Short- and long-term results after laparoscopic floppy Nissen fundoplication in elderly versus non-elderly patients

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Abstract

Background: Laparoscopic anti-reflux surgery could be of benefit in a subset of elderly patients with gastroesophageal reflux disease. However, there are few reports that have evaluated the long-term results. This study examined the effects of age on the short- and long-term (for at least 5 years) outcomes after laparoscopic Nissen fundoplication (LNF).

Patients and Methods: Patients were divided into four groups as follows: young (18–49); adult (50–69); and elderly (70–84), and very elderly (85–91). The database (recorded prospectively) included operating duration, conversion, intra- and early post-operative complication and late outcomes. Mean follow-up was 14.5 years (range 5–24 years).

Results: Five hundred and sixty-nine patients met the inclusion criteria: young n = 219 (38.4%); adult n = 248 (43.5%); elderly n = 91 (16.0%) and very elderly n = 11 (1.9%). Hiatal hernia (type I and III) was significantly less frequent in young and adult patients (P < 0.0001). The operation was significantly longer in elderly and very elderly patients (P < 0.001); the use of drains (P < 0.001) and grafts (P < 0.0001) for hiatal hernia repair was less in young and adult patients. The hospital stay, conversion (5.4%), intra-operative and early post-operative complications were not influenced by age. Dysphagia was evenly distributed among the groups. Forty-eight (8.4%) patients had recurrence: 15 in the young group (6.8%), 18 in the adult group (7.2%), 11 in the elderly group (12%) and 4 in the very elderly group (36.3%) (P < 0.0001).

Conclusions: Age does not influence short- and long-term outcomes following LNF. Control of reflux in the elderly is worse than adult patients. Therefore, ageing is a relative contraindication to LNF.

Keywords: Elderly, follow-up, gastroesophageal reflux disease, laparoscopic Nissen fundoplication

INTRODUCTION

Gastroesophageal reflux disease (GERD) is now the most common disorder of the upper gastrointestinal tract in the Western Countries, with 10%–20% of the population experiencing weekly symptoms, with great impact on quality of life.[1] Although there is a tendency to reduced symptom frequency of the usual complaints of heartburn and acid regurgitation in older patients, the frequency of GERD complications, such as erosive oesophagitis, oesophageal stricture, Barrett’s...
oesophagus and oesophageal cancer is significantly higher.[8] Therefore, elderly patients with GERD are a greater risk than younger patients for developing serious complications of GERD. Although the vast majority of elderly patients with complications associated with GERD can be successfully managed with medical therapy,[3] antireflux surgery may be warranted in some cases. The availability of laparoscopic antireflux surgery (LARS) has changed the threshold for referring patients to surgery. Several studies have reported excellent short- and long-term results for this procedure. Some studies have already shown that the benefits of a shorter hospital stay and reduced post-operative morbidity associated with laparoscopic techniques for anti-reflux surgery also apply to elderly patients.[6–8] Hence, it can be argued that age should not be a contraindication to LARS. However, there are few reports that have evaluated the long-term results after 5 years or more[9,10] in the elderly patients, after LARS. In this study, we examined the effects of age on the immediate operative outcome and complications of LARS (Nissen fundoplication) in a prospective fashion. Furthermore, the long-term efficacy (for at least 5 years) of laparoscopic Nissen fundoplication (LNF) in controlling reflux with respect to age is also investigated.

PATIENTS AND METHODS

This study was a retrospective analysis of prospectively collected data. Between April 1994 and July 2018, 808 consecutive patients underwent LARS for symptomatic GERD. In this study, we included patients who met the following criteria: LNF with at least 5 years of follow-up data available (April 1994–July 2013). Patients were excluded if they had type II hiatal hernia (pure paraoesophageal hernia), a history of the previous fundoplication or were undergoing other LARS (Toupet, Dör, etc…) or additional surgical procedures. Patients were divided into four groups according to their age: young (aged 18–49); adult (aged 50–69); elderly (aged 70–84) and very elderly (aged ≥85). The outcome was determined for each category of age. All patients referred to us with probable GERD (oesophageal symptoms and or extraoesophageal symptoms) were comprehensively evaluated.

