrathoracic herniation of 2.8 ± 0.8 cm, was present (***Table 3***). Eight out of the eleven patients with a radiologic recurrent

large hiatal hernia had a fundoplication added at the time of surgery. Overall recurrent herniation was also more frequent in patients with an added fundoplication, although not statistically significant (12 / 31, 38.7% vs. 6 / 29, 20.7%; P = .128).

Two out of 18 patients (11.1%) with abnormal anatomy during radiologic follow-up, one with a recurrent large hiatal hernia and the other with telescoping, were symptomatic failures, whereas five out of 42 patients (11.9%) with an intact repair were unsatisfied with the outcome. All patients available for symptomatic follow-up but refusing barium oesophagogram rated symptomatic outcome as successful. There was no statistical significant correlation between the outcome of symptomatic and radiologic follow-up (r = -0.015; P = .908).

In patients with a recurrent large hiatal hernia at follow-up, one (9.1%) had a type II, nine (81.8%) type III, and one (9.1%) type IV hiatal hernia before operation, whereas this was 5 (11.9%), 32 (76.2%), and 5 (11.9%), respectively, in patients with an intact repair at follow-up.

Table 3   *Outcome of radiologic follow-up*

	Total (n = 60)
Repairs without antireflux procedure	
intact anatomical repair	23 (38.3%)
type I hiatal hernia	3 (5.0%)
large hiatal hernia (type II-IV)	3 (5.0%)
Repairs with antireflux procedure	
intact anatomical repair	19 (31.7%)
intrathoracic wrap migration	1 (1.7%)
telescoping	3 (5.0%)
large hiatal hernia (type II-IV)	8 (13.3%)

Predictors of symptomatic and radiologic outcome during follow-up

In the univariable analysis, duration of follow-up was the only significant predictor of successful symptomatic outcome (***Table 4***). For successful radiologic outcome, the addition of an antireflux procedure was a negative predictor in the univariable analysis (***Table 5***). Because there was only one variable of significant predictive value in the univariable analysis for both outcome parameters, a predictive model could not be constructed.

Table 4   *Results of univariable analysis of successful symptomatic follow-up*

	Odds ratio	95% confidence interval	P-value*
Male	1.037	0.183 - 5.874	.968
Age (years)	0.986	0.910 - 1.069	.735
Body mass index (kg/m²)	1.019	0.872 - 1.191	.810
Type of large hiatal hernia	0.639	0.070 - 5.826	.678
Addition of an antireflux procedure	0.804	0.165 - 3.913	.786
Duration of follow-up (months)	1.025	0.988 - 1.062	.165

*Binary logistic regression analysis.

Table 5   *Results of univariable analysis of successful radiologic follow-up*

	Odds ratio	95% confidence interval	P-value*
Male	0.897	0.276 - 2.913	.856
Age (years)	1.034	0.980 - 1.091	.222
Body mass index (kg/m²)	0.953	0.863 - 1.052	.341
Type of large hiatal hernia	0.640	0.153 - 2.671	.531
Addition of an antireflux procedure	0.413	0.130 - 1.308	.125
Duration of follow-up (months)	1.003	0.980 - 1.026	.820
Successful symptomatic follow-up	0.900	0.158 - 5.140	.905

*Binary logistic regression analysis.

Surgical reinterventions

Eight patients had surgical reintervention after primary repair with a mean intermediate period of 16.8 ± 13.3 months; in four it was because of a symptomatic recurrent large hiatal hernia or intrathoracic migration of the wrap, in two other patients Nissen fundoplication was converted to a partial fundoplication for troublesome dysphagia because of motility disorders of the oesophagus, in one other patient surgery was performed for symptomatic type I hiatal hernia, and in another patient it was because of troublesome dysphagia based on a too tight cruraplasty. At follow-up, the symptomatic outcome was successful (Visick score) in half of these patients. Two patients again showed a recurrent hiatal hernia on postoperative barium oesophagogram, and both scored their symptomatic outcome as unsuccessful.

Discussion

In this prospective study, the symptomatic outcome of laparoscopic repair of large hiatal hernias was successful in almost 90% of patients after a mean follow-up of nearly four years. Radiologic follow-up, however, showed a recurrent large hiatal hernia in 18% of patients, intrathoracic wrap migration in 1%, and a small type I hiatal hernia in another 10%. Given the fact that this type of surgery is mainly done to correct the anatomy at the level of the hiatus and gastro-oesophageal junction, there is a 30% failure in this study. However, the restoration of the anatomical defect, obviously, is not the only reason for surgery because a variety of symptoms is the reason for these patients to seek medical help.

The symptomatic success rate in this study was slightly higher than in other studies reporting success rates at long-term follow-up ranging from 80-86%, whereas radiologic or anatomical success, reported between 65% and 70%, was comparable[11,26]. In these studies, however, only about two thirds of patients were available at follow-up, which is in contrast to 86% in this study. Patients operated in early experience of the surgeons with laparoscopic large hiatal hernia repair were also included in the current study, but subgroup analysis revealed that this did not influence the symptomatic as well as the anatomical outcome, as was found by others[30]. The discrepancy between the symptomatic and objective success rate is also known from studies conducted for gastro-oesophageal reflux disease[31,32]. Information about the natural history of asymptomatic recurrences is absent in the current literature, and there is a need for evaluation over a longer period of time. Anyhow, in this study, surgical treatment was not performed in patients with minimally symptomatic or asymptomatic recurrences.

Younger age and obesity were independent predictors of higher incidence of a radiologic recurrent hiatal hernia in the study by Aly et al.[26], whereas others found longer follow-up to be a significant predictor of objective outcome[27]. Duration of follow-up was the only factor with significant predictive value of symptomatic outcome in univariable analysis in the current study. Age and body mass index were also analysed but appeared not to be of predictive value of symptomatic as well as anatomical outcome.

An antireflux procedure was only selectively performed in the current study in case of preoperative established gastro-oesophageal reflux disease. Analysis of the addition of an antireflux procedure to the large hiatal hernia repair during logistic regression analysis revealed that its use was a predictor of radiologic recurrence in the univariable analysis. In other studies[8,26,27], the predictive value of this variable for recurrence was not analysed. We do not have a solid explanation for the predictability of this variable for radiologic recurrence. Although it is suggested by some authors that an antireflux procedure prevents reherniation of the stomach by functioning as an intra-abdominal buttress[25,33], there is currently no evidence that supports its routine use for this purpose. Information of the addition of

antireflux procedures to treat or prevent gastro-oesophageal reflux in the repair of large hiatal hernias is yet lacking. Therefore, we currently perform a prospective study with standardised preoperative workup and postoperative symptomatic and objective evaluation to decide on the routine or selective use of an antireflux procedure in the repair of large hiatal hernias. Until the results of that study are available, it is difficult to recommend either the selective or routine use or complete avoidance of an antireflux procedure.

The use of mesh is gaining popularity, especially with large hiatal hernia repair to prevent recurrences. Two randomised controlled trials showed a significant reduction of recurrence from 22-24% to 0-9%[34,35]. Follow-up is still short, and (long-term) complications can occur such as troublesome dysphagia and oesophageal erosions possibly causing perforation[36-38]. Hazebroek et al.[39] evaluated these complications in a small cohort of 19 patients who underwent large hiatal hernia repair with mesh at a mean follow-up of 34 months, and none of them had oesophageal erosions during upper endoscopy. An increase in the incidence and severity of dysphagia was also not observed. Because the efficiency and safety of mesh in the short-term seem to be promising, a more liberal attitude regarding the use of mesh was recently introduced in our institute. The long-term results, however, have to support the use of mesh in large hiatal hernia repair routinely. Moreover, different shapes and materials of the mesh and types of repair were used in different studies[36,38]. Future research should therefore be performed to determine what type of mesh and which technique are the safest and most efficient.

In summary, symptomatic outcome in this study was very satisfactory, but objective large hiatal hernia recurrence was found in 18% of the patients. Symptomatic and anatomical outcome showed no correlation. The addition of an antireflux procedure does not prevent recurrent herniation after the repair of large hiatal hernias. Therefore, this study lends no support to the routine addition of a fundoplication to an anatomical repair of large hiatal hernias. However, the function of a fundoplication in the prevention or treatment of gastro-oesophageal reflux disease is unsure, and, therefore, future studies have to prove either its selective or routine use.

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7

Tailored or Routine Addition of an Antireflux Fundoplication in Laparoscopic Large Hiatal Hernia Repair; *A Comparative Cohort Study*

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Abstract

Background

There is controversy on the tailored or routine addition of an antireflux fundoplication in large hiatal hernia (type II-IV) repair. We investigated the strategy of selective addition of a fundoplication in patients with a large hiatal hernia and concomitant gastro-oesophageal reflux disease.

Methods

Between 2002 and 2008, 60 patients with a large hiatal hernia were evaluated by medical history, upper endoscopy, and oesophageal 24-hour pH monitoring. In patients with documented gastro-oesophageal reflux disease, an antireflux fundoplication was added.

Results

In 35 patients, an antireflux procedure was added; 25 underwent hiatal hernia repair only. In patients with fundoplication, oesophagitis was present in six patients (22.2%) after surgery, and abnormal oesophageal acid exposure persisted in eleven (39.3%). Seven patients (38.9%) with hernia repair only developed abnormal oesophageal acid exposure, and oesophagitis was postoperatively generated in five (27.8%). In neither group, patients had new-onset daily heartburn and dysphagia.

Conclusion

In patients with a large hiatal hernia associated with gastro-oesophageal reflux disease, addition of a fundoplication gives acceptable reduction of symptoms and does not generate symptomatic side-effects. Objective control of reflux, however, is only moderate. Omission of an antireflux procedure in the absence of gastro-oesophageal reflux disease induced oesophagitis in 28%, and abnormal oesophageal acid exposure in 39% of patients. Therefore, routine addition of an antireflux fundoplication deserves recommendation.

