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ORIGINAL ARTICLE

Surgical outcomes and over one-year follow-up results of laparoscopic Nissen fundoplication for gastroesophageal reflux disease: Single-center experiences

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Summary *Background:* Laparoscopic antireflux surgery is a standard surgical treatment method for gastroesophageal reflux disease (GERD) in Western countries. However, the procedure has not been actively carried out in Korea because of concerns regarding surgical complications. Here, we conducted this study to evaluate short-term surgical outcomes of laparoscopic Nissen fundoplication (LNF) performed at a single institution.
Methods: From January 2010 to August 2016, totally 29 patients underwent LNF for GERD performed by three surgeons at Asan Medical Center, Korea. All patients participated in a telephonic survey including the presence of symptoms and the status of quality of life (QOL).
Results: The median age at operation and BMI were 54 years and 23.8 kg/m^2, respectively. Preoperatively, 27 patients (93.1%) underwent PPI therapy. All patients had typical or atypical GERD symptoms. One patient (3.4%) required reoperation because of total gastroesophageal junction obstruction. 24 patients (82.8%) reported complete or partial resolution of symptoms, whereas 21 (72.4%) reported partial or complete improvement in quality of life. In patients with reflux esophagitis, GERD symptoms were significantly relieved after LNF ($P = 0.005$). LNF responders tended to perceive an improvement in quality of life post operation ($P < 0.001$).
Conclusion: LNF is a feasible, safe, and effective treatment option for controlling GERD symptoms as well as improving the quality of life. Presence of reflux esophagitis was a

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predictor of successful outcomes.

1. Background

Gastroesophageal reflux disease (GERD) is the most common upper gastrointestinal tract disease. It is caused by gastric (acid) or duodenal (alkali) refluxate, which leads to troublesome symptoms and complications. GERD has a negative effect on the patients' quality of life because of its chronic nature and the frequent recurrence tendency. The reported symptom-based GERD prevalence ranges from 10% to 20% and from 5.2% to 8.5% in the Western and Eastern population, respectively.[1,2] In Korea, the prevalence of GERD is 7.3%, which is lower than that in Western countries; however, a gradual increase in prevalence has been reported over the years.[3] Proton pump inhibitors (PPIs) show significant efficacy and have become the first choice of treatment for GERD. Despite the high efficacy of PPIs, clinical failure rate increased up to 20—30% because of lack of response to PPI.[4] Because chronic nature of the disease, long-term PPI administration is usually required. However, chronic use of PPIs can cause adverse events such as chronic kidney disease, dementia, bone fracture, spontaneous bacterial peritonitis, and atypical pneumonia.[5]

Laparoscopic antireflux surgery is a standard surgical treatment method for GERD and is presented as an alternative modality to patients not responding to PPI therapy in Western countries. According to the guidelines recommended by the Society of American Gastrointestinal and Endoscopic Surgeons in 2010, the indications for surgery in patients with GERD are as follows: 1) failed medical management; 2) patient preference for surgery despite successful medical management; 3) development of GERD complications (i.e., peptic stricture and Barrett's esophagus); and 4) extra-esophageal manifestations (i.e., asthma, hoarseness in voice, cough, chest pain, and aspiration).[6] However, laparoscopic fundoplication is not a common procedure in Korea. Because surgical treatment for functional gastrointestinal disease is not familiar for the patients, they have much more concerns about surgical complications. Moreover, lack of Korean data on surgical outcomes of antireflux surgery makes it more difficult to establish as an effective treatment option for GERD.[7,8] Recently, although a few Korean studies reported successful control of GERD symptoms after laparoscopic fundoplication as well as demonstrated the feasibility and safety of the surgery, the data is still lacking.[7,9,10]

In the present study, we evaluated the surgical outcomes of laparoscopic Nissen fundoplication (LNF) performed at a single institution over a follow-up period of more than one year.

2. Methods

From January 2010 to August 2016, totally 29 patients underwent LNF for GERD performed by three surgeons at Asan Medical Center, Korea. After obtaining approval from the institutional review board, their medical records were reviewed. Data pertaining to demographic and clinical characteristics, including age at operation, sex, body mass index (BMI), history of abdominal surgery, duration of PPI therapy, history of GERD, chief symptoms, presence of reflux esophagitis or hiatal hernia, preoperative examinations, operation time, and postoperative complications were included in the analysis.

