

Characteristics and Outcomes of Laparoscopic Surgery in Patients with Gastroesophageal Reflux and Related Disease: A Single Center Experience

Tsutomu Nomura¹, Katsuhiko Iwakiri², Takeshi Matsutani¹, Nobutoshi Hagiwara¹,
Itsuo Fujita¹, Yoshiharu Nakamura¹, Yoshikazu Kanazawa¹, Hiroshi Makino³,
Noriyuki Kawami², Masao Miyashita⁴ and Eiji Uchida¹

¹Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan

²Division of Gastroenterology, Department of Internal Medicine, Nippon Medical School, Tokyo, Japan

³Department of Surgery, Nippon Medical School Tama Nagayama Hospital, Tokyo, Japan

⁴Department of Surgery, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan

Background: Laparoscopic anti-reflux surgery (LARS) is generally the treatment of choice for patients with gastroesophageal reflux disease (GERD). This report describes our experiences in performing LARS on patients with GERD, and focuses retrospectively on the pathophysiology of individual patients and the current status of Japanese patients who have undergone LARS. We demonstrate that patients with non-erosive reflux disease resistant to proton pump inhibitors (PPI-resistant NERD) and high-risk giant hernia, whom we are sometimes hesitant to treat surgically, can be safely and successfully treated with LARS (depending on the pathophysiology of individual patients).

Methods: Between January 2007 and June 2015, 37 patients underwent LARS at Nippon Medical School Hospital. These patients were retrospectively subgrouped according to pathophysiology; 9 of them had PPI-resistant NERD (Group A), 19 had a giant hiatal hernia (Group B), and 9 had erosive esophagitis (Group N). Patient characteristics, intraoperative bleeding, operation duration, perioperative complications, and length of hospital stay were determined, along with symptomatic outcomes and patient satisfaction.

Results: Patients in Group A were the youngest (average: 43.9 years), and those in Group B were the oldest (75.9 years) ($P=0.002$). The percentage of high-risk patients, as determined by performance status ($P=0.047$) and American Society of Anesthesiologists physical status classification ($P=0.021$), was highest in Group B, whereas the percentage of patients with mental disorders was highest in Group A ($P=0.012$). There were no significant differences among the groups in terms of intraoperative bleeding, surgery duration, or postoperative hospital stay. Thirty-three patients (89.2%), including all 19 in Group B, expressed excellent or good postoperative satisfaction levels.

Conclusions: The characteristics of the patients who underwent LARS at our hospital differed according to pathophysiology and from those in western countries. Satisfactory outcomes depended on the pathophysiology of individual patients. (J Nippon Med Sch 2017; 84: 25–31)

Key words: laparoscopic anti-reflux surgery, proton pump inhibitor resistant non-erosive reflux disease, giant hiatal hernia

Introduction

Laparoscopic anti-reflux surgery (LARS) is widely performed as the preferred surgical treatment for gastroesophageal reflux disease (GERD). Esophageal surgeons

have reached a consensus on current indications for LARS, and these conform to the guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)¹. The number of patients undergoing LARS at

Correspondence to Tsutomu Nomura, Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan

E-mail: nomura-t@nms.ac.jp

Journal Website (<http://www.nms.ac.jp/jnms/>)

our hospital for unusual types of GERD has been increasing. These include patients undergoing LARS for non-erosive reflux disease (NERD) resistant to proton pump inhibitors (PPIs), and older patients with mixed-type giant hernias presenting with aspiration pneumonia or dysphagia. Because the demographic and clinical characteristics of these patients differ, so too should indications and operative procedures, which should depend on the clinical status of individual patients. Concerning this issue, no evident distinctions have been reported, which has sometimes led to confusion among surgeons and physicians.

