

One- and ten-year outcome of laparoscopic anterior 120° versus total fundoplication: a double-blind, randomized multicenter study

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Received: 19 November 2014 / Accepted: 19 March 2015 / Published online: 1 April 2015
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Abstract

Background Nissen fundoplication is an effective treatment for gastroesophageal reflux disease (GERD) but can cause adverse effects like flatulence and dysphagia. The aim was to compare laparoscopic anterior 120° fundoplication (APF) to total fundoplication (Nissen) concerning flatulence and other adverse effects, in a randomized blinded study.

Methods Seventy-two patients were randomized to APF ($n = 36$) or Nissen ($n = 36$). Gastroscopy, 24-h pH monitoring and evaluation for symptoms and quality of life using questionnaires (GSRS, PGWB and 7-graded Likert scales) were performed preoperatively, at 1 and 10 years postoperatively. Patients and the researchers were blinded to operative method.

Results When entering the study, most patients had mild–moderate reflux disease according to the symptom score, the 24-h pH measurements, and frequency and grade of esophagitis. At 1-year ($n = 68$) flatulence, dysphagia, heartburn and acid regurgitation did not differ between groups. More patients could belch ($p = 0.005$), and pH monitoring showed a higher time with $\text{pH} < 4$ in the APF

group ($p = 0.006$). At 10 years ($n = 61$), the APF group reported less dysphagia ($p < 0.001$), more heartburn ($p = 0.019$) and more patients could belch ($p = 0.012$) and vomit ($p < 0.001$) compared to the Nissen. No difference remained at 10 years in pH monitoring ($n = 23$) between groups. Symptoms of heartburn and acid regurgitation were less than preoperatively in both groups ($p < 0.001$). No revisional operations were performed.

Conclusions Both procedures offer good long-term control of reflux symptom, with modest post-fundoplication symptoms. Anterior 120° fundoplication results in less dysphagia, better ability to belch and vomit than total fundoplication at 10-year follow-up. The results suggest that APF could be an alternative to Nissen fundoplication in the surgical treatment of mild–moderate GERD.

Keywords Gastroesophageal reflux disease · Laparoscopic surgery · Fundoplication · Adverse effects · Randomized controlled trial · Long-term effects

Laparoscopic total fundoplication, referred to as the Nissen fundoplication, is one of the most common surgical treatments of gastroesophageal reflux disease (GERD). Excellent acid control has been reported to the cost of adverse effects, like dysphagia, increased flatulence and inability to belch or/and vomit. This can impair quality of life for the patients and sometimes results in a revisional operation [1–5].

In an attempt to decrease the negative side effects of total fundoplication, while hopefully maintaining good acid control, an anterior partial (120°) fundoplication (APF) was described by Watson et al. [6]. This procedure was intended to be a more physiological antireflux procedure by emphasizing several of the factors involved in the

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antireflux barrier such as creating an elongated intraabdominal length of the esophagus and, by suturing the fundus toward the esophagus and the crural sling, augment the angle of His. By an APF, Watson et al. could demonstrate both a normal esophageal pH profile and a normal pressure in the lower esophageal sphincter up to 5 months postoperatively and good symptomatic reflux control up to 5 years [6, 7]. However, very little is known about long-term outcome of APF and follow-up beyond the reported 5 years. To the best of our knowledge, no study has compared APF with the Nissen procedure.

Recently, a meta-analysis was published suggesting fewer adverse effects and equal reflux control for the more extensive anterior 180° fundoplication compared to the Nissen fundoplication both at 1- and 5-year follow-up [8]. There is also a recently published 14-year follow-up from a randomized trial comparing anterior 180° fundoplication to Nissen fundoplication [9]. In this trial, the anterior group reported less dysphagia but more heartburn than the Nissen group with no differences in gas-related symptoms or patients' satisfaction.

The objective of this prospective double-blind randomized multicenter study was to investigate if the treatment of GERD with anterior 120° fundoplication resulted in fewer adverse effects with equally good reflux control as the total fundoplication of Nissen, both in the short- and long-term perspective. For this purpose, patients were evaluated using questionnaires, gastroscopy and 24-h pH monitoring preoperatively, at 1 and 10 years postoperatively.

Materials and methods

The study was approved by the Local Ethical committee at Lund University (Dnr 222-00). Informed consent was obtained from all enrolled patients. The study was registered on ClinicalTrials.gov ID NCT01669330, unique protocol ID NW20012011. The flowchart diagram summarizes the trial design and is presented in Fig. 1.

Patient selection

Patients 18–65 years of age with reflux symptoms, having GERD confirmed by gastroscopy, 24-h pH monitoring and manometry, together with decreased heartburn and acid regurgitation when treated with PPI during 3 months, were eligible for inclusion. Exclusion criteria were previous gastric surgery, paraesophageal hernias, irritable bowel syndrome according to ROM II-criteria, severe illnesses that might affect long-term follow-up (severe systemic diseases, insulin-dependent diabetes and severe heart, lung and/or kidney diseases and mental disorders) and patients with drug abuse.