Pre-operative studies

Pre-operative studies performed preoperatively laboratory investigations included upper alimentary endoscopy, oesophagogram, stationary oesophageal high-resolution manometry, ambulatory 24-h pH-impedance testing of the oesophagus and upper abdominal ultrasound.

Indications for surgery

Indications for surgery were failed medical management (inadequate symptom control, or medication side effects); patients who opt for surgery despite successful medical management (due to quality of life considerations, life-long need for medication intake); large symptomatic type III paraoesophageal hernia (>50% of the stomach located in the thoracic cavity) which was causing mechanical/obstructive symptoms; complications of GERD (Barrett’s oesophagus, peptic stricture), and extraoesophageal manifestations (asthma, hoarseness, cough, chest pain and aspiration). All patients underwent a LNF. This technique has been described previously.[5,11] The patients who underwent surgery for a hiatal hernia (type I and type III) underwent a procedure that entailed dissection of the hernia sac, reduction of the hernial sac and its contents from the mediastinum into the abdominal cavity. The posterior hiatal repair was routinely performed. If hiatal hernia was ≤3 cm, the posterior hiatal repair was performed by positioning of non-resorbable mesh (PolyTetraFluoroEthilene – PTFE). Dimension of mesh used vary from 2 cm × 4 cm to 5 cm × 6 cm, profiled to “U” form; if hiatal hernia was >3 cm, posterior hiatal repair was performed by the positioning of mesh and stitches.

Post-operative care

Nasogastric tubes initially were placed on suction overnight but were not used routinely after the first 65 procedures. On the day after surgery, after radiological control, patients were started first on clear liquids and later that day a soft diet was instituted. The patients were given detailed counselling on avoiding meats, breads and raw vegetables for 3 weeks after the operation. Discharge generally occurred on the 2nd post-operative day. All patients were evaluated 1 week and 3 months after surgery and yearly thereafter. Patients who could not come for their yearly visit were contacted by phone and asked about their symptom status. In all patients, symptomatic and asymptomatic were performed gastroscopy and pH-metry. These studies were performed at the presentation of symptoms in symptomatic patients and every year in asymptomatic patients. The database used to collect information, included the following details: patient age at the moment of operation, type of fundoplication performed, duration of the operation, eventual conversion from laparoscopic to an open procedure, intra- and early post-operative complications, late outcomes, timing and reasons for any revisional surgery. Complications severity was graded according to the Clavien-Dindo classification.[13] All patients included in the study had been followed up for at least 5 years. Failure of the surgical treatment was defined as recurrence of symptoms severe enough to
require at least intermittent medical therapy when the results of post-operative functional studies correlated with these symptoms, or the occurrence of serious surgical complications (slipped Nissen, severe gas bloat, dysphagia, dumping syndrome, etc.) that necessitated re-operation. An intention-to-treat analysis was performed. Patients who required conversion to open procedure, as well as those requiring later surgical revision, were included in the analysis.

**Statistical analysis**

Statistical analysis was performed using commercially available statistical software (GraphPad InStat, version 3.06 for Windows Vista, GraphPad Software, San Diego California USA, http://www.graphpad.com/). Spearman rank correlation, ANOVA and Chi-squared tests were used to determine the significance of any differences between the study groups. Statistical significance was determined if values of $P < 0.05$.

**RESULTS**

Out of 808 patients, 569 met the inclusion criteria for this study. Table 1 reports baseline characteristics of patients. There were no statistically significant differences between young, adult, elderly and very elderly patients in terms of gender [Table 1]. Preoperatively, disease severity, assessed by type and duration of symptoms, endoscopic, manometric and pH-metric data, was significantly worse in elderly and very elderly patients [Table 1]. Furthermore, the American Society of Anaesthesia score and number of hiatal hernia were significantly higher in these patients [Table 1]. Mean follow-up was 14.5 years (range 5–24 years) [Table 1]. The duration of the operation was significantly ($P < 0.001$) longer in elderly and very elderly patients and the use of drains and grafts for hiatal hernia repair was less in the young and adult patients ($P < 0.001$ and $P < 0.0001$) [Table 2]. The higher number of grafts used in the elderly and very elderly can be explained by the significantly high number of hiatal hernias in elderly and very elderly patients [Table 1]. The hospital stay did not differ among the groups. Thirty-one (5.4%) patients required conversion from a laparoscopic to an open procedure, nine out of the first 50 cases of the series. Eleven (5%) of these patients were young, 14 (5.6%) were adult and 6 (6.5%) were the elderly. No conversion in very elderly patients [Table 2]. Conversion to an open