The symptom response rate of patients with NERD treated once daily with PPI for 4 weeks is reported to be 56%², which is significantly lower than the response rate of patients with erosive esophagitis (EE)³. Therefore, surgical treatment is recommended for patients with PPI-resistant NERD³. This condition cannot be diagnosed with endoscopy, so combined multichannel intraluminal impedance (MII)-pH examination is necessary for definitive diagnosis. Patients with giant hiatal hernias have different characteristics from patients with other types of GERD, in that the former tend to be older and more debilitated.

Herein, we describe our experiences of performing LARS on patients with unusual types of GERD, and the current status of Japanese patients who have undergone LARS. The main aim of this study was to retrospectively evaluate the patients' demographic and clinical characteristics, the results of preoperative examinations, and the indications for and outcomes of LARS. The secondary aim was to demonstrate that patients with PPI-resistant NERD and high-risk giant hernias, whom we are sometimes hesitant to treat surgically, can be safely and successfully treated with LARS, depending on the pathophysiology of individual patients.

Patients and Methods

All procedures were in accordance with the ethical standards of the relevant committees on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions. Informed consent was obtained from all patients involved.

Between January 2007 and June 2015, 37 patients (17 men and 20 women, mean age 66.7 years) underwent LARS at Nippon Medical School Hospital. These patients were retrospectively subgrouped according to pathophysiology. Nine patients (5 men and 4 women, mean age 48.1 years) had PPI-resistant NERD (Group A), 19 (6

men and 13 women, mean age 76.2 years) had giant hiatal hernias (Group B), and 9 (6 men and 3 women, mean age 65.0 years) had ordinary GERD with erosive esophagitis (EE) (Group N). We used barium swallow, abdominal computed tomography (CT), and endoscopy to diagnose hiatal hernias, and barium swallow and CT to diagnose Giant hernias with at least 30% of the stomach intussuscepted in the chest⁴. When hiatal hernias could not be identified by abdominal CT or barium swallow, we determined whether hiatal hernias >2 cm could be diagnosed by endoscopy. With type III hernias, it is difficult to measure the sliding component by endoscopy, so we used CT to measure the paraesophageal component as the distance from the hiatus to the top of the fundus. Operative indications in Group A were determined by MII-pH monitoring; specific indications for LARS included a positive (>50%) symptom index⁵, extreme adverse impact on quality of life, and desire for surgery³. Esophageal manometry was performed with a 21-channel manometric assembly (Dentsleeve, Wayville, SA, Australia)⁶. Indications for LARS in Group B consisted of diagnosis of any symptom caused by a giant hiatal hernia, such as dysphagia or aspiration pneumonia, even in older and high-risk patients. Indications for LARS in Group N were based on SAGES guidelines¹.

Regarding surgical treatment, Nissen fundoplication was adopted as an initial anti-reflux procedure. Thereafter, Toupet fundoplication was used, because it reduces postoperative dysphagia better than Nissen fundoplication⁷. Crural repair was not performed in Groups A or N if the hiatus did not widen during the operation. In Group B, cruroplasty and hernia sac removal was performed in all cases.

Study Endpoint

The study endpoint was to clarify the differences in clinical characteristics, symptoms, methods of examination, and surgical procedures and outcomes among the three groups. Objective assessments included demographic and clinical characteristics, intraoperative bleeding, duration of surgery, perioperative complications, and length of hospital stay. Subjective assessments included dysphagia, heartburn and other symptoms, as well as patient satisfaction. The efficacy of LARS was evaluated by postoperatively interviewing all patients about symptom improvement, with improvement graded as excellent, good, fair, or poor. Our assessment showed that patients with PPI-resistant NERD and high-risk giant hernias, whom we are sometimes hesitant to treat surgically, should, like patients with GERD, be treated with LARS.