Outcome measure

The primary outcome was to compare the level of flatulence between the two groups at 1 year postoperatively. The secondary outcome measures were frequency of dysphagia, ability to belch and vomit, gastroesophageal reflux (monitored by symptoms, 24-h pH and gastroscopy), overall gastrointestinal symptoms measured by the Gastrointestinal Symptom Rating Scale (GSRS) and Quality of life measured by the Psychological General Well-Being index (PGWB) at 1 and 10 years postoperatively and flatulence at 10 years. Both GSRS and PGWB have been validated [10–12]. Other secondary outcomes were short-term complications, hospital stay and revisional surgery.

Power calculation

The assumption was that reflux control did not differ between groups, but the adverse effects like flatulence would be less after APF. The primary outcome was to compare the level of flatulence scored on a 7-graded Likert scale (described below) at 1 year. The sample size calculation was based on a reported incidence of flatulence causing discomfort following the Nissen procedure of 40 % [1, 13]. The reported incidence of adverse effects causing discomfort following the APF was less than 5 % [6]. However, this assumption was deemed too optimistic, and the power calculation was instead made on an assumption of 15 % incidence of flatulence causing discomfort in the APF. Level of flatulence causing discomfort was considered as Likert 2 or more and referred to as symptomatic flatulence. To detect a 25 % decrease in symptomatic flatulence, with a two-sided 5 % significance level and a power of 90 %, a sample group of 65 patients was required in each group.

Randomization and blinding

Randomization to either APF or Nissen was performed using sealed, sequentially numbered, opaque envelopes, in blocks of ten, organized before the trial began by a research nurse. Sets of random numbers of envelopes were sent to each participating unit. The surgeons were unaware of the block size. Patients were not stratified according to any other criteria. Randomization was performed during the operation after the dissection of the esophagus, and the hiatus had been completed. If the operation had to be converted to an open procedure, the allocated fundoplication was performed and the patient remained within the study.

The patients, the healthcare providers at the ward and in the outpatient clinic, the research nurse and the independent researcher performing the follow-up were under the whole study period unaware of the type of operation that