Introduction

Surgery is the only available curative treatment for symptomatic large hiatal hernias (type II-IV). Surgical repair exists of dissection of the hernia sac from the posterior mediastinum, reduction of the herniated intra-abdominal organs with a tension-free intra-abdominal position of the distal oesophagus, and posterior cruroplasty[1,2]. The surgical strategy, however, has not been fully clarified and controversies, like the appropriate use of antireflux procedures to treat or prevent gastro-oesophageal reflux disease, still persist[3]. The frequent presence of reflux-related symptoms is one of the reasons to routinely add an antireflux procedure in the repair of large hiatal hernias[4]. Furthermore, some authors argue that, due to extensive dissection at the level of the gastro-oesophageal junction, the restoration of the gastro-oesophageal anatomy during repair of the hiatal hernia interferes with the natural antireflux mechanism, and therefore advocate the standard use of an antireflux procedure[5,6]. Others argue against such an approach because, in their view, restoring the gastro-oesophageal anatomy is accompanied with repair of the antireflux mechanism preventing reflux-related symptoms after surgery[7]. Finally, addition of an antireflux procedure (ie, a Nissen or Toupet fundoplication) may cause postoperative troublesome dysphagia[4,8]. As a result, some authors advise to selectively perform an antireflux procedure during large hiatal hernia repair in patients with preoperatively diagnosed gastro-oesophageal reflux disease[4,8,9], whereas others recommend its routine addition[5,7]. However, these recommendations are not evidence-based and not supported by data on the combination of both subjective and objective analyses of pre- and postoperative presence of gastro-oesophageal reflux disease, and the postoperative incidence of troublesome dysphagia. Therefore, evidence for a tailored approach of antireflux procedures in large hiatal hernia repair is lacking.

We investigated the strategy of selective addition of an antireflux fundoplication in patients with a large hiatal hernia in whom gastro-oesophageal reflux disease was documented before surgery.

Methods

Patients

Between 2002 and 2008, all patients over 18 years with a large hiatal hernia (type II-IV), confirmed with barium oesophagogram, were considered for enrolment in the study protocol. Patients who underwent surgical repair of recurrent hiatal herniation, those who needed emergency surgery, and patients with hiatal hernia repair after primary antireflux surgery were excluded.

Study design

All patients who agreed upon participation were preoperatively evaluated. First, medical history was taken with special emphasis on symptoms related to gastro-oesophageal reflux disease (ie, heartburn and/ or regurgitation). Secondly, all patients were objectively assessed by upper endoscopy, and stationary oesophageal manometry and ambulatory 24-hour pH monitoring. Gastro-oesophageal reflux disease was considered to be present if at least two of these three preoperative workup components were in support of this diagnosis. When pH monitoring failed or, due to anatomical obstruction, could not be reliably conducted, the combination of symptomatic assessment and upper endoscopy had to confirm or rule out gastro-oesophageal reflux disease. In patients with preoperatively proven gastro-oesophageal reflux disease, an antireflux procedure was added to the repair. After surgery, both symptomatic and objective analyses were repeated.

The study protocol was approved by the Medical Ethics Committee, and informed consent was obtained from all patients who agreed with participation.

Symptomatic assessment

To obtain symptomatic information, patients filled out standardised questionnaires. Reflux-related symptoms were evaluated with the Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) score (possible range 0 [best] – 45 [worst])[10], and general quality of life was assessed using a visual analogue scale (VAS, possible range 0 [worst] – 100 [best])[11]. In addition, patients were asked to score their symptoms after surgery compared to baseline. This was measured on a four-point scale, according to the Visick grading system, which ranges from "resolved" to "worsened"[12].

Objective assessment

To evaluate the presence and extent of oesophagitis and the presence or absence of a (recurrent) hiatal hernia, upper endoscopy was performed by senior gastroenterologists. Reflux oesophagitis was graded according to the Los Angeles classification (grade A-D)[13].

Stationary oesophageal manometry was performed using a water-perfused system with a multiple-lumen catheter with an incorporated sleeve sensor (Dentsleeve Pty Ltd, Adelaide, Australia). In response to 10 standardised wet swallows (5-mL water bolus), mean end-expiratory lower oesophageal sphincter (LOS) pressure, residual LOS relaxation pressure, intraluminal oesophageal pressure at 5, 10 and 15 cm above the upper margin of the LOS, and the peristaltic pattern of the body of the oesophagus were recorded. Herein, the end-expiratory gastric baseline pressure served as the zero reference point. LOS pressure of 0.6-3.5 kPa, and residual LOS relaxation pressure for at most 1.4 kPa was defined as normal.

Immediately after oesophageal manometry, patients underwent ambulatory 24-hour pH monitoring after suspending antisecretory drugs for seven days. Intraluminal oesophageal pH was measured using a pH glass electrode (model LOT 440, M3; Medical Instruments Corporation, Solothurn, Switzerland) which was positioned 5 cm above the manometrically determined proximal margin of the LOS. During 24-hour of measurement, intraluminal pH was stored in a portable digital data logger (Orion, Medical Measurements Systems B.V., Enschede, the Netherlands) with a sample frequency of 1 Hz. Acid reflux was considered abnormal when the percentage of total time with pH < 4 was more than 5.8%, for upright time more than 8.2% and for supine time more than 3.5%[14]. The symptom association probability (SAP) was calculated, and with SAP more than 95%, symptoms were considered to be related to acid reflux[15].

Surgical technique

All patients were operated laparoscopically by two senior surgeons with substantial experience in laparoscopic and gastro-oesophageal surgery (I.A.M.J.B. and E.J.H.). The operative technique consisted of dissection of the peritoneal hernia sac from the posterior mediastinum, and reduction of its contents into the abdominal cavity. The oesophagus was thoroughly mobilised until at least 3 cm of the distal oesophagus was tensionless intra-abdominally. After complete exposure of the right crus, the hiatus was narrowed using interrupted non-absorbable sutures until approximately 1 cm between the crus and oesophagus remained. Neither pledgets nor mesh were used for any of the repairs, and no oesophageal lengthening procedures were performed. In patients with preoperatively demonstrated gastro-oesophageal reflux disease, according to the study protocol, proximal short gastric vessels were ligated to completely mobilise the gastric fundus using ultrasonic dissection, and a fundoplication of 3-4 cm was then constructed with non-absorbable stitches. A total fundoplication was common, however, in patients with inadequate oesophageal peristalsis or low-amplitude contractions in the distal part of the oesophagus, a partial fundoplication was added.

Endpoints

The primary symptomatic endpoint of this study was postoperative presence of daily heartburn and daily dysphagia. The presence of abnormal oesophageal acid exposure during pH monitoring and oesophagitis on upper endoscopy after surgery were primary objective endpoints. Secondary endpoints included the Visick grading system and general quality of life.

Statistical analysis

Values were expressed as mean ± SD. Data were analysed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA). To statistically analyse the differences between preoperative and postoperative values, the paired samples t test was used for continuous values and the McNemar test for categorical values. Statistical analysis of continuous values between groups was performed by using the t test for independent samples. Differences were considered statistically significant with P < .050.
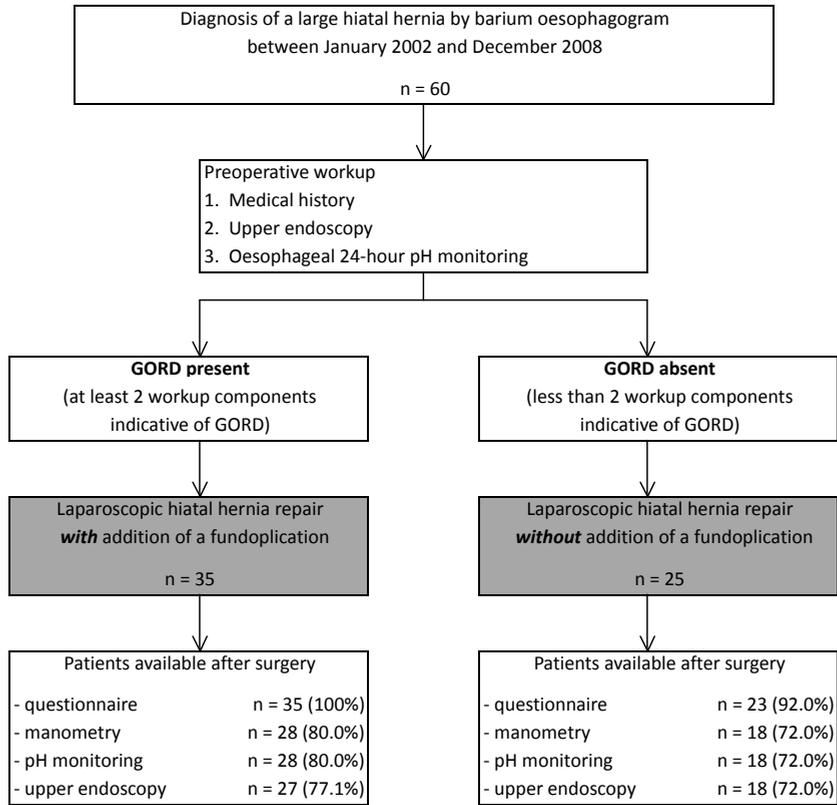
Results

Sixty consecutive patients with a large hiatal hernia enrolled the study protocol. Preoperative presenting symptoms were heartburn in 40 (66.7%), dysphagia in 32 (53.3%), regurgitation in 30 (50.0%), both epigastric and retrosternal pain in 25 (41.7%), and 12 patients (20.0%) had anaemia. Overall, preoperative heartburn and/ or regurgitation was experienced by 46 patients (76.7%). According to the study protocol, all patients were subsequently objectively evaluated. Preoperative pH monitoring was attempted in all included patients. Because of technical failure to position the pH catheter in the distal oesophagus due to obstruction, pH monitoring appeared impossible in three patients and one patient refused cooperation after problematic oesophageal manometry. Abnormal oesophageal acid exposure was present in 38 of the 56 patients (67.9%) in whom pH monitoring was successful. Upper endoscopy was performed in 58 patients. Two patients who refused preoperative endoscopy had both already shown pathological oesophageal acid exposure in addition to complaints of heartburn. Since endoscopy was therefore not strictly necessary to complete the study protocol, both were included in the study. Oesophagitis was present in 17 patients (29.3%), grade A in five, grade B in nine, and grade C in three.

Overall, the combination of preoperative symptomatic and objective assessment revealed that in 35 patients (58.3%) at least two of the preoperative workup factors were indicative of gastro-oesophageal reflux disease. According to the study protocol, these patients had a fundoplication added during their hiatal hernia repair (Nissen fundoplication in 29 and partial fundoplication in six patients). The remaining 25 patients underwent hiatal hernia repair only. Baseline characteristics and time to follow-up of the group of patients with and those without an added fundoplication are presented in *Table 1*.

Symptomatic assessment

All patients, except two refusing patients in the group without fundoplication, returned symptom questionnaires after surgery (*Figure 1*).