Table 1 Demographic characteristics of the 3 groups of patients

	Group A (n=9)	Group B (n=19)	Group N (n=9)	p value
Age (median, IQR in years)	43, 9	75, 9	70, 17	0.002 ^a
Gender (Male/Female)	5/4	6/13	6/3	0.176 ^b
BMI (median, IQR kg/m ²)	20.1, 4.0	24.0, 5.2	24.3, 2.0	0.328 ^a
Preoperative performance status				0.047 ^b
PS 0	8	3	4	
PS 1	1	9	3	
PS 2	0	3	0	
PS 3	0	1	1	
PS 4	0	3	1	
Gibbus	0/9	4/19	0/9	0.12 ^b
ASA-PS Classification				0.021 ^b
ASA 1	4	0	1	
ASA 2	5	15	7	
ASA 3	0	4	1	
Emergency operation	0/9	7/19	2/9	0.104 ^b
Mental disorder				0.012 ^b
none	3	17	7	
depression	5	0	1	
Schizophrenia	0	1	1	
Panic disorder	1	0	0	
Dementia	0	1	0	
Previous abdominal operation	3/9	1/19	1/9	0.124 ^b
Preoperative hospital stay (median, IQR days)	2, 1	2, 20	2, 1	0.048 ^a

^a Kruskal-Wallis test; ^b Pearson's χ^2 test

Abbreviations: BMI, body mass index; PS, performance status; ASA, American Society of Anesthesiologists physical status classification; IQR, interquartile range

Statistical Analyses

Data are presented as median and interquartile ranges. Where appropriate, Pearson's χ^2 and Kruskal-Wallis tests were used for comparisons. A *P* value <0.05 was considered statistically significant. All statistical analyses were performed with SPSS version 20.0 (SPSS, Chicago, IL, USA).

Results

Table 1 shows the demographic characteristics of the 3 patient groups. The patients in Group A (43.9 years) were the youngest, and those in Group B (75.9 years) were the oldest (*P*=0.002). The percentages of high-risk patients, as determined by performance status (PS) (*P*=0.047) and American Society of Anesthesiologists (ASA) physical status classification (*P*=0.021), were highest in Group B. Seven patients in this group required immediate hospitalization for dysphagia, aspiration pneumonia or general wasting, whereas 2 patients in Group N required immediate hospitalization for aspiration pneumonia. Preoperative hospital stay was significantly longer in Groups B

and N than in Group A (*P*=0.048). The percentage of patients with mental disorders was significantly higher in Group A than in the other 2 groups (*P*=0.012), with somatic complaints and mental symptoms, including insomnia, depression and panic disorder, observed.

Table 2 shows the results of preoperative examinations and patient symptoms. In Group B, all the patients had type III hernias with sliding and paraesophageal components. In Group A, no patients were diagnosed endoscopically with hiatal hernias. In Group N, 6 patients had sliding type hiatal hernias >2 cm diagnosed endoscopically. Objective factors determining the need for LARS in Groups A and B were the results of MII-pH monitoring and abdominal CT, respectively. EE was observed in all 9 patients in Group N and in 9 of 19 in Group B.

The most frequently observed subjective symptom in Group B was dysphagia, with 7 of the 19 patients requiring emergency surgery. In contrast, heartburn and chest pain were predominant in Group A, whereas patients in Group N manifested a variety of symptoms (*P*<0.001).

Anti-reflux procedures in Group A included Nissen

Table 2 Results of preoperative examinations and patients' symptoms

	Group A (n=9)	Group B (n=19)	Group N (n=9)	p value
Objective factors (Examination)				
The Los Angeles classification				0.004 ^b
Grade N	9	10	0	
Grade A	0	6	6	
Grade B	0	3	1	
Grade C	0	0	1	
Grade D	0	0	1	
Hernia size				<0.001 ^b
<2 cm	9	0	3	
2 to <5 cm	0	0	5	
≥5 cm	0	19	1	
Subjective factors (Chief symptom)				
Dysphagia	0	16	0	<0.001 ^b
Regurgitation, Pneumonia	0	2	4	
Heartburn, Chest pain	8	1	4	
Belch	1	0	1	

^b Pearson's χ^2 test

Abbreviations: CT, computed tomography; LA, Los Angeles classification

fundoplication in 5 patients and Toupet fundoplication in 4. Anti-reflux procedures in Group N included Nissen fundoplication in 1 patient, Toupet fundoplication in 7 and Dor fundoplication in 1. LARS in Group B patients included cruroplasty as well as fundoplication. After the incarcerated organ was repositioned, the weakened hiatus was repaired prior to fundoplication. Cruroplasty reinforcement required prosthetic mesh in 13 patients, whereas the other 6 required only simple closure of the hiatus (Table 3).