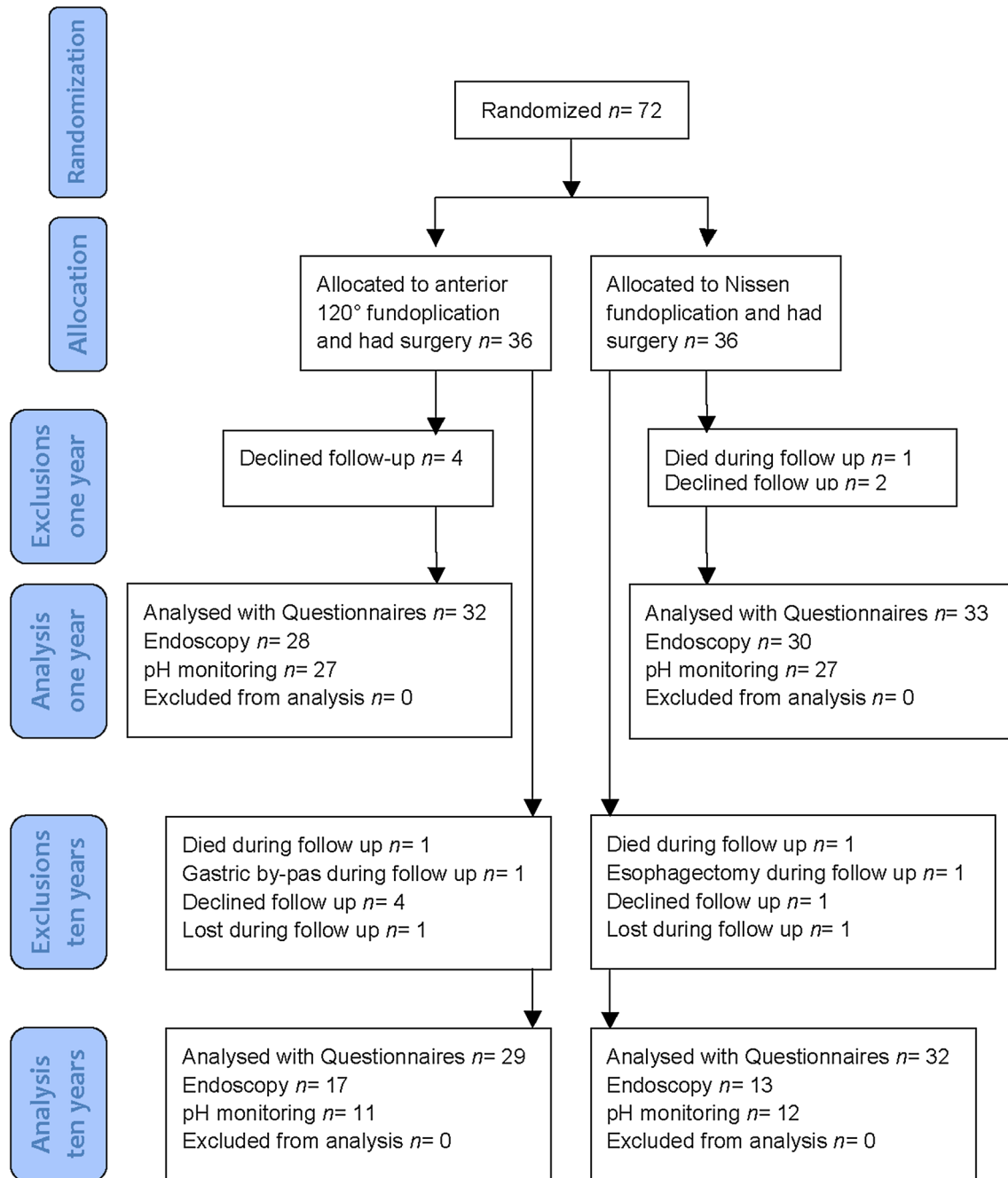


Fig. 1 CONSORT diagram of patients included in the study with 1- and 10-year follow-up

had been performed. The responsible surgeons did not collect data or evaluated the outcome measures.

Investigations and preoperative assessment

Questionnaires

Flatulence Symptoms of flatulence were graded on a 7-graded Likert scale: 0 = No symptoms; 1 = Minimal,

very mild symptoms without discomfort; 2 = Mild, symptoms exist but are easily tolerated; 3 = Moderate, symptoms exist and sometimes disturb normal activities; 4 = Moderate severe, symptoms exist that regularly disturb normal activities; 5 = Severe, symptoms exist that inhibits the performance of normal activities; and 6 = Very severe, Worst imaginable symptoms. Level of flatulence causing discomfort was considered as Likert 2 or more and referred to as symptomatic flatulence.

GSRs, Gastrointestinal Symptom Rating Scale The GSRs is a self-administered questionnaire used for assessment of gastrointestinal symptoms. It includes 15 questions combined into five syndrome domains: diarrhea (3 items), indigestion (4 items), constipation (3 items), abdominal pain (3 items) and reflux (2 items). The questionnaire uses a 7-graded Likert scale: 1 = No discomfort; 2 = Minimal discomfort; 3 = Mild discomfort; 4 = Moderate discomfort; 5 = Moderate severe discomfort; 6 = Severe discomfort; and 7 = Very severe discomfort. The mean value was calculated for each domain, and the total GSRs value consists of a mean value from the five domains.

Reflux symptoms The two questions in the GSRs regarding reflux, heartburn and acid regurgitation, were separately analyzed.

Dysphagia Symptoms of dysphagia were graded on a 7-graded Likert scale: 0 = No dysphagia, can eat all kinds of food; 1 = Minimal, occasionally a normal chew can pass slowly; 2 = Mild, at several occasions a normal chew can pass slowly; 3 = Moderate, must always think of chewing carefully, but can eat normal food; 4 = Moderate severe, can only eat food that is easily chewed or is liquid and have to drink to get the food pass; 5 = Severe, can only eat liquid food; and 6 = Very severe, very hard to swallow liquid food or completely stop/not able to get anything down.

PGWB, Psychological General Well-Being index PGWB is a self-administered questionnaire that measures subjective well-being or distress. It includes 22 questions combined into six dimensions anxiety (5 items), depressed mood (3 items), positive well-being (4 items), self-control (3 items), general health (3 items) and vitality (4 items). The questionnaire uses a 6-graded Likert scale. The score is calculated from the sum of the grading of the 22 questions, which gives a total range value between 22 and 132. A low score corresponds to a poor level and a higher score to a better level of well-being. The reference value for the average Swedish population is 103 [12].

Ability to belch or vomit Answered by yes or no.

Gastroscopy, 24-h pH monitoring and manometry

Erosive esophagitis was evaluated by gastroscopy and graded according to Los Angeles classifications [13]. Methodology for 24-h pH monitoring and for manometry has been described previously [14].

Surgical techniques

Laparoscopy was initiated by open access through the umbilicus, and the abdomen insufflated using carbon dioxide to a pressure of 10 mmHg. Trocars were placed up to the choice of the surgeon.

APF

The APF has been described in detail previously [6]. Blunt dissection was performed of the esophageal hiatus, full mobilization (5–6 cm segment) of intraabdominal esophagus preserving the hepatic branch of the vagus nerve. The posterior hiatal repair was performed with at least three non-absorbable sutures, leaving only a small hiatal opening alongside the esophagus. The esophagus was anchored to the left hiatal pillar with three or four sutures. The anterior 120° fundoplication was performed by suturing the superior-medial aspect of the gastric fundus to the superior arch of the crural sling with two sutures and with three sutures to the right side of the anterior wall of the esophagus, taking care to avoid branches of the anterior vagus nerve. Short gastric vessels were left intact.