Figure 1   *Study profile with preoperative workup and postoperative evaluation*

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┌─────────────────────────────────────────────────────────┐
│   Diagnosis of a large hiatal hernia by barium           │
│   oesophagogram between January 2002 and December 2008   │
│                                                          │
│                        n = 60                            │
└─────────────────────────────────────────────────────────┘
                            │
                            ▼
        ┌─────────────────────────────────────────┐
        │ Preoperative workup                     │
        │ 1.  Medical history                     │
        │ 2.  Upper endoscopy                     │
        │ 3.  Oesophageal 24-hour pH monitoring   │
        └─────────────────────────────────────────┘
              │                          │
              ▼                          ▼
┌──────────────────────┐     ┌──────────────────────┐
│   GORD present       │     │    GORD absent       │
│ (at least 2 workup   │     │ (less than 2 workup  │
│   components          │     │   components         │
│ indicative of GORD)  │     │ indicative of GORD)  │
└──────────────────────┘     └──────────────────────┘
              │                          │
              ▼                          ▼
┌──────────────────────┐     ┌──────────────────────┐
│ Laparoscopic hiatal  │     │ Laparoscopic hiatal  │
│ hernia repair        │     │ hernia repair        │
│ *with* addition of a │     │ *without* addition   │
│ fundoplication       │     │ of a fundoplication  │
│      n = 35          │     │      n = 25          │
└──────────────────────┘     └──────────────────────┘
              │                          │
              ▼                          ▼
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Patients available after surgery		Patients available after surgery	
- questionnaire	n = 35 (100%)	- questionnaire	n = 23 (92.0%)
- manometry	n = 28 (80.0%)	- manometry	n = 18 (72.0%)
- pH monitoring	n = 28 (80.0%)	- pH monitoring	n = 18 (72.0%)
- upper endoscopy	n = 27 (77.1%)	- upper endoscopy	n = 18 (72.0%)

Abbreviation: GORD, gastro-oesophageal reflux disease.

Table 1   *Baseline characteristics*

	Large hiatal hernia repair with fundoplication (n = 35)	Large hiatal hernia repair without fundoplication (n = 25)
Male / female	10 (28.6%) / 25 (71.4%)	10 (40.0%) / 15 (60.0%)
Age at enrolment (years)	58.2 ± 10.8	61.0 ± 9.2
Body mass index (kg/m^2)	28.0 ± 4.5	29.9 ± 5.7
Time to follow-up (months)	13.5 ± 16.7	10.9 ± 2.9
Type of large hiatal hernia		
type II	1 (2.9%)	5 (20.0%)
type III	32 (91.4%)	15 (60.0%)
type IV	2 (5.7%)	5 (20.0%)

Values are given as mean ± SD, unless otherwise stated.

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Patients with fundoplication
After surgery, daily heartburn was absent in 31 patients (88.6%). All four patients who still experienced heartburn had pathological oesophageal acid exposure after surgery, and three used a proton pump inhibitor. Daily complaints of dysphagia were present in three patients (8.6%), and all three had dysphagia before operation. The self-rated effect of surgery showed that symptoms were resolved or improved in 31 patients (88.6%). General quality of life and GERD-HRQoL scores improved significantly (***Table 2***).

Patients with hiatal hernia repair only
Twenty patients (87.0%) rated their symptoms as resolved or improved. Five patients (21.7%) experienced that surgery did not affect heartburn. In four of these five patients, postoperative pH monitoring was performed showing abnormal oesophageal acid exposure in two. Both before and after surgery, daily dysphagia was present in two patients (8.7%). General quality of life was significantly increased, and GERD-HRQoL score remained unchanged (***Table 2***).

Table 2   *Symptomatic outcome*

	Large hiatal hernia repair with fundoplication (n = 35)	Large hiatal hernia repair without fundoplication (n = 23)
Self-rated change in symptoms compared with preoperative status (Visick grading system)		
resolved	15 (42.9%)	8 (34.8%)
improved	16 (45.7%)	12 (52.2%)
unchanged	0 (0%)	1 (4.3%)
worsened	4 (11.4%)	2 (8.7%)
GERD-HRQoL score		
preoperative	16.7 ± 9.4	7.4 ± 9.7
postoperative	5.4 ± 6.9*	6.9 ± 8.5†
General quality of life score (VAS)		
preoperative	32.3 ± 27.7	32.2 ± 25.3
postoperative	52.5 ± 23.2‡	54.4 ± 24.4§

Values are given as mean ± SD, unless otherwise stated.
P-value with regard to the difference between the preoperative and postoperative value was <.001*, .679†, .001‡ and .005§.
Abbreviations: GERD-HRQoL, Gastro-Esophageal Reflux Disease Health Related Quality of Life; VAS, visual analogue scale.

Objective assessment

As some patients refused cooperation, upper endoscopy and 24-hour pH monitoring were performed in a total of 45 (75.0%) and 46 patients (76.7%) after surgery, respectively (***Figure 1***).

Patients with fundoplication

Eleven patients with oesophagitis before surgery had postoperative endoscopy, showing that oesophagitis was resolved in eight (72.7%). After surgery, three patients had grade A, one B, one grade C, and one grade D oesophagitis. Grades of oesophagitis before and after surgery are depicted in ***Figure 2***. One patient refused endoscopy before surgery, therefore, preoperative status was only known in five of these six patients.

After surgery, mean LOS pressure was not significantly changed. In total, upright and supine time, oesophageal acid exposure was reduced. However, for supine reflux time, this was not statistically significant (***Table 3***). Oesophageal acid exposure was normalised in most patients after surgery (60.7%). In seven of the eleven patients who had persisting pathological reflux, total acid exposure was decreased after surgery, but an increase was present in the remaining four (***Figure 3***). Four of the eleven patients with persisting pathological reflux experienced daily heartburn postoperatively. In none of the patients, pathological reflux was induced.

Figure 2   *Grades of oesophagitis before and after surgery in patients with oesophagitis after large hiatal hernia repair **with** fundoplication (n = 5)*
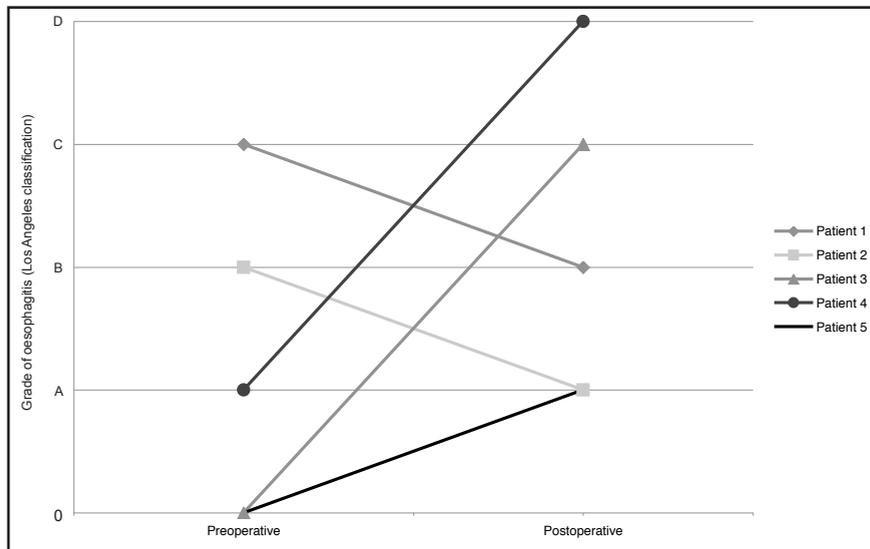
Table 3   *Outcome parameters of pre- and postoperative oesophageal manometry and 24-hour pH monitoring*

	Large hiatal hernia repair with fundoplication		Large hiatal hernia repair without fundoplication	
	Preoperative (n = 32)	Postoperative (n = 28)	Preoperative (n = 24)	Postoperative (n = 18)
Oesophageal manometry				
Lower oesophageal sphincter				
end-expiratory pressure (kPa)	1.0 ± 1.1	1.5 ± 1.0*	2.0 ± 1.8	1.1 ± 0.6†
incomplete nadir pressure	2 (6.3%)	0 (0%)	2 (8.3%)	0 (0%)
Oesophageal 24-hour pH monitoring				
Oesophageal acid exposure (pH < 4)				
total time (%)	14.5 ± 8.5	5.8 ± 8.8‡	3.6 ± 3.1	5.3 ± 5.3*
upright time (%)	15.9 ± 10.6	4.0 ± 5.7‡	4.4 ± 3.3	4.2 ± 3.8*
supine time (%)	12.7 ± 11.4	8.1 ± 18.4*	2.2 ± 4.3	7.2 ± 8.8*
Pathological oesophageal acid exposure	31 (96.9%)	11 (39.3%)	7 (29.2%)	8 (44.4%)

Values are given as mean ± SD, unless otherwise stated.
*Difference between the preoperative and postoperative value was not statistically significant.
P-value with regard to the difference between the preoperative and postoperative value was .026† and < .001‡.

Figure 3   *Total oesophageal acid exposure before and after surgery in patients with persistent abnormal acid exposure after large hiatal hernia repair **with** fundoplication (n = 11)*
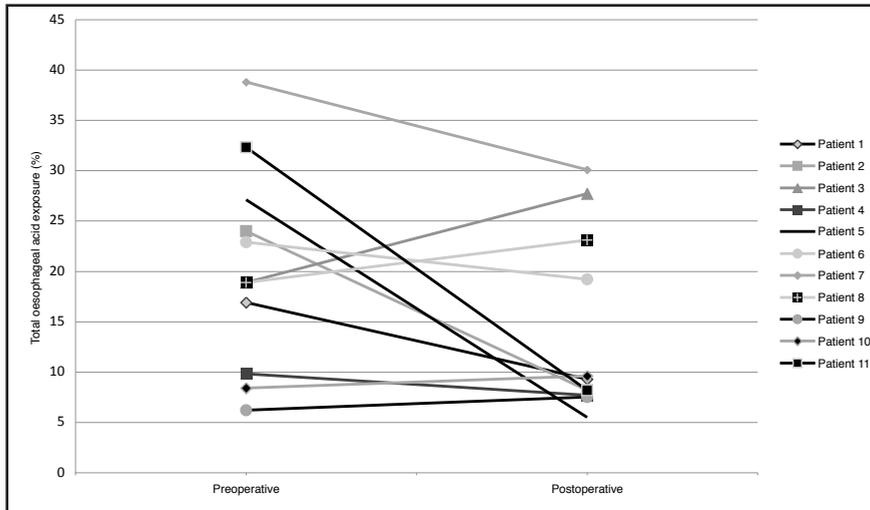
Patients with hiatal hernia repair only
After surgery, three patients had grade A, and another three had grade B oesophagitis. With the exception of one patient who preoperatively had grade A oesophagitis, none of these patients had oesophagitis before surgery.

After surgery, there was a significant decrease in mean LOS pressure (**Table 3**). During postoperative pH monitoring, eight patients had pathological acid exposure, and this was new-onset in seven of them. In four, this was merely due to an increase in supine reflux, and a combination of pathological upright and supine reflux was found in the other three patients. Preoperative and postoperative total oesophageal acid exposure times in the eight patients with pathological acid exposure after surgery are depicted in **Figure 4.** Two of these eight patients experienced daily heartburn after surgery, and three were taking antisecretory drugs. In the seven patients with pathological reflux before surgery, five underwent postoperative pH monitoring showing normalised acid exposure in four of them.