There were no significant differences among the 3 groups in intraoperative bleeding or duration of surgery. None of the patients was switched to open surgery or experienced any critical postoperative complications, and postoperative hospital stay was similar in the 3 groups (Table 4). Rates of postoperative dysphagia were comparable in the 3 groups, but no patient complained of long-standing severe dysphagia. Of the 37 patients, 33 (89.2%), including all 19 in Group B, reported excellent or good postoperative satisfaction levels. Patients in Group B experienced resolution of symptoms, allowing oral intake and discharge from the hospital. For PPI medication before and after the operation, there were no significant differences among the 3 groups.

Discussion

We analyzed the characteristics of patients who underwent LARS at our hospital, subgrouped by pathophysiol-

ogy. Although the total number of patients was small, the characteristics of the 3 groups showed definite tendencies. The patients in Group B were significantly older (median age, 75.9 years) than those in the other 2 groups, as well as being older than patients in western countries who undergo surgery for giant hiatal hernias (mean age, 59–72 years)^{8–10,11}. LARS is less frequently performed in Japan than in western countries, with <200 patients per year in Japan undergoing this operation¹², the main reasons being that severe esophagitis is uncommon in Japan¹³ and that Japanese surgeons are not yet accustomed to performing LARS. Thus, Japanese patients generally undergo this operation only after the disease has progressed significantly, whereas western patients may undergo surgery during earlier stages of the disease.

The patients in Group A were significantly younger than those in the other 2 groups, but were similar in age to patients in other Japanese studies of NERD^{14–16}. Although epidemiological studies do not show any age-related increase in the prevalence of GERD symptoms, the real prevalence of GERD may well increase with age¹⁷. The pathophysiology of NERD includes hypersensitivity in the proximal esophagus, with symptoms possibly caused by increases in reflux volumes, which cause distension and defects of secondary peristalsis¹⁸. This pathophysiology might be unaffected by aging.

A meta-analysis of 20 studies reported a positive association between increased body mass index (BMI) and

Table 3 Characteristics of surgical treatments

	Group A (n=9)	Group B (n=19)	Group N (n=9)	p value
Fundplication (Nissen/Toupet/Dor)	5 / 4 / 0	3 / 15 / 1	1 / 7 / 1	0.137 ^b
Crural repair (None/simple closure/mesh use)	9 / 0 / 0	0 / 6 / 13	4 / 4 / 1	<0.001 ^b

^b Pearson's χ^2 test

Table 4 Objective and symptomatic outcomes after the operation

	Group A (n=9)	Group B (n=19)	Group N (n=9)	p value
Surgery duration (median, IQR min)	181, 33	193, 60	197, 27	0.428 ^a
Amount of bleeding (median, IQR mL)	5, 14	5, 20	10, 25	0.839 ^a
Postoperative stay (median, IQR day)	7, 1	7.0, 1.8	7.0, 0.5	0.528 ^a
Postoperative dysphagia (n)				0.623 ^b
None/Mild	7	12	7	
Moderate	2	7	2	
Severe	0	0	0	
Patient satisfaction (n)				0.113 ^b
Excellent/good	7	19	7	
Fair	2	0	1	
Poor	0	0	1	
PPI medication (%)				0.051 ^b
Before operation	66.7	73.7	100	
After operation	22.2	21.1	22.2	

^a Kruskal-Wallis test; ^b Pearson's χ^2 test

Abbreviations: IQR, interquartile range; PPI, proton pump inhibitor

the presence of GERD in the US¹⁹. Furthermore, the prevalence of a defective lower esophageal sphincter (LES) was reported to be higher in patients with higher BMI, with obese patients being more than twice as likely as normal weight patients to have a mechanically defective LES²⁰. The mean BMI of our patients was within normal limits, which is consistent with previous reports about Japanese patients with GERD^{15,16}. Thus, despite the generally accepted role of obesity in the pathophysiology of GERD, it would appear that it is not caused by obesity alone and that more complicated mechanisms are involved.