Nissen

Briefly, the initial steps for the laparoscopic Nissen were similar to those for the APF fundoplication, commencing esophageal mobilization. Posterior hiatal repair by adopting the crural muscles with interrupted 2/0 non-absorbable braided sutures was performed letting a 10-mm instrument passing easily along the esophagus through the hiatus after the repair. The frontal wall of fundus was wrapped around the esophagus creating a loose 360° fundoplication which was anchored with three or four 2/0 non-absorbable braided sutures, one secured to the esophagus. The fundoplication had to be loose enough to let instrument pass through the fundoplication. Division of short gastric vessels was optional.

Surgery and postoperative care

The operations were performed by four surgeons working in four different surgical departments in Sweden (Skåne University Hospital, Lund; Skåne University Hospital, Malmö; Kalmar County Hospital, Kalmar and Norra Älvsborg County Hospital, Trollhättan). All were experienced in laparoscopic antireflux surgery and performed both techniques. To ensure surgical technique, all four surgeons got together for a 2-day surgical instruction course led by Professor Watson, the creator of APF.

No bougie was used during operation neither was a gastric tube used postoperatively. The patient was allowed

to drink in the evening of the operation day, to consume liquid food the first postoperative day and soft food the second when they also were allowed to leave the hospital.

Follow-up

Up to 8 weeks postoperatively

During the first eight postoperative weeks, a research nurse called the patients once a week making a telephone interview and registered symptoms of flatulence and dysphagia on the 7-graded Likert scale and notified if they were able to belch or vomit.

One and ten years

One-year and ten-year postoperative patients were offered gastroscopy and 24-h pH monitoring. Symptoms of flatulence, dysphagia, heartburn and acid regurgitation were assessed using the above described 7-graded Likert scales, and general gastrointestinal symptoms were assessed by GSRS, and quality of life by PGWB. The ability to belch and vomit was registered.

Statistical analysis

A two-tailed Mann–Whitney *U* test was used to compare ordered scales. Unpaired Student's *t* test was employed on interval scale for operation time, hospital stay and differences in GSRS and PGWB. Categorical data were analyzed using the Fisher's exact test. Wilcoxon matched-pairs signed-rank test was used to compare results over time. Values from ordered scales were expressed as median and interquartile range (IQR). Values from interval scales were expressed as mean \pm 95 % CI. Analyses were performed using Prism, version 6.0c (GraphPad Software, LaJolla, CA). Data were analyzed on an intention-to-treat basis.

Results

The first patient was included in September 2000. After initiation of the study, the number of antireflux operations declined dramatically in Sweden because of increased use of proton pump inhibitors. After mature consideration, enrollment was stopped prematurely in November 2003 because of slow recruitment. In total, 72 patients were included, 36 patients were randomized to APF and 36 to a Nissen fundoplication. When making this decision, it was taken into account that the primary endpoint flatulence was to be reduced by 25 % in the power calculation performed. When based on the actual incidence reported on 40 % for Nissen and 5 % for APF, the decrease was 35 % [1, 6, 15].

With a two-sided 5 % significance level and a power of 90 %, a sample size of 56 patients (28 patients in each group) would have been needed.

Operation and complications

Patient demographics and baseline characteristics were similar between the groups (Table 1).

Operation time was slightly longer in the APF group than in the Nissen group with a median of 120 min (IQR 30) and 102 min (IQR 34), respectively ($p = 0.044$). Median hospital stay was 2 days (range 1–6) in the APF and 2 days (range 1–10) in the Nissen group ($p = 0.508$). One complication, a perioperative injury of the brachial plexus, occurred in the Nissen group. No reoperations were performed.

One patient in the APF group was later diagnosed with gastroparesis and got a gastric pacemaker. It is unclear if the gastroparesis existed preoperatively or was a result of a nerve injury during dissection. One patient was converted (Nissen operation) to open surgery because of adhesions from previous abdominal surgery. This patient later developed an incisional hernia.