Figure 4   *Total oesophageal acid exposure before and after surgery in patients with abnormal oesophageal acid exposure after large hiatal hernia repair **without** fundoplication (n = 8)*
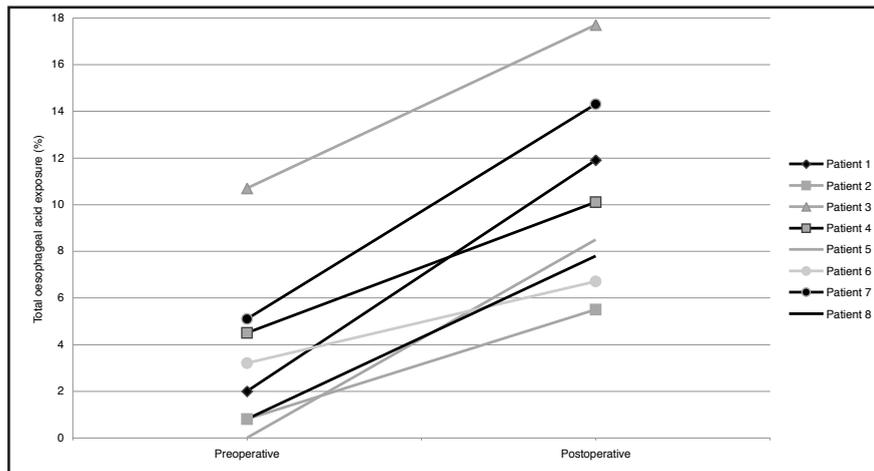
Surgical reinterventions

After a mean period of 18.0 ± 12.2 months after primary repair, eight patients (13.3%), four in each group, underwent surgical reintervention.

Patients with fundoplication
One patient had a Belsey Mark IV procedure because of intrathoracic wrap migration with associated reflux symptoms, and in two patients Nissen fundoplication was converted to a partial fundoplication (Toupet fundoplication and Belsey Mark IV, respectively) for troublesome dysphagia. The fourth patient had laparoscopic reduction of an intrathoracic Nissen fundoplication which caused troublesome dysphagia.

Patients with hiatal hernia repair only
Due to rupture of crural repair, two patients had a recurrent large hiatal hernia; in one of them, a new crural repair was performed with mesh, and in the other a Belsey Mark IV procedure was performed. Because of a narrow crural repair, a third patient was reoperated for troublesome dysphagia, and a fourth patient had reflux symptoms with a type I hiatal hernia and underwent a Nissen fundoplication by laparotomy.

Discussion

This prospective study showed that in most patients the addition of an antireflux procedure in the repair of large hiatal hernias both subjectively and objectively resolved gastro-oesophageal reflux disease, without new-onset of troublesome dysphagia. With persistence of pathological reflux in 39% of patients, the effect on objective gastro-oesophageal reflux was less than expected, however, without the induction of abnormal acid exposure in any patient. In contrast, in patients who, in the absence of preoperatively established gastro-oesophageal reflux disease, had hernia repair only, pathological oesophageal acid exposure was induced in 39% and reflux oesophagitis in 28%.

Normalisation of oesophageal acid exposure was seen in 61% of patients who had a fundoplication. The remaining 39% had persisting pathological acid exposure with improvement of exposure time in 64%. These results are in contrast to the outcome of surgery for gastro-oesophageal reflux disease carried out in patients with normal gastro-oesophageal anatomy, or type I hiatal hernias. In this group, persistent abnormal acid exposure is reported in 4.1-12.5% of patients[16]. Apparently, in patients with a large hiatal hernia, other mechanisms contribute to gastro-oesophageal reflux. The more prominent anatomical disturbances which require more extensive dissection, thereby destroying anatomical structures which

contribute to the natural antireflux mechanism, like the phreno-oesophageal membrane and pre-aortic fascia, have previously been reported as possible cause[5]. In our opinion, however, these structures are also dissected during a Nissen fundoplication primarily performed for gastro-oesophageal reflux disease. An evident explanation for the to some extent disappointing objective results of large hiatal hernia repair is lacking.

Although preoperative oesophagitis or pathological oesophageal acid exposure was resolved in one third of the patients without fundoplication added during hernia repair, oesophagitis and/ or pathological oesophageal acid exposure was induced in more than half of all patients. As mentioned before, some authors hypothesise that correction of the anatomy in patients with a large hiatal hernia destroys the natural antireflux mechanism[5,6], whereas others are of different opinion and believe that this antireflux mechanism, the natural synergy between the diaphragm and the lower oesophageal sphincter, is restored during surgery[7]. As the first hypothesis seems correct for patients in whom by the repair pathological acid exposure or oesophagitis was induced and the latter one may apply to the subgroup with both oesophagitis and pathological oesophageal acid exposure resolved after surgery, both hypotheses may be applicable. In our opinion, however, it is not predictable which of both hypotheses apply to which patient. Therefore, it deserves recommendation to add an antireflux fundoplication in all patients with a large hiatal hernia. In the group of patients with resolved oesophagitis or normalised oesophageal acid exposure, however, this concept would be an "over-treatment" which could possibly lead to an increase in the frequency of post-fundoplication dysphagia. In the group of patients with fundoplication, however, postoperative frequency of daily troublesome dysphagia was low (8.6%) and new-onset dysphagia was absent. Others have also reported that post-fundoplication dysphagia after hiatal hernia repair was transient[5]. An antireflux fundoplication in the repair of large hiatal hernias can therefore be added routinely, without substantial risk of the induction of troublesome dysphagia.

Postoperative daily heartburn was present in 22% of patients without an added fundoplication. Although all of these experienced the same complaints before surgery, an antireflux procedure was not added because oesophagitis and abnormal pH profiles were preoperatively absent. This indicates that symptoms may contradict objective assessment. This finding was also reported earlier[6,8,9]. In a number of these patients, abnormal oesophageal acid exposure could be established after surgery. Therefore, they could potentially have benefited from routine addition of a fundoplication. Some authors suggest that in patients with a large hiatal hernia preoperative oesophageal pH monitoring is not accurate[6,8]. In the current study, pH monitoring was technically feasible in 93% of patients. One might discuss the induction of false negative results due to the grossly abnormal gastro-oesophageal anatomy in these patients. The concept of routine addition of a fundoplication in patients with a large hiatal hernia based on the aforementioned high frequency of induction of postoperative

gastro-oesophageal reflux disease, would abandon pH monitoring from the preoperative workup. The postoperative anatomical status of the repair was not evaluated in the current study, because this was subject of a previous study by our group[17].

In conclusion, the omission of an antireflux procedure in the repair of large hiatal hernias in patients without preoperatively diagnosed gastro-oesophageal reflux disease induced oesophagitis in 28% of patients and pathological oesophageal acid exposure in 39%. Since the postoperative incidence of troublesome dysphagia was acceptable in patients with a fundoplication, we support the routine addition of an antireflux procedure in patients with a large hiatal hernia. However, the objective outcome with regard to reflux control in patients who underwent large hiatal hernia repair with fundoplication was less than expected.

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Dyspeptic Symptoms after Laparoscopic Large Hiatal Hernia Repair and Primary Antireflux Surgery for Gastro-oesophageal Reflux Disease; *A Comparative Study*

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Abstract

Background

Several patients with gastro-oesophageal reflux disease (GORD) suffer from functional dyspepsia. After laparoscopic Nissen fundoplication, these symptoms persist in a substantial number of patients. We hypothesised that, due to a higher chance of vagal nerve impairment during extensive hernia sac resection and oesophageal mobilisation, dyspeptic symptoms are more frequent after laparoscopic large hiatal hernia (type II-IV) repair than after primary antireflux surgery.

Methods

From January 2003, 61 consecutive patients who primarily underwent an antireflux fundoplication for GORD and 27 consecutive patients who had large hiatal hernia repair with fundoplication for concomitant GORD were included. According to a system combining frequency and severity, patients scored eight dyspeptic symptoms (ie, postprandial fullness, early satiation, epigastric pain and burning, bloating, nausea, vomiting, and excessively belching). Additionally, preoperative presenting symptoms were, according to the Visick grading system, scored as resolved, improved, unchanged, or worsened. General quality of life was obtained using the Short Form 36.

Results

In 43 of the 50 available patients (86.0%) who primarily underwent antireflux surgery and in all 24 available patients who had hiatal hernia repair (100%), preoperative symptoms resolved or improved. Mean symptom scores of all eight dyspeptic symptoms after surgery were comparable between both cohorts. General quality of life was equal in both cohorts, but was below the previously defined score in the general Dutch population.

Conclusion

After laparoscopic large hiatal hernia repair, dyspeptic symptoms were present in similar figures as after primary antireflux surgery.

Introduction

According to the Rome III consensus, functional dyspepsia is divided into two categories. In the first category, the postprandial distress syndrome, symptoms are meal-induced and comprise postprandial fullness and early satiation. The second category, the epigastric pain syndrome, is characterised by meal-unrelated epigastric burning and pain. Other symptoms which may be associated with functional dyspepsia are bloating, nausea, vomiting, and belching[1]. In 27-70% of patients, gastro-oesophageal reflux disease (GORD) is accompanied by one or more of these dyspeptic symptoms[2-4]. This prevalence has been shown to be higher than in the general population[2,5]. The concomitant presence of these symptoms negatively influences quality of life in patients with GORD[6]. Laparoscopic Nissen fundoplication largely improves or resolves the most prominent GORD symptoms (ie, heartburn and regurgitation), but in a substantial number of patients dyspeptic symptoms persist or develop[7-11].

Patients with a large hiatal hernia (type II-IV) frequently present with a broad variety of upper abdominal symptoms. Heartburn, regurgitation, dysphagia and chest pain are the most frequently reported symptoms[12-15], but many patients have other upper abdominal symptoms like nausea, vomiting, postprandial discomfort, and early satiation[16-19]. Although these symptoms are generally attributable to mechanical gastric emptying disturbances in patients with a large hiatal hernia, these may also be considered dyspeptic symptoms associated with large hiatal hernias as was previously described in patients with GORD as well. In our clinical experience, a subset of patients complains of dyspeptic symptoms after laparoscopic large hiatal hernia repair. Since the mechanical gastric emptying disturbances are resolved by the surgical repair, these symptoms may be due to delayed gastric emptying, a major pathophysiologic mechanism of dyspeptic symptoms[20], caused by iatrogenic dysfunction of the vagus nerve. The latter is thought to be caused by traction induced neuropraxia or iatrogenic transsection of branches during extensive dissection of the hernia sac during repair of the large hiatal hernia. The symptomatic outcome after large hiatal hernia repair reported in previous studies generally emphasises reflux-related symptoms, chest pain, general quality of life, or a more general symptomatic outcome[12-15,17-19,21-24]. Reports on the frequency of dyspeptic symptoms after laparoscopic large hiatal hernia repair are lacking.