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**Table 1: Pre-operative patient details**

|                      | All        | Young    | Adult     | Elderly   | Very elderly |
|----------------------|------------|----------|-----------|-----------|--------------|
| **Patients, n (%)**  | 569 (100)  | 219 (38.4) | 248 (42.5) | 91 (16.0) | 11 (1.9)     |
| **Age (years), mean (range)** | 50.6 (18-91) | 38.8 (18-49) | 62.4 (50-69) | 74.6 (70-84) | 87.8 (85-91) |
| **Sex ratio, n (%)** |            |          |           |           |              |
| Female               | 331 (58.1) | 136 (62.1) | 135 (54.4) | 54 (59.3) | 6 (54.5)     |
| Male                 | 238 (41.8) | 83 (37.9)  | 113 (45.5) | 37 (40.6) | 5 (45.4)     |
| **Follow-up period (years), mean (range)** | 14.5 (5-24) | 16.1 (5-24) | 15.8 (5-24) | 15.6 (5-24) | 15.6 (5-24) |
| **Symptom type, n (%)** |            |          |           |           |              |
| Typical              | 390 (50.7) | 169 (55.9) | 181 (54.6) | 38 (30.9) | 2 (15.3)     |
| Mixed                | 187 (24.3) | 68 (22.5)  | 82 (24.7)  | 33 (26.8) | 4 (30.7)     |
| Atypical             | 192 (24.9) | 65 (21.5)  | 68 (20.5)  | 52 (42.2) | 7 (53.8)     |
| **Duration of symptoms (month), mean (range)** | 21.3 (14-38) | 23.4 (16-28) | 22.8 (14-26) | 33.6 (29-38) | 33.4 (31-36) |
| **Endoscopic data, n (%)** |            |          |           |           |              |
| No oesophagitis (NERD) | 138 (24.2) | 65 (29.6)  | 64 (25.8)  | 8 (8.8)   | 1 (9.0)      |
| Oesophagitis (ERD)   | 431 (75.7) | 154 (70.3) | 184 (74.2) | 83 (91.2) | 10 (90.1)    |
| Grade 1              | 108 (25.0) | 46 (29.8)  | 45 (24.4)  | 15 (8.0)  | 2 (20.0)     |
| Grade 2              | 154 (35.7) | 70 (45.4)  | 69 (37.5)  | 14 (16.8) | 1 (10.0)     |
| Grade 3              | 91 (21.1)  | 23 (14.9)  | 35 (19.2)  | 30 (36.1) | 3 (30.0)     |
| Grade 4              | 78 (18.0)  | 15 (9.7)   | 35 (19.2)  | 24 (28.9) | 4 (40.0)     |
| **Manometric data, mean (range)** |            |          |           |           |              |
| Total length of LES (cm) | 2.8 (1.4-5) | 2.9 (1.5-4.5) | 3.1 (1.6-4.6) | 2.8 (1.4-2) | 2.9 (1.6-4.8) |
| Abdominal length of LES (cm) | 0.6 (0-1.9) | 0.7 (0.6-1.8) | 0.8 (0.6-1.4) | 0.7 (0.1-6) | 0.9 (0.8-1.8) |
| Resting pressure of LES (mmHg) | 8 (0-23) | 9.2 (0-21) | 8.8 (1.2-24) | 5 (0-16) | 4 (0.2-14.2) |
| Amplitude of contractile waves (mmHg) | 41 (4-146) | 40 (6-140) | 46 (7-146) | 31 (4-130) | 28 (5-128) |
| **PH-metric data, mean (range)** |            |          |           |           |              |
| Percentage total time with pH <4 | 32 (15-88) | 20.8 (18-44) | 20.6 (15-48) | 36.4 (32-74) | 50.5 (39-88) |
| ASA score            |            |          |           |           |              |
| I                    | 326 (57.2) | 152 (69.4) | 154 (62.0) | 20 (21.9) | /            |
| II                   | 217 (38.1) | 65 (29.6)  | 86 (34.6)  | 58 (63.7) | 8 (72.2)     |
| III                  | 26 (4.5)   | 2 (0.3)    | 8 (3.2)    | 13 (14.2) | 3 (27.2)     |
| Hiatal hernia, n (%) | 62 (7.3)   | 11 (4.4)   | 38 (14.7)  | 6 (54.4)  | /            |
| Type I               | 46 (4.7)   | 8 (3.2)    | 32 (35.1)  | 2 (18.1)  | /            |
| Type III             | 16 (1.9)   | 4 (1.6)    | 6 (6.6)    | 4 (36.3)  | /            |
| Previous abdominal operation, n (%) | 115 (20.2) | 30 (13.0) | 45 (18.1) | 36 (39.5) | 4 (36.3) |