Table 1 Baseline demographic and clinical characteristics

	APF, <i>n</i> = 36	Nissen, <i>n</i> = 36
Male/female	20/16	20/16
Age (years)	47 (28–70)	47.5 (22–61)
Percent time pH < 4 ^a	8.4 (9.3)	8.4 (4.4)
Heartburn ^{a,b}	4.0 (2.7)	4.0 (2.0)
Acid regurgitation ^{a,b}	3.5 (3.2)	3.0 (2.0)
Flatulence ^{a,c}	2.0 (3.0)	2.0 (3.0)
Dysphagia ^{a,c}	0.0 (1.0)	0.0 (1.0)
GSRS ^d	2.7 (2.3–3.1)	2.9 (2.5–3.2)
PGWB ^d	101 (95–107)	94 (88–100)
Esophagitis		
No	24 (67 %)	28 (78 %)
Grade A	6 (17 %)	3 (8 %)
Grade B	5 (14 %)	5 (14 %)
Grade C	1 (3 %)	0
Grade D	0	0

Age: median (range)

APF anterior partial (120°) fundoplication, GSRS the Gastrointestinal Symptom Rating Scale, PGWB the Psychological General Well-Being index

^a Median (IQR)

^b Measured on a 7-graded Likert scale (1–7)

^c Measured in a 7-graded Likert scale (0–6)

^d Mean (95 % CI)

8-week outcome

There were no differences detected between the groups regarding flatulence and dysphagia symptoms, neither in the ability to belch or vomit, at four and at 8 weeks post-operatively. Table 2.

One-year outcome

At 1-year follow-up, 65 patients out of the 71 patients still alive (91.5 %) answered the questionnaires, 58 patients (82 %) had a gastroscopy and 54 patients (76 %) had a 24-h pH monitoring (Fig. 1). One patient in the Nissen group had died before the 1-year follow-up of an unrelated cause. No patient had undergone revisional surgery.

Both the APF and the Nissen group had improved their quality of life from preoperatively to 1 year (APF $p = 0.038$, Nissen $p = 0.044$). Dysphagia decreased from 8 weeks to 1 year for both APF and Nissen ($p < 0.001$ for both groups), whereas flatulence did not show any difference over time (APF $p = 0.465$, Nissen $p = 0.327$). No differences were detected in flatulence, dysphagia, general gastrointestinal symptom scale (GSRs) or quality of life (PGWB) between the groups (Tables 3, 4; Fig. 2). More patients in the APF group could belch at 1 year (Table 4). No difference was found regarding ability to vomit at 1 year but almost one-third of the patients in both groups did not know if they were able to vomit or not (Table 4).

At 1 year, 4/28 patients in the APF group had erosive esophagitis (all of them grade A) compared to 1/30 in the Nissen group (one grade B) ($p = 0.067$). The 24-h pH monitoring was within the normal range in both groups. A higher acid exposure time was noted in the APF group compared to the Nissen group (Table 5). No differences in reflux symptoms between the groups were detected (Table 3; Fig. 2).

Ten-year outcome

Long-term follow-up was performed at median 10 years and 1 month (IQR 16 months). One patient in the APF

group had died between 1- and 10-year follow-up of unrelated cause. Another patient in the APF group had been operated on with a gastric bypass, and one patient in the Nissen group had undergone an esophagectomy due to high-grade Barrett's dysplasia (Fig. 1). None of the included patients had undergone revisional surgery.

A total of 61 out of the 68 patients still alive at 10 years and without further esophagogastric surgery (90 %) answered the questionnaires. The APF group reported less symptomatic flatulence and less dysphagia than the Nissen group (Table 3; Fig. 2). More patients in the APF group could belch and vomit compared to the Nissen group at 10-year follow-up (Table 4). When comparing the preoperative results with those at 10-year follow-up, no changes in flatulence and dysphagia were found in the APF group ($p = 0.531$ and $p = 0.629$, respectively), whereas in the Nissen group, an increase in both flatulence and dysphagia was found over time ($p < 0.001$ and $p = 0.022$, respectively). Comparison between the results at 1 and 10-year follow-up did not detect any changes in flatulence and dysphagia in the APF group ($p = 0.218$ and $p = 0.531$), neither was any change in flatulence found in the Nissen group ($p = 0.118$), although there was an increase in dysphagia in the Nissen group ($p = 0.014$). GSRs improved for both groups at 10-year follow-up compared to preoperatively (APF $p = 0.007$; Nissen $p < 0.001$). No differences were detected at 10-year follow-up in GSRs or quality of life (PGWB) between the groups (Table 4).

At 10 years, the APF group had a higher incidence of heartburn compared to the Nissen group (Table 3; Fig. 2), although the symptom levels in both group were modest. For both groups, the symptoms of heartburn and acid regurgitation were less severe at 10-year follow-up compared to preoperatively ($p < 0.001$ for all four comparisons over time). A total of 23 patients participated in the pH monitoring. No difference between the APF and the Nissen group was detected (Table 5). These 23 patients did not differ as a group compared to the whole cohort, nor to the group of 38 patients who did not undergo pH monitoring, regarding symptoms of reflux, dysphagia, flatulence, ability