We hypothesised that dyspeptic symptoms are more frequent after laparoscopic large hiatal hernia repair than after laparoscopic Nissen fundoplication for refractory gastro-oesophageal reflux disease.

Methods

Patients

From January 2003, 88 consecutive patients who presented with refractory reflux-related symptoms with proven pathological oesophageal acid exposure during 24-hour pH monitoring, as previously defined[25], were included. These were subdivided into two different cohorts; 61 patients who primarily had GORD (primary antireflux surgery cohort) and 27 patients with a large hiatal hernia (large hiatal hernia repair cohort). During upper endoscopy, 55 patients (90.2%) in the primary antireflux surgery cohort had a type I hiatal hernia. In the large hiatal hernia repair cohort, preoperative barium oesophagogram showed a type II hiatal hernia in one (3.7%), type III in 24 (88.9%), and type IV in two patients (7.4%).

Patients who underwent surgical reintervention for recurrent hiatal herniation or failed primary antireflux surgery were excluded.

Surgical technique

During laparoscopy in the primary antireflux surgery cohort, dissection of the hiatus and oesophagus was performed until at least 3 cm of the distal part of the oesophagus was intra-abdominally located. In the large hiatal hernia repair cohort, repair consisted of laparoscopic dissection of the hernia sac from the mediastinum, followed by reduction of the herniated stomach and oesophagus. All patients in both cohorts subsequently underwent posterior crural repair without the use of mesh. Finally, after division of the short gastric vessels, an antireflux fundoplication was added; in the primary antireflux surgery cohort a 360° Nissen fundoplication was added in all patients, except one who had a 270° Toupet fundoplication, and in the large hiatal hernia repair cohort, 22 had a Nissen and a Toupet was added in the remaining five patients.

Symptomatic assessment

After surgery, a questionnaire directed on eight dyspeptic symptoms (ie, postprandial fullness, early satiation, epigastric pain and burning, bloating, nausea, vomiting and excessively belching) was sent to all patients. These symptoms were scored according to a system as used in the Gastro-Esophageal Reflux Disease Health Related Quality of Life (GERD-HRQoL) score[26], which combines frequency and severity, yielding a score between zero and five per symptom. Mean scores were reported for each of the eight symptoms. If one or more dyspeptic symptoms were experienced, patients were asked if they were taking any drugs for these symptoms and in addition, whether they had changed meals to reduce symptoms.

Additionally, patients were asked to rate their preoperative most prominent presenting symptoms, according to the Visick grading system, as resolved, improved, unchanged or worsened[27]. General quality of life scores were obtained by the Dutch translated Short Form 36 questionnaire which contains eight different domains of quality of life; physical functioning, physical role limitations, emotional role limitations, bodily pain, vitality, mental health, social functioning, and general health[28]. For each domain, a score between 0 and 100 can be yielded; the higher the score, the better the quality of life. Quality of life scores were compared to previously reported scores in the general Dutch population[29].

Data analysis

Values were expressed as mean ± SD. Data were analysed using SPSS for Windows version 15.0 (SPSS Inc., Chicago, Illinois, USA).

Results

In the primary antireflux surgery cohort, 11 patients were lost. In the large hiatal hernia repair cohort, one patient was unwilling to return the questionnaire and, due to physical and/ or mental status, two more patients were unable to answer the questions. Eventually, a total of 50 patients (82.0%) in the primary antireflux surgery cohort, and 24 (88.9%) in the large hiatal hernia repair cohort returned the questionnaire. Baseline characteristics and time of follow-up of both cohorts are presented in *Table 1*.

Symptomatic assessment

In the primary antireflux surgery cohort, the most prominent preoperative presenting symptoms were resolved or improved in 43 patients (86.0%) and in all 24 patients in the large hiatal hernia repair cohort (*Figure 1*). In both cohorts, there was no difference in the mean scores of symptoms characteristic of the postprandial distress syndrome and epigastric pain syndrome of functional dyspepsia, and of the other four dyspeptic symptoms (*Table 2*). In both cohorts, symptom scores of nausea and vomiting were low.
Twenty patients (40.0%) in the primary antireflux surgery cohort and five (29.2%) in the large hiatal hernia repair cohort daily experienced one or more dyspeptic symptoms, and for these symptoms, 14 (28.0%) and five patients (29.2%), respectively, were medically treated. In both cohorts, daily complaints of early satiation, bloating and excessively belching were the most experienced dyspeptic symptoms. In addition, 25 patients (50.0%) in the primary antireflux surgery cohort, and eleven (45.8%) in the large hiatal hernia repair cohort used more frequent but smaller meals during the day, or had otherwise changed their diet for these complaints.

Table 1   *Baseline characteristics*

	Primary antireflux surgery cohort (n = 61)	Large hiatal hernia repair cohort (n = 27)
Male / female	38 (62.3%) / 23 (37.7%)	7 (25.9%) / 20 (74.1%)
Age (years)	43.8 ± 12.2	58.3 ± 11.1
Body mass index (kg/m²)	26.7 ± 4.4	26.3 ± 4.5
Body weight		
preoperative (kg)	80.9 ± 14.5	76.9 ± 14.2
follow-up (kg)	82.4 ± 15.8	79.8 ± 16.7
Time to follow-up (months)	58.8 ± 13.2	30.0 ± 20.5

Values are given as mean ± SD, unless otherwise stated.

General quality of life (Short Form 36)
Quality of life scores of the eight domains of the Short Form 36 are presented in *Figure 2*. In all eight domains, the primary antireflux surgery cohort and large hiatal hernia repair cohort showed comparable quality of life scores. In both cohorts, all quality of life scores were below the previously defined scores in the general Dutch population.
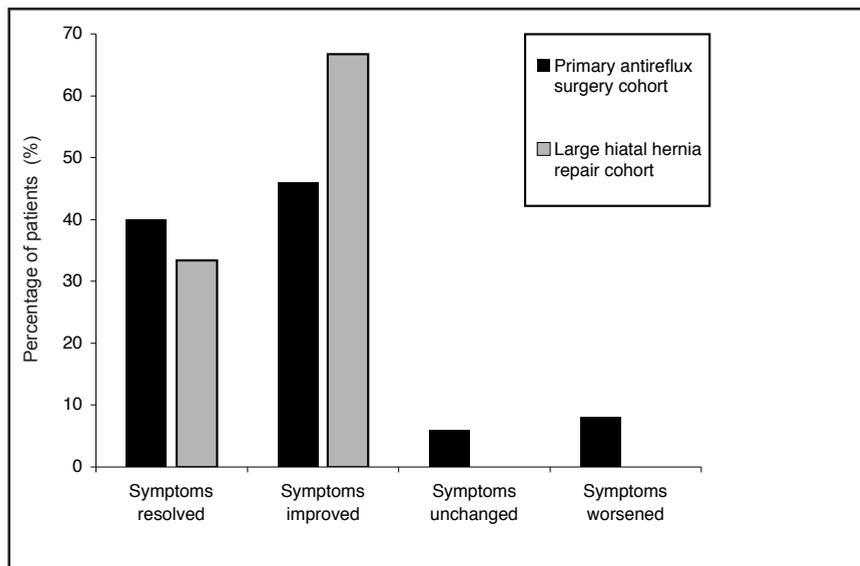
Figure 1   *Self-rated change in the most prominent preoperative symptoms after surgery (Visick grading system)*

Table 2   *Mean dyspeptic symptom scores after surgery*

	Primary antireflux surgery cohort (n = 50)	**Large hiatal hernia repair cohort (n = 24)**
Postprandial distress syndrome		
postprandial fullness	1.5 ± 1.2	0.8 ± 1.2
early satiation	1.6 ± 1.3	1.2 ± 1.2
Epigastric pain syndrome		
epigastric pain	1.1 ± 1.4	0.7 ± 1.1
epigastric burning	0.8 ± 1.2	0.6 ± 1.2
Other dyspeptic symptoms		
bloating	1.5 ± 1.5	0.9 ± 1.3
nausea	0.4 ± 0.9	0.5 ± 0.7
vomiting	0.3 ± 0.9	0.1 ± 0.5
excessively belching	1.5 ± 1.4	1.1 ± 1.3

Values are given as mean ± SD, unless otherwise stated.
Symptom scores were obtained according to a system combining frequency and severity with a minimum of 0, and a maximum of 5 for each symptom.

Figure 2   *General quality of life (Short Form 36)*
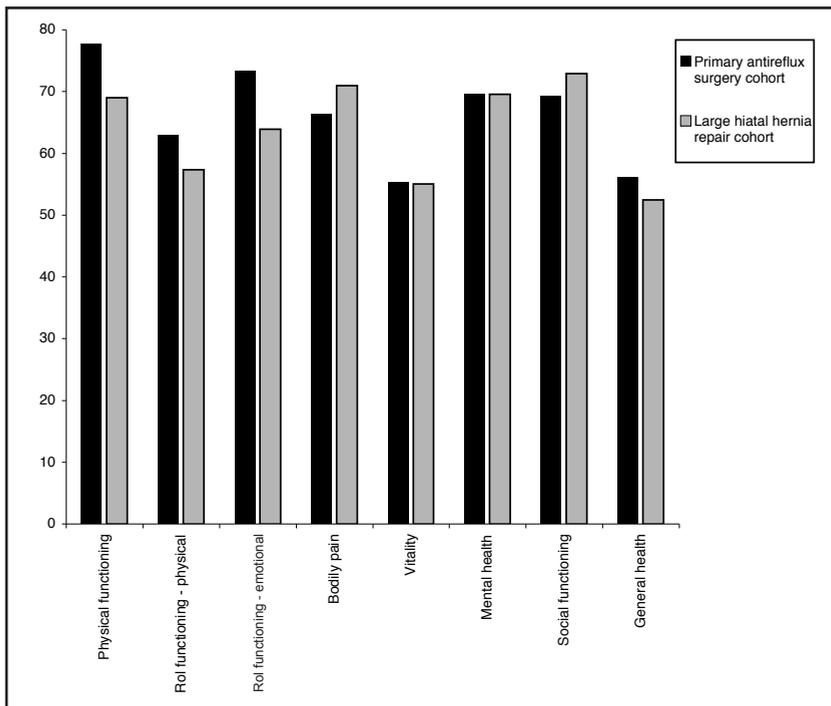
Discussion

In this study, evaluation of the frequency of dyspeptic symptoms after laparoscopic repair of large hiatal hernias showed figures which were similar to those found after primarily for refractory gastro-oesophageal reflux disease performed laparoscopic fundoplication.