NERD: Non-erosive reflux disease, ERD: Erosive reflux disease, LES: Lower esophageal sphincter, ASA: American society of anesthesiologists
surgical operation was not influenced by age. The following conditions required conversion to an open laparotomy: inability to reduce a very large hiatal hernia (9 patients: 2 young, 4 adults and 3 elderly), dense upper abdominal adhesions (14 patients: 6 young, 6 adults and 2 elderly), technical difficulties with oesophageal dissection due to peri-esophagitis (7 patients: 2 young, 3 adults and 2 elderly) and bleeding due to a liver laceration (one adult patient). During the 14.5 years mean follow-up, pH-metry-proven reflux recurrence occurred in two patients (elderly group). Insufficiency of the fundoplication (wrap undone) was diagnosed in one patient who subsequently underwent a laparotomic re-operation after 13 years. Nineteen (3.3%) intra-operative complication in 17 patients [Table 3] and 39 (6.8%) post-operative complications in 36 patients occurred [Table 3].

Intra-operative complications
Most of the intra-operative complications were minor (Clavien 1–2; n = 14), whereas major complications (Clavien 3–4) were five [Table 3]: one patient required conversion to laparotomy to control the bleeding due to a liver laceration (one adult patient). Three gastric and one oesophageal perforations occurred and were sutured laparoscopically. The patients had good recovery, without further complications.

Early post-operative complications
Furthermore, most of the post-operative complications were minor (Clavien 1–2; n = 33), whereas major complications (Clavien 3–4) were six [Table 3]: pneumonia occurred in four cases and was treated successfully with antibiotics. Two intra-abdominal abscesses were diagnosed 9 and 11 days after the operation and treated conservatively without drainage.

The four groups were similar regarding the rate of intra-operative and early post-operative complications.

Long-term follow-up data
Follow-up information was available for 538 patients (94.5%) [Table 4].

A total of 61 patients (11.3%) reported dysphagia 2 months after the operation, but these symptoms persisted in only 12 patients (2.2%) at 6 months. Out of these 12 patients, 5 presented with severe dysphagia. Five were in the first 50 cases of operative series. Dysphagia, resolving spontaneously or requiring intervention (dilatation or...
re-operation), was distributed evenly among the groups. Seven patients (1.3%) required endoscopic dilatation. Five patients were successfully managed with a single dilatation procedure, whereas two patients required several dilatations before the condition of suitable swallowing was achieved. Five patients (0.9%) required re-operation for prolonged dysphagia (three for a tight wrap and two for a tight oesophageal hiatus) after failed dilatation attempts. All underwent laparoscopic conversion from Nissen procedure to Toupet, with enlargement of hiatal opening in two. Dysphagia was resolved completely in all patients. None of the patients who required dilatation or re-operation had pre-operative endoscopic evidence of an oesophageal stricture.

The rate of bloating was evenly distributed among the groups.