Table 2 Outcome at 4 and 8 weeks

	4-week APF <i>n</i> = 35	4-week Nissen <i>n</i> = 36	<i>p</i>	8-week APF <i>n</i> = 35	8-week Nissen <i>n</i> = 35	<i>p</i>
Flatulence ^a	2.0 (1.0)	1.0 (1.0)	0.299	1.0 (1.0)	2.0 (2.0)	0.201
Dysphagia ^a	3.0 (1.0)	3.0 (0.8)	0.356	2.0 (1.0)	2.0 (2.0)	0.176
Can belch ^b	29/35 (83 %)	31/36 (86 %)	0.753	31/35 (88 %)	31/35 (88 %)	1.00
Unable to vomit ^b	27/35 (77 %)	29/36 (81 %)	0.353	27/35 (77 %)	29/35 (83 %)	0.353

APF anterior partial (120°) fundoplication

^a Scored on a 7-graded Likert scale (0–6), Median (IQR); Mann–Whitney *U* test

^b Fisher's exact test

Table 3 Symptom score at 1 and 10 years

	1-year APF	1-year Nissen	<i>p</i>	10-year APF	10-year Nissen	<i>p</i>
Flatulence ^{a,c}	2.0 (3.0) <i>n</i> = 31	2.0 (2.0) <i>n</i> = 32	0.384	2.0 (2.8) <i>n</i> = 24	2.5 (2.0) <i>n</i> = 30	0.051
Symptomatic flatulence ^b	17/31 (55 %)	19/32 (59 %)	0.801	16/24 (67 %)	27/30 (90 %)	0.046
Dysphagia ^{a,c}	0.0 (1.0) <i>n</i> = 32	1.0 (1.0) <i>n</i> = 33	0.102	0.0 (1.0) <i>n</i> = 24	1.0 (2.0) <i>n</i> = 30	<0.001
Heartburn ^{a,d}	1.0 (1.0) <i>n</i> = 32	1.0 (1.0) <i>n</i> = 33	0.675	2.0 (2.0) <i>n</i> = 29	1.0 (1.0) <i>n</i> = 32	0.019
Acid regurgitation ^{a,d}	1.0 (0.0) <i>n</i> = 32	1.0 (0.0) <i>n</i> = 33	0.512	1.0 (1.5) <i>n</i> = 29	1.0 (0.0) <i>n</i> = 31	0.053

APF anterior partial (120°) fundoplication

^a Median (IQR); Mann–Whitney *U* test

^b Scored Likert 2 or more, Fisher's exact test

^c Scored on a 7-graded Likert scale (0–6)

^d Scored on a 7-graded Likert scale (1–7)

Table 4 Outcome at 1 and 10 years

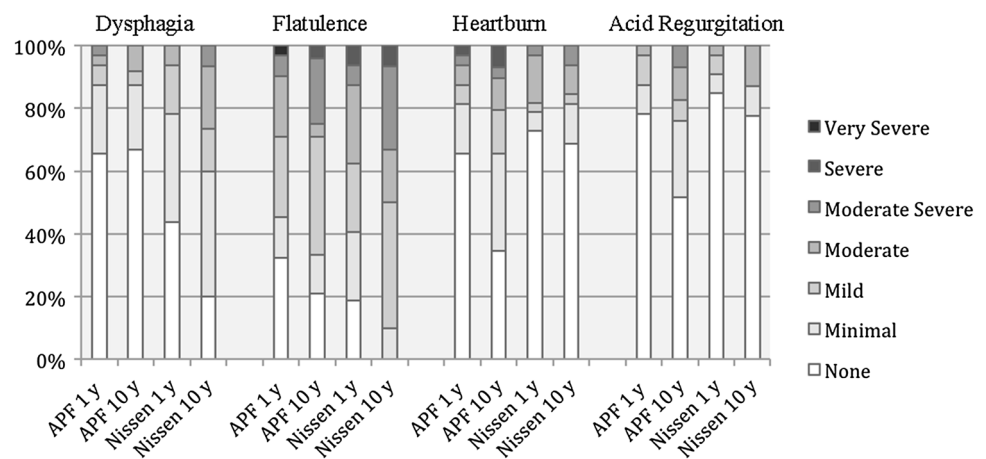
	1-year APF <i>n</i> = 32	1-year Nissen <i>n</i> = 32	<i>p</i>	10-year APF <i>n</i> = 29	10-year Nissen <i>n</i> = 32	<i>p</i>
Can belch ^a	30/32 (94 %)	20/32 (63 %)	0.005	27/29 (93 %)	21/32 (66 %)	0.012
Unable to vomit ^a	15/23 (47 %)	17/19 (53 %)	0.083	10/26 (34 %)	29/31 (90 %)	<0.001
GSRs ^b	2.0 (1.7–2.3)	2.2 (1.9–2.5)	0.298	2.3 (1.9–2.5)	2.2 (1.9–2.5)	0.752
PGWB ^b	110 (104–115)	102 (94–109)	0.064	103 (95–111)	106 (100–112)	0.552
Taking PPI ^a				10/29 (34 %)	8/32 (25 %)	0.575

APF anterior partial (120°) fundoplication

^a Fisher's exact test

^b Mean (95 % CI), *t* test

Fig. 2 Symptom score at 1 and 10 years according to a 7-graded Likert scale. APF anterior partial (120°) fundoplication, y year



to belch or vomit and outcomes of quality of life. Daily or weakly use of PPI at 10 years was 34 % in the APF group and 25 % in the Nissen group ($p = 0.575$) (Table 4). Of those patients using PPI, only 3/8 in the Nissen group and

4/10 in the APF group performed a 24-h pH monitoring, all with a normal result.