Because of the more extensive dissection of the hernia sac, and therefore the concomitant higher change of iatrogenic injury of the vagus nerve, we had expected that dyspeptic symptoms would be more frequent after large hiatal hernia repair than after surgery primarily performed for GORD. In the past, truncal, selective and highly gastric vagotomy was performed for the treatment of duodenal ulcer. Studies on the long-term outcome in patients who underwent one of these vagotomies reported dyspeptic symptoms in 18-37% of patients[30,31]. Dissection during large hiatal hernia repair, however, may be mainly accompanied with neuropraxia of the vagus nerve rather than with complete transsection. This neuropraxia may cause dyspeptic symptoms. If neuropraxia resolves within a few months after surgery, however, these symptoms will disappear. In this study, however, duration of follow-up was much longer and data regarding the presence of dyspeptic symptoms in the first few months after surgery were not obtained. Although injury of the vagus nerve is not the sole contributor to dyspeptic symptoms, the difference in oesophageal and gastric dissection required during large hiatal hernia repair and primary antireflux surgery did therefore not influence the frequency and severity of dyspeptic symptoms at long-term follow-up after surgery. The number of included patients in both cohorts, however, was small due to the scarcity of patients with a large hiatal hernia.

After surgery, all patients in the large hiatal hernia repair cohort considered the most prominent preoperative presenting symptoms as resolved or improved. Nevertheless, a substantial number of patients experienced dyspeptic symptoms at follow-up. As 29% of patients used drugs for these symptoms and almost half of all patients had more or less changed their meals, these symptoms had substantial impact on daily life. Unfortunately, data regarding the preoperative presence of one or more of the eight dyspeptic symptoms were not obtained. Therefore, it is not clear whether these symptoms were of postoperative onset (ie, iatrogenic), or persisted from before operation. We currently verify the presence of these symptoms routinely and preoperatively inform patients on the possible persistence of dyspeptic symptoms after surgery. A previous study on dyspeptic symptoms after antireflux surgery for gastro-oesophageal reflux disease reported that these symptoms were preexistent in a proportion of patients, but developed postoperatively in another part of patients[9]. The presence of dyspeptic symptoms after laparoscopic large hiatal hernia repair was previously reported, but only regarding a limited number of symptoms (ie, bloating, nausea, vomiting and early satiation)[16,32]. Additionally, differences between patients with and without

the addition of an antireflux fundoplication in the repair of large hiatal hernias were not found[32].

Although in almost all patients the most prominent preoperative presenting symptoms were resolved or improved, general quality of life after surgery was found to be inferior in both cohorts compared to the general Dutch population. Results of other reports on quality of life scores after laparoscopic large hiatal hernia repair are comparable to those obtained in the current patient population[21]. As mentioned before, a previous study has shown that in patients with gastro-oesophageal reflux disease, the associated presence of dyspeptic symptoms negatively influences quality of life[6]. In view of this, the presence of dyspeptic symptoms may have caused inferior general quality of life in the participating patients in the current study as well.

In conclusion, the difference in oesophageal and gastric dissection required during laparoscopic large hiatal hernia repair and laparoscopic fundoplication primarily performed for gastro-oesophageal reflux disease does not influence the outcome with regard to dyspeptic symptoms as these complaints were present in similar figures after both surgical interventions.

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9

Summary and Conclusions

In this thesis, the complexity of surgical treatment of failed antireflux procedures and large hiatal hernias (type II-IV) is described. The studies in the first part of this thesis have addressed morbidity, mortality, and symptomatic as well as objective outcome of antireflux surgery after previous endoscopic or surgical procedures for gastro-oesophageal reflux disease. The second part has focused on two important issues regarding the surgical treatment of large hiatal hernias; the long-term results of laparoscopic repair and the strategy of selective addition of a fundoplication.

Part 1   Surgical reintervention after failed antireflux procedures for gastro-oesophageal reflux disease

In the long run, primary antireflux surgery fails in 10-15% of patients[1]. Although conservative treatment is adequate in the majority of patients, surgical reintervention is necessary in 3-6%[2-7]. Several small series have reported on the symptomatic outcome after reinterventions, but data on objective outcome is essentially lacking. In *chapter 2*, part of this gap was filled in by reporting on the objective outcome of surgical reintervention for recurrent gastro-oesophageal reflux disease or troublesome dysphagia after failed antireflux surgery in a prospective cohort of 130 patients. These patients underwent open or laparoscopic Nissen fundoplication, or partial fundoplication by an abdominal or thoracic approach. During redo surgery, an anatomical explanation for failure of the primary procedure, including wrap disruption, telescoping, intrathoracic wrap migration, or para-oesophageal hiatal herniation, was found in 90% of the patients. Oesophageal or gastric injury was the most frequent intraoperative complication. Mortality was 1.5%, in both cases after thoracic surgery. After five years of follow-up, symptomatic outcome was successful in 70% of patients. Mean lower oesophageal sphincter pressure was significantly reduced after surgery in patients reoperated for troublesome dysphagia, but did not change in patients who underwent redo surgery for recurrent reflux. Oesophageal acid exposure normalised in 70% of patients.

With a failure rate of 30% and not negligible morbidity, results of redo surgery are suboptimal. Predictors of outcome were sought in *chapter 3* to tailor the intervention to the individual patient and to inform candidates about the outcome of reoperation. For this purpose, the predictive value of different pre- and intraoperative variables was assessed by logistic regression analysis for the outcome after redo surgery performed for recurrent reflux and for troublesome dysphagia. None of the variables were identified as independent predictor of the outcome after redo antireflux surgery for recurrent reflux on multivariable analysis. However, low-amplitude distal oesophageal contractions, an abdominal approach and intrathoracic wrap migration were isolated on multivariable analysis as independent predictors of the persistence of troublesome dysphagia after redo surgery.

Although the group of patient described in *chapter 2 and 3* is larger than most of the studies in the literature, the groups are still too small to successfully categorise patients in relevant subgroups to benefit preoperative counselling. Therefore, a review of the literature on this type of surgery was performed and described in *chapter 4*. The most frequent indications for reoperation were recurrent reflux and troublesome dysphagia. As a cause for failure, wrap disruption and telescoping was more frequent after open abdominal primary surgery, whereas disruption of hiatal repair and a too tight wrap were more frequent after laparoscopic primary surgery. Intraoperative complications were lower in open compared to laparoscopic surgery, and postoperative complications were in the same range. Mortality was slightly higher after open abdominal redo surgery. The conversion rate of the laparoscopic redo procedures was higher than in primary surgery. Successful symptomatic outcome was slightly higher than in the series reported in *chapter 2 and 3*. As in the studies a different definition of success was used, this must be interpreted with some caution. Symptomatic outcome of laparoscopic and open abdominal redo surgery was comparable. Successful objective outcome, if reported at all, was slightly higher after laparoscopic compared to open redo surgery.

To offer an alternative for life-long use of antisecretory drugs and to avoid prolonged recuperation of antireflux surgery, endoscopic treatment modalities for gastro-oesophageal reflux disease were recently introduced[8,9]. The EsophyX plications system is the most recently introduced endoscopic antireflux therapy. In this procedure, an antireflux fundoplication is created by an endoluminal approach. In a subset of patients, however, the symptomatic and functional outcome after endoluminal EsophyX fundoplication is disappointing and a subsequent antireflux fundoplication may be required[10]. If surgery is needed, the outcome of antireflux surgery under these circumstances, is completely unknown. Therefore, the influence of previous EsophyX on the feasibility and outcome of laparoscopic Nissen fundoplication was studied in *chapter 5*, showing that patients with previous EsophyX were more prone to intraoperative complications (ie, gastric perforations) than primary cases. Symptomatic and objective reflux control was adequate, but a subset of patients experienced daily complaints of dysphagia.

Conclusions

Symptomatic and objective outcomes of surgical reintervention for failed primary antireflux surgery are substantially lower than those of primary operation, and redo surgery is accompanied with relative high morbidity, and even mortality. Risk factors for renewed failure are difficult to identify, so patients facing the need for redo surgery should be informed in even greater detail than those before primary surgery. Full scale subjective and objective evaluation is demanded. Laparoscopy should be attempted as the first step, but a higher conversion rate needs to be anticipated. If troublesome dysphagia represents the indication

for redo surgery, patients with low-amplitude distal oesophageal contractions should be informed about the possible disappointing outcome in terms of postoperative dysphagia. In addition, during abdominal reoperations for troublesome dysphagia, the crus should be thoroughly inspected as the cause of dysphagia. Although antireflux surgery after previous endoluminal EsophyX fundoplication may be accompanied with a higher risk of postoperative troublesome dysphagia compared to primary surgery, it does not influence the outcome with regard to reflux control, and should, at this stage, not be considered an additional risk factor.

Part 2   Surgical repair of large hiatal hernias

Because of the documented advantages over the open repair, including less complications, less postoperative pain and shorter hospital stay, laparoscopic repair is the preferred approach in the surgical treatment of large hiatal hernias[11-14]. The long-term durability of the laparoscopic repair, however, is questioned by many authors[15-17]. Therefore, in *chapter 6*, the long-term outcome of laparoscopic large hiatal hernia repair was studied in a prospective cohort of 70 patients showing successful symptomatic outcome in 89% of patients, and intact gastro-oesophageal anatomy in 70% of patients after a mean follow-up of four years. Anatomical recurrence was either due to a small type I hiatal hernia, or full-blown recurrent herniation. Only 10% of these recurrences appeared to have symptoms, while the same percentage of patients with intact gastro-oesophageal anatomy was unsatisfied with symptomatic outcome. An antireflux fundoplication, as selectively added in patients with preoperatively established gastro-oesophageal reflux disease, did not prevent anatomical recurrence.

The addition of an antireflux fundoplication to treat or prevent concomitant gastro-oesophageal reflux disease is a second controversy in the repair of large hiatal hernias[18]. Routine use is advised by those who believe that the natural antireflux mechanism of the gastro-oesophageal junction is destroyed during surgical dissection in the repair of large hiatal hernias, and gastro-oesophageal reflux disease will be the result in the majority, to justify the addition of a fundoplication[19,20]. Others, however, are convinced that the natural antireflux mechanism is re-established by anatomical restoration only, and in their view, the addition of a fundoplication only means an additional, unnecessary risk[21]. Both concepts are not evidence-based. Therefore, in *chapter 7*, a comparative cohort study was performed to evaluate the strategy of selective addition of an antireflux fundoplication during large hiatal hernia repair. In a consecutive cohort of patients with a symptomatic large hiatal hernia, an antireflux fundoplication was added if at least two of three items – clinical history, oesophagitis during upper endoscopy, or pathological acid exposure on pH monitoring – indicated the presence of gastro-oesophageal reflux disease. Symptomatic outcome was successful in

about 90% in both the group of patients with and without a fundoplication, without the new-onset of dysphagia in either group. As 40% still had pathological acid exposure, the addition of a fundoplication did not simply protect from further reflux. In the group without fundoplication, a similar number of patients developed abnormal oesophageal acid exposure after surgery, with reflux oesophagitis in about a quarter of patients.