The diagnosis of GERD was made in all patients prior to the operation based on clinical symptoms, esophagogastroduodenoscopy, esophageal manometry, and 24-h pH monitoring. Presence of reflux esophagitis were observed through endoscopes and degree of esophagitis was classified according to Los Angeles grades. Presence of hiatal hernia was diagnosed by endoscope which was conducted before surgery and laparoscope images during operation.

LNF were carried out in accordance with the guidelines recommended by the Society of American Gastrointestinal and Endoscopic Surgeons in 2010.[6] A 46 Fr bougie was used during surgery and the wrap was made 2—3 cm in length around gastroesophageal junction. All patients visited outpatient clinic after 2—3 weeks after surgery after discharge, however only 6 patients (20.7%) continued to visit clinic of surgery, 5 patients (17.2%) continued to visit clinic of gastroenterology, and the rest were lost to follow up. Therefore, we developed a questionnaire to evaluate the postoperative status. All patients were enrolled in a telephonic survey conducted on August 31, 2017 and all of them answered it. Median follow-up period after surgery was 55.6 months (range, 12.6—89.3 months). The questionnaire comprised the following four questions: 1) improvement of patients' main symptoms, 2) discontinuation or reduction of PPI medication, 3) history of additional surgery or endoscopic treatment due to treatment failure, and 4) improvement in quality of life after surgery (Fig. 1). GERD symptom relief was categorized into three categories: markedly improved (complete resolution of symptoms), partially improved (partial resolution of symptoms), and no improvement. Patients who answered 'markedly improved', 'partially improved' and 'not improved' were regarded as good responders, partial responders, and non-responders, respectively. Typical symptoms of GERD were defined as heartburn and regurgitation which most of the patients complaint about. Atypical symptoms of GERD, or extra-esophageal manifestations were defined as cough, chest pain, aspiration, etc. PPI medication status after

Question	Answer
Have you noticed any improvement in your main symptoms?	Markedly improved Partially improved Not improved
If you administered PPI before surgery, have you reduced the dose or stopped the intake now?	Stopped Reduced Maintained
Have you ever received surgery or endoscopic therapy at another hospital after the surgery?	Yes/No
Do you think that your quality of life improved after the surgery?	Markedly improved Partially improved Not improved

Figure 1 Tele-questionnaire for evaluation of surgical outcomes of antireflux surgery.

antireflux surgery was classified into three categories: treatment cessation, reduction, and maintenance. Improvement in patients' quality of life (QOL) was graded as 'markedly improved', 'partially improved', and 'not improved'. Patients who were highly satisfied with the surgery were assigned to the markedly improved group, and those who were satisfied but continued to experience some symptoms were assigned to the partially improved group.

2.1. Statistical analysis

SPSS ver. 21.0 (IBM Co., Armonk, New York, USA) was used for all data analyses. The Fisher's exact test was used to identify factors that affected symptom relief and QOL after surgery. A *P*-value <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

The study population included 22 males and 7 females. The median age at operation and BMI were 54 years and 23.8 kg/m^2, respectively. The mean PPI therapy duration before surgery was 27 months (range, 1–120 months). 27 patients (93.1%) underwent PPI medication preoperatively. All patients experienced GERD symptoms and the mean duration of symptoms was 36 months (range, 2–480). Of these, 22 (75.9%) experienced typical symptoms while 4 (13.8%) experienced atypical symptoms. Three patients (10.3%) experienced both typical and atypical symptoms. Reflux esophagitis was observed in 18 patients (62.1%) and hiatal hernia was seen in 13 patients (44.8%) (Table 1).

Table 1 Demographic and clinical characteristics of 29 patients that underwent laparoscopic Nissen fundoplication.