During the 14.5-year mean follow-up, phmetry-proven reflux recurrence occurred in 48 patients, giving an overall recurrence rate of 8.4%. A striking correlation existed between recurrence rate and age. Of the elderly and very elderly patients, 12% and 36.3%, respectively, had failed operation, in contrast to only 6.8% of young and 7.2% of adult patients. Insufficiency of the fundoplication (wrap undone) was diagnosed in 6 patients, who underwent re-operation, five by laparoscopy after 5 years (very elderly group), 7 years (elderly group), 9 and 10 years (young and adult group) and 11 years (very elderly group), respectively, and one by laparotomy after 3 years (adult group). Once, a patient’s symptoms were treated with medication only. A barium contrast study showed an intra-thoracic herniation of the fundoplication in four patients, with severe regurgitation. This failure was among patients who had a fundoplication only. These patients underwent re-operation by laparoscopic approach after 4, 8, 10 and 11 years. At this writing, all patients who underwent a re-operation (5 for dysphagia, 6 for wrap undone and 4 for fundoplication herniation) are free of symptoms.

Five incisional hernias (two young groups, two adult groups, and one elderly group) were corrected.

During the late follow-up 27 patients (5%) died at a mean time of 8.6 years (range 1–20 years) following surgery. The causes of death were not related to the original operation. Seven patients died for cerebrovascular accidents, eight for myocardial infarction, six for cancer: stomach (two patients), lung (two patients), liver and bowel, four for trauma and two for pneumonia.

Finally, to better highlight the data relating to patients with paraoesophageal hernia (type III), these are summarised in Table 5.

**DISCUSSION**

Elderly patients with GERD are at greater risk than younger patients for developing serious complications of GERD.\[2,13,14\]

In our series, elderly and very elderly patients had a significantly lower prevalence of typical symptoms (heartburn, acid regurgitation and epigastric pain) than young and adult patients [Table 1]. Conversely, the prevalence of other symptoms (anorexia, weight loss, anaemia, vomiting and dysphagia and severe oesophagitis) significantly increased with age [Table 1]. There is no difference among the four groups as for extraoesophageal symptoms. These findings concordant with data from a previous study.\[15\]

Surgery is an option for some patients with GERD and is now more frequently considered because of the ability to perform anti-reflux surgery laparoscopically. Several studies have demonstrated that LARS is safe,
effective, improves quality of life and has low-morbidity and low-mortality.\[16-18\]

With increasing age of the population, treatment options for the elderly are becoming more important and some of these patients will demand alternative therapy if medical treatment fails.

Several studies have shown the safety and excellent results for LARS also in elderly patients.\[8,10,19-21\]

Fei et al.\[10\] prospectively evaluated 620 consecutive patients underwent total laparoscopic fundoplication for GERD. Five hundred and twenty-four patients were younger than 65 years and 96 patients were 65 years or older. An excellent outcome was observed in 93% of young patients and in 88.9 in elderly patients (\(P = \text{NS}\)). In the young patients, the mean follow-up was 89.7 ± 8 months (range 6–180), whereas in elderly patients, it was 71.2 ± 9 months (range 6–107).

With the studies that brought up the discussion on the effect and safety of LARS in the elderly patients with GERD, all of them reported similar surgical results between the elderly group and nonelderly group including similar operation time, post-operative hospital stay and low-morbidity and low-mortality.\[19] However, most previous aforementioned studies\[19,20\] addressing this issue as weakness because of either a short follow-up. In fact, there have been few reports that have evaluated the long-term outcomes after 5 years or more\[9,10\] in the elderly patients. Furthermore, the retrospective nature of some of the studies\[20\] were additional shortcomings of most of these papers.

In the present study, a single surgeon performed all the operations; data were collected in prospectively maintained database. The mean follow-up was 14.5 years (range 5–24 years). All previous studies\[10,19,20\] showed no significant increase in peri-operative complications after LARS in elderly patients. In our series, there was not a significantly increased risk associated with LNF in elderly and very elderly patients with respect to operative and early post-operative complications.