In patients with a large hiatal hernia, the gastro-oesophageal anatomy is considerably disturbed and to restore this, extensive surgical dissection is required during laparoscopic repair. It was hypothesised in *chapter 8*, that the dissection required during the repair of large hiatal hernias may be accompanied with an increased risk of iatrogenic injury of the vagus nerve, and that this may lead to dyspeptic symptoms. It was shown, however, that after surgery, dyspeptic symptoms were present in the same frequency in patients who underwent laparoscopic large hiatal hernia repair compared to those who had a laparoscopic antireflux fundoplication primarily performed for refractory gastro-oesophageal reflux disease.

Conclusions

Long-term symptomatic outcome of laparoscopic large hiatal hernia repair is satisfactory in 90% of patients, but a substantial part of these patients has anatomical recurrence (30%). However, there is no difference in symptomatic outcome between patients with anatomical recurrence and intact gastro-oesophageal anatomy. The addition of an antireflux fundoplication does not prevent anatomical recurrence. Nevertheless, as in a substantial number of patients reflux oesophagitis or pathological acid exposure is induced if a fundoplication is omitted, the addition of an antireflux fundoplication during large hiatal hernia repair is strongly recommended. Herein, the addition of a fundoplication in the repair of large hiatal hernias does not negatively influence the symptomatic outcome in terms of new-onset daily complaints of dysphagia. Furthermore, the disturbed gastro-oesophageal anatomy in large hiatal hernias, and the extensive surgical dissection required to restore these anatomical disturbances, is not accompanied with more frequent or more severe dyspeptic symptoms as compared to an antireflux fundoplication primarily performed for refractory gastro-oesophageal reflux disease.

The natural history of patients with a minimal symptomatic or asymptomatic anatomical recurrence after laparoscopic large hiatal hernia repair is currently unknown. Therefore, future research should be performed to show the significance of these anatomical recurrences over a longer period of time in terms of developing symptoms and complications. In addition, mesh has been introduced in the repair of large hiatal hernias to reduce the high number of anatomical recurrences. Recently, two randomised trials have shown a significant decrease of recurrences[22,23]. Therefore, mesh seems to be promising, but long-term results should be awaited. Additionally, different shapes and materials of mesh are available, and future

studies have to show which technique is the most efficient and safest. However, given the scarcity of patients with a symptomatic large hiatal hernia, it will be difficult to collect series large enough to be able to reach these research goals. Collaboration between different clinical centres could possibly offer a solution to continue prospective studies to provide evidence-based guidelines on the surgical treatment of large hiatal hernias.

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Samenvatting en Conclusies
(Summary and Conclusions in Dutch)

In dit proefschrift wordt de complexiteit van chirurgische reïnterventies na voorgaande antireflux procedures en de chirurgische behandeling van grote hiatus hernia diafragmatica (type II-IV) beschreven. In de studies in het eerste deel van dit proefschrift worden de morbiditeit, mortaliteit en de symptomatische en objectieve uitkomsten van antireflux chirurgie na eerdere endoscopische en chirurgische procedures, verricht vanwege refractaire gastro-oesofageale refluxziekte, behandeld. In het tweede deel zijn de studies gericht op twee belangrijke onderwerpen met betrekking tot de chirurgische behandeling van grote hiatus hernia diafragmatica, namelijk de lange termijn resultaten van laparoscopische correctie en de strategie van het selectief toevoegen van een antireflux fundoplicatie.

Deel 1   Chirurgische reïnterventies na antireflux procedures voor gastro-oesofageale refluxziekte

Primaire antireflux chirurgie heeft op de lange termijn een teleurstellend resultaat bij 10-15% van de patiënten[1]. Hoewel de meerderheid van de patiënten adequaat kan worden behandeld met conservatieve maatregelen, is bij 3-6% van de patiënten een chirurgische reïnterventie noodzakelijk[2-7]. De symptomatische uitkomst van deze reïnterventies is in diverse kleine studies beschreven, maar objectieve resultaten zijn nauwelijks beschikbaar. In *hoofdstuk 2* werd dit hiaat gedeeltelijk opgevuld door de objectieve uitkomst van chirurgische reïnterventies, die werden verricht in verband met recidief gastro-oesofageale refluxziekte of ernstige dysfagie na voorgaande antireflux chirurgie, vast te stellen in een prospectief cohort van 130 patiënten. De reïnterventies die bij deze patiënten werden verricht, betroffen conventionele of laparoscopische Nissen fundoplicaties en transabdominale of transthoracale partiële fundoplicaties. Tijdens de chirurgische reïnterventie verklaarde bij 90% van de patiënten een anatomische afwijking het teleurstellende resultaat van de primaire ingreep. Deze anatomische afwijkingen betroffen manchet disruptie, telescopering (migratie van de gastro-oesofageale overgang boven de antireflux manchet), intrathoracale migratie van de manchet en para-oesofageale herniatie. De meest voorkomende peroperatieve complicaties betroffen letsels van de oesofagus en maag. De mortaliteit was 1.5%, waarbij in beide gevallen werd geopereerd door middel van een transthoracale benadering. Bij 70% van de patiënten was de symptomatische uitkomst na een follow-upduur van vijf jaar succesvol. De gemiddelde druk van de onderste slokdarmsfincter was postoperatief significant gedaald in de groep patiënten die een reïnterventie voor ernstige dysfagie ondergingen, terwijl deze druk postoperatief ongewijzigd was in de groep patiënten waarbij de reïnterventie werd verricht voor recidief reflux. De zuurexpositie in de distale slokdarm was postoperatief genormaliseerd bij 70% van de patiënten.

De resultaten van chirurgische reïnterventies na voorgaande antireflux chirurgie zijn suboptimaal aangezien de symptomatische en objectieve uitkomsten teleurstellend zijn bij 30% van de patiënten. Daarnaast gaan deze reïnterventies gepaard met een aanzienlijke morbiditeit. In **hoofdstuk 3** werd naar significante voorspellers gezocht van de symptomatische en objectieve uitkomst van deze reïnterventies om het type operatie af te kunnen stemmen op het probleem van de individuele patiënt en daarnaast om patiënten te kunnen informeren over de uitkomst van de reïnterventie. Daartoe werd, door middel van logistische regressie analyse, de voorspellende waarde van diverse pre- en peroperatieve variabelen vastgesteld voor de uitkomst van chirurgische reïnterventies verricht vanwege recidief reflux of ernstige dysfagie na voorgaande antireflux chirurgie. Geen van de geanalyseerde variabelen bleek tijdens multivariabele analyse een onafhankelijke voorspeller te zijn voor de uitkomst van chirurgische reïnterventies verricht vanwege recidief reflux. Daarentegen waren een lage contractieamplitude van de distale slokdarm, een transabdominale benadering en intrathoracale migratie van de antireflux manchet tijdens multivariabele analyse onafhankelijke voorspellers voor het postoperatief persisteren van dysfagie.

Hoewel de groep patiënten zoals beschreven in **hoofdstuk 2 en 3** groter is dan in de meeste overige studies in de literatuur omtrent chirurgische reïnterventies na voorgaande antireflux chirurgie, zijn de groepen nog altijd te klein om patiënten in te delen in relevante subgroepen om hen preoperatief effectief voor te kunnen lichten. In **hoofdstuk 4** werd een overzicht van de literatuur gegeven met betrekking tot studies waarin de resultaten van chirurgische reïnterventies na voorgaande antireflux chirurgie worden beschreven. De meest voorkomende indicaties voor de reïnterventies waren recidief reflux en ernstige dysfagie. Manchet disruptie en telescopiering werden, als oorzaak van het falen van de voorgaande antireflux procedure, frequenter aangetroffen na voorgaande conventionele transabdominale chirurgie, terwijl disruptie van de hechtingen van de cruraplastiek en een te strakke manchet frequenter aanwezig waren indien de primaire ingreep laparoscopisch was verricht. Peroperatieve complicaties traden minder frequent op tijdens conventionele dan tijdens laparoscopische reïnterventies, terwijl de frequentie van postoperatieve complicaties vergelijkbaar was tussen beide benaderingen. De mortaliteit was hoger na conventionele transabdominale chirurgie. Het aantal conversies van laparoscopische reïnterventies was hoger in vergelijking met primaire antireflux chirurgie. De symptomatische uitkomst was succesvol bij een enigszins groter percentage patiënten dan in de patiëntenpopulatie zoals beschreven in **hoofdstuk 2 en 3**, hoewel verschillende definities van een succesvolle uitkomst werden gerapporteerd in de diverse studies. De symptomatische uitkomst van conventionele en laparoscopische reïnterventies was vergelijkbaar. De objectieve uitkomst was succesvol in een groter percentage patiënten die een laparoscopische reïnterventie ondergingen in vergelijking met patiënten die door middel van een conventionele transabdominale benadering werden geopereerd, hoewel objectieve resultaten slechts in een beperkt aantal studies werden beschreven.

Diverse endoscopische behandelingen voor gastro-oesofageale refluxziekte zijn geïntroduceerd als alternatief voor levenslange behandeling met zuurremmers en daarnaast om langdurig herstel na antireflux chirurgie te voorkomen[8,9]. Het EsophyX plicatie systeem is de meest recent geïntroduceerde endoscopische behandelingsmethode waarbij een endoluminale antireflux fundoplicatie wordt aangelegd. Aangezien de symptomatische en objectieve uitkomsten na een endoluminale EsophyX fundoplicatie bij een deel van de patiënten teleurstellend zijn, is antireflux chirurgie mogelijk in tweede instantie noodzakelijk[10]. De resultaten van antireflux chirurgie onder deze omstandigheden zijn echter geheel onbekend. De invloed van een voorgaande EsophyX fundoplicatie op de uitkomst van een laparoscopische Nissen fundoplicatie werd vastgesteld in *hoofdstuk 5*. In vergelijking met primaire antireflux chirurgie ontstonden peroperatief frequenter maagperforaties. Hoewel de symptomatische en objectieve controle van reflux na laparoscopische Nissen fundoplicatie adequaat was, had een gedeelte van de patiënten postoperatief dagelijks klachten van dysfagie.