Variable	Value
Age in years, median (range)	54 (17–77)
Sex	
Male	22 (75.9%)
Female	7 (24.1%)
BMI, median (range)	23.8 (17.9–30.4)
Laparotomy history	3 (10.3%)
PPI treatment duration	
<6 months	6 (20.7%)
6 months–1 year	4 (13.8%)
>1 year	19 (65.5%)
History of GERD	
≤1 year	4 (13.8%)
1 year–5 years	13 (44.8%)
>5 years	12 (41.4%)
GERD symptoms	
Typical	22 (75.9%)
Atypical	4 (13.8%)
Mixed	3 (10.3%)
Reflux esophagitis	
Present	18 (62.1%)
Absent	11 (37.9%)
Degree of esophagitis, Los Angeles grade	
None or minimal	20 (69.0%)
A	3 (10.3%)
B	4 (13.8%)
C	2 (6.9%)
Barrett's esophagus	3 (10.3%)
Hiatal hernia	
Present	13 (44.8%)
Absent	16 (55.2%)
pH monitoring (n = 24)	
Acid reflux	17 (70.8%)
No acid reflux	7 (29.2%)
Esophageal manometry (n = 26)	
Normal	17 (65.4%)
Ineffective esophageal motility	7 (27.0%)
Hypertensive/hypotensive LES	2 (7.6%)

BMI: body mass index, PPI: proton pump inhibitor, GERD: gastroesophageal reflux disease, LES: Low esophageal sphincter.

Table 2 Surgical outcomes of laparoscopic Nissen fundoplication in 29 patients.

Variable	Value
Operation time, median (min)	83 (43–248)
Conversion to open surgery	0
Complications	
Bleeding	0
Infection	0
Pneumothrorax	0
Esophageal obstruction	1 (3.4%)
Mortality	0

Table 3 Follow-up results based on the telephonic survey.

Variable	Value
Relief of main symptoms	
Markedly improved (Good responder)	17 (58.6%)
Partially improved (Partial responder)	7 (24.2%)
Not improved (Nonresponder)	5 (17.2%)
Discontinuation of PPI at present	
Stop	21 (77.8%)
Reduction	4 (14.8%)
Maintenance	2 (7.4%)
History of reoperation/endoscopic treatment	
Yes	0
No	29 (100%)
Improvement of life quality	
Markedly improved	18 (62.1%)
Partially improved	3 (10.3%)
Not improved	8 (27.6%)

PPI: proton pump inhibitor.

3.2. Preoperative evaluations

Among the 29 patients, 24 patients received 24-h pH monitoring and 26 underwent esophageal manometry before surgery. A 24-h pH monitoring showed 17 cases compatible with acid reflux and 7 cases with normal results. A manometry revealed that 17 patients showed normal pressure of low esophageal sphincter and 7 presented ineffective esophageal motility (Table 1).

3.3. Surgical outcomes

The median operation time was 83 min (range, 43–248). None of the patients required conversion to open laparotomy. A 53-year-old male patient developed total gastroesophageal junction obstruction on the third day after surgery and underwent reoperation. The suture used to approximate hiatus was too tight and led to esophageal obstruction. The postoperative period after revision surgery was uneventful, and the patient was discharged on day 8 of hospitalization.

Table 4 Factors affecting symptom relief after antireflux surgery.

Variable	Good responder	Partial responder	Nonresponder	*P*-value
Age in years				0.334
≤50	6 (46.2%)	5 (38.5%)	2 (15.4%)	
>50	11 (68.8%)	2 (12.5%)	3 (18.8%)	
Sex				0.343
Male	11 (50.0%)	6 (27.3%)	5 (22.7%)	
Female	6 (85.7%)	1 (14.3%)	0	
BMI (kg/m^2)				0.460
≤25	9 (56.3%)	3 (18.8%)	4 (25.0%)	
>25	8 (61.5%)	4 (30.8%)	1 (7.7%)	
PPI treatment duration				0.583
<6 months	5 (83.3%)	0	1 (16.7%)	
6 months–1 year	2 (50.0%)	1 (25.0%)	1 (25.0%)	
>1 year	10 (52.6%)	6 (31.6%)	3 (15.8%)	
Hx. of GERD				0.503
≤1 year	3 (75.0%)	0	1 (25.0%)	
1 year–5 years	7 (53.8%)	5 (38.5%)	1 (7.7%)	
>5 years	7 (58.3%)	2 (16.7%)	3 (25.0%)	
GERD symptoms				0.199
Typical	14 (63.6%)	3 (13.6%)	5 (22.7%)	
Atypical	2 (50.0%)	2 (50.0%)	0	
Mixed	1 (33.3%)	2 (66.7%)	0	
Reflux esophagitis				0.005
Present	12 (66.7%)	6 (33.3%)	0	
Absent	5 (45.5%)	1 (9.1%)	5 (45.5%)	
RE, LA grade				0.353
None/minimal	10 (50.0%)	5 (25.0%)	5 (25.0%)	
A	1 (33.3%)	2 (66.7%)	0	
B	4 (100.0%)	0	0	
C	2 (100.0%)	0	0	
Hiatal hernia				0.460
Present	8 (61.5%)	4 (30.8%)	1 (7.7%)	
Absent	9 (56.3%)	3 (18.8%)	4 (25.0%)	