The prevalence of hiatus hernia and the size of hiatus hernia also significantly increased with age [Tables 1 and 5]. An increased number of paraoesophageal hernias (type III) in elderly patients was also reported by other studies.\[19\]

Actually, the mortality and morbidity of laparoscopic and open paraoesophageal hernia repair are reported to be high.\[19,22\]

In our study, in all 16 patients with paraoesophageal hernia (type III), the indication for surgery was the presence of mechanical and/or obstructive symptoms [Table 5].
Laparoscopic repair of a large paraoesophageal hernia can be a challenging procedure. This is also supported by our study. Indeed, mean operation time was significantly longer in patients undergoing surgery for a large hiatus hernia, conversion to open surgery was required more often, median post-operative hospital stay was longer, intra and post-operative complications were more frequently, but we had no mortality [Table 5]. Furthermore, Bammer et al[8] reported no mortality.

All the four groups in the study presented dysphagia and bloating as long-term post-operative problems. We reported five cases of reoperation due to dysphagia (0.9%) and 7 cases of endoscopic dilatation (1.3%). Among these, five patients were in the first 50 cases of the operative series. The rate of dilatation and re-operation for dysphagia was higher in elderly patients, but without a statistically significant difference [Table 4]. Nevertheless, all studies[10,19] reported no effect of aging on general dysphagia status after LARS. Moreover, this high rate of serious dysphagia necessitating re-intervention at 11 months, decreased at 5, 11 years and beyond of follow-up. Furthermore, bloating was uniformly distributed in all groups of patients.

The problem of recurrence requires special attention. In many studies, the reported recurrence rate of reflux after LARS differs greatly from one series to another, depending on the parameter considered for the definition of recurrence. In our study, we used to define recurrence reflux the pH monitoring, which is actually considered the most objective assessment to define whether or not the patient has GERD.[23] Several studies have also proven that an abnormal 24-h pH score is the best predictor of a good surgical outcome.[24] A pathological increased oesophageal acid exposure is better revealed by prolonged pH monitoring (48 h or more).[25] It should also be noted that heartburn score and proton pump inhibitor (PPI) use are clearly not objective indicators of recurrent gastroesophageal reflux.[26] In support of this, it seems that only 30–35 percentages of PPI use after anti-reflux surgery is actually used to treat gastroesophageal reflux.[27,28] Despite the importance that some studies give to the heartburn score reported by the patient,[29] Engström et al.[30] affirm that would be desirable to validate and quantify these symptoms with pH monitoring. On the other hand, it is also well known that aggressive and extended follow-up protocols (routine post-operative pH-metry and endoscopic control) would result in much higher recurrence rates.

In this study, we observed a higher recurrence rate in elderly and very elderly patients than in young and adult patients [Table 4], with a mean follow-up duration of 14.5 years (range 5–24 years) and without any difference in follow-up duration between four groups [Table 1]. We also found that elderly and very elderly patients had similar short outcomes than other patients (P = 0.72), while they showed a higher failure rate (P = 0.024) after follow-up of 5 years or more. We consider that our aggressive follow-up protocols (routine post-operative pH-metry and endoscopic control) could explain a higher recurrence rate than in other studies.[10,19,20] Many mechanisms had been described that could explain why ageing adversely affects the durability of anti-reflux operations, including lower oesophageal sphincter (LES) pressure,[14] abnormal oesophageal clearance,[29] reduced salivary production,[30] altered oesophageal mucosa resistance[3] and delayed gastric emptying.[3] Furthermore, many drugs frequently taken by the elderly for co-morbid illnesses (i.e., nitrates, calcium channel blockers, benzodiazepines, nonsteroidal anti-inflammatory drugs, etc.[32,29]) are known to decrease LES pressure, to modify oesophageal and gastric motility or to directly damage the oesophageal mucosa. These alterations should explain not excellent results in our elderly patients who underwent fundoplication surgery.

CONCLUSIONS

In elderly and very elderly patients symptoms of reflux esophagitis are blurred and aspecific; the disease is progressively more severe with advancing age. The aging does not seem to influence short-term and long-term (incisional hernia, dysphagia and bloating) outcomes following surgery, but long-term control of reflux overall is worse in elderly patients compared to young or adult ones. Therefore, ageing is a relative contraindication to LNF. Thus, antireflux surgery by an experienced surgeon is appropriate for low-risk elderly and very elderly patients. Further studies should be carried out to evaluate the long-term outcomes, cost-effectiveness and quality of life in these patients.

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Conflicts of interest
There are no conflicts of interest.

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