LARS for paraesophageal hiatal hernias is a challenging procedure^{21,22}, with most patients being older individuals with a higher risk of postoperative complications^{11,23,24}. Accordingly, LARS for these patients is associated with higher mortality and morbidity rates than LARS for non-elderly GERD patients^{23,25}. In our study, the patients in Group B had lower preoperative PS and ASA scores, and longer preoperative hospital stays because of

dysphagia, aspiration pneumonia, and general debility than the patients in the other groups; these results are consistent with those of previous studies. In contrast, none of the patients in any group experienced serious complications, and intraoperative bleeding, duration of surgery, and postoperative hospital stay were comparable in the 3 patient groups. Postoperative satisfaction level was good or excellent in all Group B patients, as oral ingestion became possible after surgery. These excellent outcomes in patients with giant hiatal hernias suggest that LARS is safe and effective, even for older patients and those with other diseases. LARS should be aggressively performed if it is expected to improve patient condition.

The surgical procedure is still controversial, especially fundoplication. However, dysphagia and inability to belch are more common after laparoscopic Nissen fundoplication than after Toupet fundoplication²⁶. It is important to balance the anti-reflux efficacy of surgery with the extent of postoperative dysphagia in selecting the

fundoplication procedure. Tan et al. reported in a comparative meta-analysis of Nissen and Toupet fundoplication that although postoperative satisfaction in the 2 groups was comparable, the latter experienced a lower occurrence of postoperative dysphagia²⁷. In the past, we initially selected the fundoplication method according to the manometry findings. However, in the present study, in consideration of the above-mentioned reports, we used only Toupet fundoplication. It is important to prevent postoperative dysphagia that might cause aspiration pneumonia, so we paid careful attention to the possibility of stenosis after fundoplication, carrying out endoscopic examinations of the lumen of the esophagus intraoperatively, especially in the frail elderly patients of Group B.

Caution should be exercised in performing LARS on patients with PPI-resistant NERD. Although MII-pH monitoring is essential for diagnosis of this disease, the concept of PPI-resistant NERD is not well known, even among physicians in Japan. Accordingly, many patients are diagnosed and treated incorrectly, resulting in no improvement or worsening of symptoms³. Our study also found a higher percentage of patients with mental disorders in Group A than in the other groups. These patients' complaints were exacerbated by NERD symptoms as well as anxiety. Despite these drawbacks, LARS outcomes in Group A were comparable with those in the other 2 groups. Good outcomes in Group A likely resulted from the strict indications for LARS of PPI-resistant NERD patients at our hospital.

GERD was evaluated preoperatively by MII-pH monitoring only in Group A. In contrast, reflux status was not evaluated in Groups B and N. MII-pH monitoring or esophageal manometry was difficult in patients with giant hiatal hernias (Group B) because of the technical impossibility of properly placing the catheter in the esophagus, especially in emergency patients. Accordingly, decisions for surgery were based on the results of CT, endoscopy, and especially, patient symptoms. LARS in Group N patients was performed when EE was observed on endoscopy and patient status met SAGES guidelines¹. Ideally, reflux status in all patients should have been assessed by MII-pH monitoring; however, except for patients with NERD, preoperative MII-pH monitoring is not essential in deciding whether to perform surgery.