BMI: body mass index, PPI: proton pump inhibitor, GERD: gastroesophageal reflux disease, RE: reflux esophagitis, LA: Los Angeles.

Except this one patient, none of the patients developed any surgical complications (Table 2).

3.4. Follow-up outcomes

GERD symptoms markedly improved in 17 patients (58.6%) and partially improved in 7 (24.2%). 5 patients (17.2%) were not improved. Twenty-one patients (77.8%) stopped PPI medication, 4 (14.8%) reduced their dosage after surgery, and 2 (7.4%) maintained PPI medication. None of patients underwent any reoperation or endoscopic treatment at any other hospital during the period. Regarding the QOL after surgery, 18 patients (62.1%) felt that their quality of life was markedly improved, 3 (10.3%) answered partially better, and 8 (27.6%) replied that there was no improvement (Table 3).

3.5. Factors affecting symptom control and QOL

Degree of GERD symptom relief was compared according to age, sex, BMI, PPI treatment duration, history of GERD, GERD symptom type, the presence of reflux esophagitis and hiatal hernia, and grade of reflux esophagitis. In patients with reflux esophagitis, GERD symptoms were significantly relieved after LNF as compared with that in patients without esophagitis ($P = 0.005$). Age, sex, BMI, PPI treatment duration, history of GERD, GERD symptom type, grade of reflux esophagitis, and presence of hiatal hernia did not significantly affect postoperative symptom relief (Table 4). There was no significant association between the QOL and the demographic and clinical factors with the exception of response to surgery. Laparoscopic antireflux surgery responders were more likely to perceive an improvement in their QOL after operation ($P < 0.001$) (Table 5).

4. Discussion

As compared with Western countries, Korea has a relatively low GERD prevalence. However, because of the gradual increase in GERD incidence, it has been recognized as a common health issue in Korea. Nevertheless, management of GERD has been largely confined to medical treatment, and data pertaining to antireflux surgery outcomes in Korea has rarely been reported. The Korean Antireflux Surgery Study group performed a survey based on data pertaining to 87 patients who underwent laparoscopic fundoplication across 8 institutions in Korea. The results reported that

Table 5 Factors affecting improvement in quality of life.

Variable	M.I.	P.I.	N.I.	*P*-value
Age				0.636
≤50	7 (53.8%)	2 (15.4%)	4 (30.8%)	
>50	11 (68.8%)	1 (6.3%)	4 (25.0%)	
Sex				0.835
Male	13 (59.1%)	3 (13.6%)	6 (27.3%)	
Female	5 (71.4%)	0	2 (28.6%)	
BMI				0.459
≤25	9 (56.3%)	1 (6.3%)	6 (37.5%)	
>25	9 (69.2%)	2 (15.4%)	2 (15.4%)	
PPI treatment duration				0.636
<6 months	4 (66.7%)	0	2 (33.3%)	
6 months—1 year	3 (75.0%)	1 (25.0%)	0	
>1 year	11 (57.9%)	2 (10.5%)	6 (31.6%)	
Hx. of GERD				0.361
≤1 year	3 (75.0%)	1 (25.0%)	0	
1 year—5 years	8 (61.5%)	0	5 (38.5%)	
>5 years	7 (58.3%)	2 (16.7%)	3 (25.0%)	
GERD symptom				0.444
Typical	15 (68.2%)	2 (9.1%)	5 (22.7%)	
Atypical	2 (50.0%)	1 (25.0%)	1 (25.0%)	
Mixed	1 (33.3%)	0	2 (66.7%)	
Reflux esophagitis				0.272
Present	13 (72.2%)	2 (11.1%)	3 (16.7%)	
Absent	5 (45.5%)	1 (9.1%)	5 (45.5%)	
Hiatal hernia				0.865
Present	9 (69.2%)	1 (7.7%)	3 (23.1%)	
Absent	9 (56.3%)	2 (12.5%)	5 (31.3%)	
Response to LARS				<0.001
Good	16 (94.1%)	0	1 (5.9%)	
Partial	2 (28.6%)	2 (28.6%)	3 (42.9%)	
None	0	1 (16.7%)	4 (80.0%)	