Gastroscopy was performed on 30 patients, 17 in the APF and 13 in the Nissen group. All patients in the Nissen

Table 5 Esophagitis and pH at 1 and 10 years

	1-year APF <i>n</i> = 28	1-year Nissen <i>n</i> = 30	<i>p</i>	10-year APF <i>n</i> = 17	10-year Nissen <i>n</i> = 13	<i>p</i>
Esophagitis ^a						
No	24 (86 %)	29 (97 %)	0.067	16 (94 %)	13 (100 %)	1.000
Grade A	4 (14 %)	0		1 (6 %)	0	
Grade B	0	1 (3 %)		0	0	
Grade C	0	0		0	0	
Grade D	0	0		0	0	
pH < 4 (% of time) ^b	1.6 (4.9) <i>n</i> = 27	0.3 (1.4) <i>n</i> = 27	0.006	0.1 (0.4) <i>n</i> = 11	0.15 (0.62) <i>n</i> = 12	0.749
Abnormal reflux ^c	10/27 (37 %)	3/27 (11 %)	0.054	0/11 (0 %)	0/11 (0 %)	
Normal reflux	17/27 (63 %)	24/27 (89 %)		11/11 (100 %)	12/12 (100 %)	

APF anterior partial (120°) fundoplication

^a Fisher's exact test

^b Median (IQR), Mann–Whitney *U* test

^c More than 4 % of time with pH < 4

group had endoscopically intact funduplications, but in the APF group, three of the partial funduplications were no longer considered intact. Of these three patients, one reported excellent symptomatic control of reflux during the first three postoperative years until he had a flu with excessive coughing, another patient reported that his reflux symptoms recurred after he had gained 40 kg in weight over a short period of time and the third patient had never had any effect on the reflux after the surgery suggesting a non-successful fundoplication. The PPI use was equal among patients who had only answered the questionnaires compared to those who had both answered the questionnaires and had been evaluated endoscopically (29 vs 30 %).

Discussion

For the primary outcome, flatulence at 1 year, no difference was detected between anterior 120° fundoplication (APF) and Nissen fundoplication. At 1 year, dysphagia had decreased in both the APF and in the Nissen group compared to the first postoperative weeks. There were no differences for dysphagia between the groups at 1 year, but more patients in the APF group could belch. The APF group had a higher acid exposure time compared to the Nissen group at 1 year, although no differences were found between the groups for symptoms of heartburn or acid regurgitation. At 10-year follow-up, the APF group reported less dysphagia and less symptomatic flatulence in the APF group, but scored higher for heartburn compared to the Nissen group. More patients could belch and vomit in the APF group at 10 years. There were no differences in quality of life between the groups.

Having flatulence as a primary endpoint is difficult since grading of what is perceived as flatulence, and when it becomes an inconvenience, differs between people. What we found though, at one and 10 years, was a clear difference between the groups regarding ability to belch. More patients were able to belch in the APF group compared to the Nissen group. Inability to belch will leave air within the gastrointestinal system, which is considered to contribute to an increase in abdominal bloating.

The long-term results in surgical treatment of GERD is important given that patients often are young or middle aged at operation with a long life expectancy. This study shows that the outcome, both with regard to adverse effects and with regard to control of reflux symptoms, changes over time. As mentioned in the introduction, no study has compared, to our knowledge, the anterior 120° fundoplication with the Nissen procedure. There are only six randomized trials comparing the symptomatic outcome of anterior partial fundoplication of other degrees of rotations, to the Nissen procedure. Four out of these six trials compared an anterior 180° [16–19] and two compared anterior 90° [20, 21] with Nissen fundoplication. Only one of these trials, a trial from Adelaide [9], comparing a 180° to Nissen fundoplication has a long-term follow-up time far above 5 years, which makes this study unique, just like ours.

Our postoperative outcomes at 8 weeks do not differ from the 1- and 3-month outcome seen in the Adelaide trial mentioned above [16], although Baigrie et al. [17] found less dysphagia at 3 months in the anterior 180° group compared to the Nissen group. The trials comparing an anterior 90° to Nissen reported in the early postoperative months less adverse effects and a higher risk of recurrent reflux [20, 21]. The lower effectiveness of reflux control for the anterior 90° fundoplication compared to both the

anterior 180° and the Nissen fundoplication studies has been confirmed at 5-year follow-up [22].