Conclusies

De symptomatische en objectieve resultaten van chirurgische reïnterventies na een teleurstellende uitkomst van voorgaande antireflux chirurgie zijn substantieel minder goed dan van primaire antireflux procedures. Daarnaast gaan deze reïnterventies gepaard met een relatief hoge morbiditeit en zelfs mortaliteit. Risicofactoren voor recidief falen zijn slechts beperkt beschikbaar en daarom dienen deze patiënten preoperatief op een nog uitgebreidere wijze te worden voorgelicht dan voorafgaand aan primaire antireflux chirurgie. Volledige preoperatieve en postoperatieve subjectieve en objectieve evaluatie is daarbij een vereiste. De laparoscopische benadering dient de eerste stap te zijn tijdens chirurgische reïnterventies, waarbij echter wel rekening moet worden gehouden met een hoog risico op conversie. Patiënten met een lage contractieamplitude in de distale slokdarm die een chirurgische reïnterventie voor ernstige dysfagie ondergaan, dienen preoperatief te worden geïnformeerd over het mogelijk teleurstellende resultaat ten aanzien van de postoperatieve dysfagie. Daarnaast moet tijdens transabdominale reïnterventies die worden verricht vanwege ernstige dysfagie, het crus uitgebreid worden geïnspecteerd als mogelijke oorzaak voor de dysfagie. Hoewel antireflux chirurgie na een eerdere endoluminale EsophyX fundoplicatie met een hoger risico op postoperatieve dysfagie gepaard lijkt te gaan in vergelijking met primaire chirurgie, wordt de uitkomst met betrekking tot de symptomatische en objectieve controle van reflux niet beïnvloed. Een voorgaande endoluminale EsophyX fundoplicatie kan daarom, in dit stadium, niet als risicofactor worden beschouwd bij antireflux chirurgie.

Deel 2   Chirurgisch herstel van grote hiatus hernia diafragmatica

De laparoscopische benadering heeft de voorkeur bij herstel van grote hiatus hernia diafragmatica aangezien deze gepaard gaat met minder complicaties, minder postoperatieve pijn en een kortere opnameduur in vergelijking met de open transabdominale benadering[11-14]. De duurzaamheid van laparoscopische correctie van grote hiatus hernia diafragmatica op de lange termijn is echter onduidelijk[15-17]. In *hoofdstuk 6* werd de lange termijn uitkomst van laparoscopisch herstel van grote hiatus hernia diafragmatica vastgesteld in een prospectief cohort van 70 patiënten. De symptomatische uitkomst was na een gemiddelde follow-upduur van vier jaar succesvol bij 89% van de patiënten en bij 70% was de gastro-oesofageale anatomie intact. Anatomische recidieven varieerden van een kleine type I tot een totale recidief hiatus hernia diafragmatica. Door 10% van de patiënten met een anatomisch recidief werd aangegeven dat er tevens sprake was van een symptomatisch recidief, terwijl hetzelfde percentage patiënten met een intacte gastro-oesofageale anatomie eveneens ontevreden was met de symptomatische uitkomst. Een antireflux fundoplicatie, zoals selectief werd toegevoegd bij patiënten met preoperatief bewezen gastro-oesofageale refluxziekte, was niet preventief voor een anatomisch recidief.

Het toevoegen van een antireflux fundoplicatie ter behandeling of preventie van gastro-oesofageale refluxziekte is een controverse bij de chirurgische correctie van grote hiatus hernia diafragmatica[18]. Enerzijds wordt het routinematig toevoegen van een fundoplicatie aanbevolen, omdat het natuurlijke antireflux mechanisme ter plaatse van de gastro-oesofageale overgang wordt aangetast door chirurgische dissectie tijdens correctie van de grote hiatus hernia diafragmatica. Dit zou resulteren in gastro-oesofageale refluxziekte bij de meerderheid van de patiënten en het toevoegen van een antireflux fundoplicatie rechtvaardigen[19,20]. Anderzijds wordt gesuggereerd dat het natuurlijke antireflux mechanisme juist wordt hersteld door correctie van de gastro-oesofageale anatomie en het toevoegen van een antireflux fundoplicatie zou daardoor een onnodig risico met zich meebrengen[21]. Beide concepten zijn echter niet evidence-based. In *hoofdstuk 7* werd een vergelijkende cohort studie verricht om de strategie van het selectief toevoegen van een antireflux fundoplicatie tijdens chirurgisch herstel van grote hiatus hernia diafragmatica te evalueren. Daartoe werd bij patiënten met een symptomatische grote hiatus hernia diafragmatica een antireflux fundoplicatie toegevoegd indien tenminste twee van drie items – symptomatische evaluatie, reflux oesofagitis tijdens oesofagogastroduodenoscopie en pathologische zuurexpositie tijdens 24-uurs pH metrie – wezen op gastro-oesofageale refluxziekte. De symptomatische uitkomst was succesvol bij 90% van de patiënten in zowel de groep met als in de groep zonder antireflux fundoplicatie. Daarbij had geen van de patiënten in beide groepen postoperatief dysfagie ontwikkeld. Aangezien 40% van de patiënten nog pathologische zuurexpositie

had tijdens postoperatieve 24-uurs pH metrie, werd met het toevoegen van een antireflux fundoplicatie de gastro-oesofageale refluxziekte niet per definitie adequaat behandeld. In de groep zonder fundoplicatie ontwikkelde een gelijk percentage patiënten postoperatief abnormale zuurexpositie in de distale slokdarm en een kwart van de patiënten reflux oesofagitis.

Bij patiënten met een grote hiatus hernia diafragmatica is de gastro-oesofageale anatomie dermate verstoord dat uitgebreide chirurgische dissectie noodzakelijk is tijdens laparoscopische correctie om de anatomie te herstellen. De hypothese in *hoofdstuk 8* was dat deze uitgebreide dissectie mogelijk geassocieerd is met een verhoogd risico op iatrogeen letsel van de nervus vagus en dat dit tot dyspeptische symptomen zou kunnen leiden. Dyspeptische symptomen bleken postoperatief bij patiënten die laparoscopisch herstel van een grote hiatus hernia diafragmatica ondergingen echter in gelijke mate aanwezig te zijn als bij patiënten die een laparoscopische antireflux fundoplicatie ondergingen die primair werd verricht in verband met refractaire gastro-oesofageale refluxziekte.

Conclusies

De symptomatische uitkomst van laparoscopisch herstel van grote hiatus hernia diafragmatica op de lange termijn is adequaat bij 90% van de patiënten. Een substantieel aantal patiënten heeft echter een anatomisch recidief (30%). Er is echter geen verschil in symptomatische uitkomst tussen patiënten met een anatomisch recidief en patiënten met een intacte gastro-oesofageale anatomie. Het toevoegen van een antireflux fundoplicatie draagt niet bij aan de preventie van een anatomisch recidief, maar wordt desalniettemin aanbevolen bij laparoscopisch herstel van een grote hiatus hernia diafragmatica aangezien pathologische zuurexpositie in de distale slokdarm en reflux oesofagitis worden geïnduceerd bij een substantieel aantal patiënten indien een dergelijke fundoplicatie achterwege wordt gelaten. De symptomatische uitkomst met betrekking tot dysfagie wordt niet negatief beïnvloed door het toevoegen van een fundoplicatie tijdens herstel van een grote hiatus hernia diafragmatica. Daarnaast is de sterk verstoorde gastro-oesofageale anatomie bij patiënten met een grote hiatus hernia diafragmatica en de uitgebreide dissectie die noodzakelijk is om deze anatomie te herstellen, niet geassocieerd met ernstigere dyspeptische klachten dan bij patiënten die een antireflux fundoplicatie ondergaan primair voor refractaire gastro-oesofageale refluxziekte.

Het natuurlijk beloop bij patiënten met een minimaal symptomatisch of asymptomatisch anatomisch recidief na laparoscopisch herstel van een grote hiatus hernia diafragmatica is op dit moment onduidelijk. Toekomstige studies zullen moeten uitwijzen wat de significantie van deze anatomische recidieven op de langere termijn is met betrekking tot het ontwikkelen van symptomen en complicaties. Mesh is geïntroduceerd om het hoge aantal anatomische recidieven na herstel van grote hiatus hernia diafragmatica te reduceren. Twee recente gerandomiseerde trials hebben aangetoond dat er een significante afname van het aantal

recidieven optreedt[22,23]. Het gebruik van mesh bij herstel van grote hiatus hernia diafragmatica lijkt dan ook veelbelovend, maar de lange termijn resultaten zullen moeten worden afgewacht. Daarnaast zijn er diverse vormen en typen materialen voor meshes beschikbaar en toekomstige studies zullen moeten uitwijzen welke techniek het veiligste en meest effectief is. Gezien het beperkt aantal patiënten met een symptomatische grote hiatus hernia diafragmatica zal het een uitdaging blijven om patiënten cohorten te verzamelen die groot genoeg zijn om deze onderzoeksdoelen te bewerkstelligen. Samenwerking tussen verschillende klinische centra kan mogelijk een oplossing bieden om het opzetten van grote prospectieve studies in de toekomst te kunnen continueren zodat voorzien kan worden in evidence-based richtlijnen voor de chirurgische behandeling van grote hiatus hernia diafragmatica.

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Curriculum Vitae Auctoris

The author of this thesis was born on 26 September 1980 in Geldrop, the Netherlands. After graduating from the Strabrecht College in Geldrop in 1999, he started his medical studies at Utrecht University. From the second until the fifth year of his studies, the author was a student-teacher at various anatomy courses. In the final two years of his studies, he followed a term of research on primary antireflux surgery at the Department of Surgery at the University Medical Centre Utrecht (Dr W.A. Draaisma).

He graduated in 2006 and subsequently worked for two years as a medical teaching assistant at the Department of Surgery at the VU Medical Centre in Amsterdam. During this period, he developed a competency-based surgical clerkship according to the CanMEDS model which was implemented in the medical education program. In addition, he participated in the development and organisation of a laparoscopic suturing course for surgical residents ("Advanced Suture Course"), and initiated a research project on technical skills training. In July 2007, he commenced the research project which resulted in the current thesis. This was initially combined with teaching at the VU Medical Centre. From January 2008, he worked for several months at the Accident and Emergency Department at the VU Medical Centre. From August 2008 until December 2009, he was a non-teaching resident at the Department of Surgery at St. Antonius Hospital, Nieuwegein/ Utrecht (Dr P.M.N.Y.H. Go).

In January 2010, he started his residency in general surgery at the University Medical Centre Utrecht (Professor I.H.M. Borel Rinkes). From January 2012, he is scheduled to follow the remaining of his surgical residency at the Diakonessenhuis in Utrecht (Dr G.J. Clevers).