BMI: body mass index, PPI: proton pump inhibitor, GERD: gastroesophageal reflux disease, LARS: laparoscopic antireflux surgery, M.I.: markedly improved, P.I.: partially improved, N.I.: not improved.

laparoscopic fundoplication is an efficient method for controlling GERD symptoms; the complete typical and atypical symptom control rates were 86.3% and 63.3%, respectively. However, antireflux surgery outcomes in the Korean context are still not well characterized.

In the United States, 6.1% patients that underwent antireflux surgery in 2006 experienced at least one complication during their postoperative hospital stay.[11] In our study, only one patient experienced postoperative complete obstruction due to too tight repair of crus (3.4%); none of the other patients developed any complications. Therefore, LNF is a feasible and safe treatment option.

In our study, GERD symptoms were controlled in 82.8% and the QOL was improved in 72.4% of patients. These findings are similar to those of another Korean study reporting that 84% of patients experienced resolution of GERD symptoms.[9] Similar to several studies that sought to identify factors predicting the fundoplication outcomes,[12] our data also revealed that demographic factors including age, sex, and BMI and clinical parameters such as PPI treatment duration and history of GERD were not associated with surgical outcomes.[9,13]

Lundell et al reported that surgery was more effective in controlling overall symptoms in patients with reflux esophagitis or chronic GERD.[14] This study also demonstrated that LNF could predict favorable outcomes in patients with reflux esophagitis. In the present study, patients with more severe esophagitis tended to show better surgical outcomes and, in all patients with Los Angeles grade B or C, GERD symptoms were resolved completely; however, the observed association was not statistically significant. In a study by Park et al, presence of hiatal hernia was a predictor of favorable surgical outcomes after antireflux surgery.[9] Although in this study, the symptom control rate among patients with hiatal hernia was higher than those without it, the association was not statistically significant. Our results demonstrated a remarkable improvement in QOL among good laparoscopic antireflux surgery responders. Contrarily, nonresponders to surgery showed less improvement in QOL. These findings suggest that antireflux surgery may have a favorable influence on QOL by alleviating GERD symptoms.

Certain limitations of our study need to be acknowledged. First, this was a single-center study and did not compare the surgical outcomes with those of medical treatment. Moreover, the sample size of patients was relatively small because fewer Korean candidates tend to opt for surgery. Secondly, not a few patients made regular follow-up visits despite of medical recommendations. Although they received the first esophagogram or esophagogastroduodenoscopy after surgery, we could not evaluate the long-term status of the patients with objective tests. Thus, the evaluation of the symptoms and QOL was performed via a one-time telephonic survey despite of some limitations. Because of unfamiliarity of antireflux surgery and lack of awareness in Korea that surgery is another treatment option for refractory GERD, patients usually did not return to clinic regularly after surgery. Nevertheless, this is the first Korean report that suggests that the presence of reflux esophagitis might be a good surgical outcome predictor after LNF and documents favorable outcomes of antireflux surgery with respect to symptom control over a follow-up period of more than one year. A controlled clinical trial and long-term follow-up results are required to draw more definitive conclusions.

In conclusion, although laparoscopic antireflux surgery is not familiar to the Korean, it is a feasible, safe, and effective treatment option for controlling GERD symptoms and improving the life quality. Patients with reflux esophagitis appear to be particularly good candidates for laparoscopic antireflux surgery.

Conflicts of interest

All the co-authors have viewed the manuscript and agree with its content, and have no financial interests to disclose.

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