The present result of a normal range of 24-h pH monitoring together with the finding that more patients could belch in the APF group gives support for APF being a more physiological fundoplication as suggested [6]. This is in line with the results from a recently published meta-analysis suggesting fewer adverse effects (dysphagia and gas-related symptoms) with equal good reflux control for the anterior 180° fundoplication compared to the Nissen fundoplication at both 1- and 5-year follow-up [8]. Our result of less dysphagia and less symptomatic flatulence at 10 years after APF compared to the Nissen procedure contrasts to the 10-year outcome in the Adelaide trial where no difference in adverse effects was demonstrated [23]. By time (after 14 years), the Adelaide trial, in line with our results, reported less dysphagia and more heartburn in the anterior compared to the Nissen group, but with no differences in patients' satisfaction between the groups [9]. Our results at 10 years with persistent ability to belch in the APF group compared to the Nissen group are in contrast to the Adelaide results at 10 and 14 years where no such difference was detected. An explanation could be the different techniques involved in the procedures. The APF involves an esophagopexy, fixing the distal esophagus to the diaphragmatic pillars, while the anterior 180° fundoplication, performed in the Adelaide trial, do not include an esophagopexy.

The pH monitoring in the Adelaide trial at 14-year follow-up showed weakly acidic reflux episodes to be more common after anterior 180° fundoplication than after Nissen fundoplication [9]. We, on the other hand, did not detect any long time differences regarding acidic reflux between the APF and the Nissen group. It could be argued that this divergence in results from pH monitoring could be due to lack of power in the present study or by selection of a subgroup of patients for pH measurements. However, the group sizes are equally small in both studies and the patients that were subjected to pH monitoring did not differ from the whole cohort at 10-year follow-up regarding symptoms of reflux, dysphagia or flatulence nor in GSRS or PGWB scores. Since the number of patients having a pH monitoring is much less than the number of patients answering the questionnaires, the pH monitoring cannot explain why patients experience more heartburn in the APF group compared to the Nissen group without any difference in objective testing. One hypothesis might be that the APF group has episodes with acid reflux, long enough to elicit mild symptoms, but short enough to be within the normal reflux time.

Daily or weekly PPI use in the APF group did not differ from the PPI use in the Nissen group in this study. The levels of PPI use are in accordance with other long-term follow-up of randomized trials [24, 25]. Both Salminen et al. and

Broeders et al. showed that regular use of PPI 10 years after laparoscopic Nissen fundoplication was 33 % respective 26 %. Neither of the studies could though detect any correlation between PPI use and acid exposure nor to endoscopic fundoplication rupture. The only correlation that Broeders et al. found was a correlation between LES dysrelaxation and retrosternal pain. PPI use is accordingly not a surrogate marker for failure of fundoplication.

Even though there were differences at 10-year follow-up in adverse effects favoring APF and in controlling reflux symptoms favoring Nissen, the symptoms were modest and long-term results were good for both procedures. This was also reflected by the results from the overall gastrointestinal symptoms scale, GSRS, and quality of life measured by PGWB that did not show any differences between the groups and was almost comparable to the average population at long-term follow-up.

The number of patients included in this study is somewhat smaller than in some of the other trials due to the premature closure. However, our follow-up rate is high. As a comparison, only 22 % of the eligible patients accepted objective measurement at 14 years in the Adelaide trial [9]. In our study, 82 % had a gastroscopy at 1 year, and 44 % at 10 years, 76 % had a 24-h pH monitoring at 1 year, and 34 % at 10 years. The 90 % reply rate of questionnaires in combination with the double-blinded design, which kept both the patient and the researcher unaware of the type of fundoplication during the whole study period, is also a strength of the study. Furthermore, the fact that this study was carried out by four different surgeons at four different centers supports the external validity of the results. It should be noted, however, that preoperative symptom score, pH measurements, and frequency and grade of esophagitis suggest that most patient had mild–moderate reflux disease when entering the study and the results may not be valid for patients with more severe reflux disease.

In conclusion, our results show that both procedures are durable at 10-year follow-up with modest post-fundoplication symptoms. Anterior 120° fundoplication results in less dysphagia, less symptomatic flatulence and better ability to belch and vomit compared to total fundoplication, while maintaining an adequate control of reflux symptoms in patient with mild–moderate reflux disease. These results suggest that APF could be an alternative to Nissen fundoplication in the surgical treatment of mild–moderate GERD.

Acknowledgments The authors thank research nurse Maria Lithner for collecting the 8-week postoperative data by calling the patients weekly and Anna and Edwin Berger's foundation for providing financial support.

Disclosures Dr Pauline Djerf has received unrestricted grant from Anna and Edwin Berger's foundation, October 2013, Lidingö,

Stockholm. Drs. Agneta Montgomery, Bengt Hallerbäck, Hans-Olof Håkansson and Folke Johnsson have no conflicts of interest or financial ties to disclose.

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