Regarding PPI medication, there were no differences among the 3 groups. Lodrup et al. reported that 5-, 10- and 15-year risks of redeeming index PPI prescriptions were 57.5%, 72.4% and 82.6%, respectively²⁸. There were

not as many patients who needed PPIs in our study; however, we also observed an increased risk of the need of PPIs over time. This would result in declining future satisfaction levels, so we think we should monitor our patients on a long-term basis.

One important limitation of this study was the small number of patients, especially when compared with studies from western countries. However, LARS is performed less frequently in Japan, especially in patients with PPI-resistant NERD, making it difficult to enroll large numbers of patients in these groups. Evaluation of additional patients, including multicenter studies, is needed to determine the characteristics and surgical outcomes of LARS in Japanese patients.

In conclusion, the characteristics of patients who underwent LARS at our hospital differed according to their pathophysiology, and also from those of western patients. Laparoscopic surgery for giant hiatal hernias, which is regarded as a challenging procedure, resulted in satisfactory outcomes despite unfavorable preoperative conditions. We attribute this to our policy of selecting Toupet fundoplication to prevent postoperative dysphagia that might cause aspiration pneumonia, especially in frail elderly patients. Patients with PPI-resistant NERD were younger and had a higher preoperative prevalence of mental disturbance. Good outcomes in these patients likely resulted from the strict indications for LARS. Overall, LARS was useful in the treatment of GERD patients at our hospital, but we believe determining the pathophysiology of individual patients is essential for satisfactory outcomes.

Conflict of Interest: We declare no conflict of interest. No funding was received for this study.

References

1. Stefanidis D, Hope WW, Kohn GP, Reardon PR, Richardson WS, Fanelli RD: Guidelines for surgical treatment of gastroesophageal reflux disease. *Surg Endosc* 2010; 24: 2647–2669.
2. Dean BB, Gano AD Jr, Knight K, Ofman JJ, Fass R: Effectiveness of proton pump inhibitors in nonerosive reflux disease. *Clin Gastroenterol Hepatol* 2004; 2: 656–664.
3. Nomura T, Iwakiri K, Matsutani T, Hagiwara N, Makino H, Maruyama H, Fujita I, Nakamura Y, Kawami N, Miyashita M, Uchida E: Laparoscopic anti-reflux surgery to treat proton pump inhibitor-resistant non-erosive reflux disease. *Esophagus* 2013; 10: 157–160.
4. Mitiek MO, Andrade RS: Giant hiatal hernia. *Ann Thorac Surg* 2010; 89: S2168–2173.
5. Wiener GJ, Richter JE, Copper JB, Wu WC, Castell DO: The symptom index: a clinically important parameter of ambulatory 24-hour esophageal pH monitoring. *Am J*

- Gastroenterol 1988; 83: 358–361.
6. Iwakiri K, Kawami N, Sano H, Tanaka Y, Umezawa M, Kotoyori M, Hoshihara Y, Sakamoto C: Mechanisms of excessive esophageal acid exposure in patients with reflux esophagitis. *Dig Dis Sci* 2009; 54: 1686–1692.
7. Broeders JA, Mauritz FA, Ahmed Ali U, Draaisma WA, Ruurda JP, Gooszen HG, Smout AJ, Broeders IA, Hazebroek EJ: Systematic review and meta-analysis of laparoscopic Nissen (posterior total) versus Toupet (posterior partial) fundoplication for gastro-oesophageal reflux disease. *Br J Surg* 2010; 97: 1318–1330.
8. Morino M, Giaccone C, Pellegrino L, Rebecchi F: Laparoscopic management of giant hiatal hernia: factors influencing long-term outcome. *Surg Endosc* 2006; 20: 1011–1016.
9. Jassim H, Seligman JT, Frelich M, Goldblatt M, Kastenmeier A, Wallace J, Zhao HS, Szabo A, Gould JC: A population-based analysis of emergent versus elective paraesophageal hernia repair using the Nationwide Inpatient Sample. *Surg Endosc* 2014; 28: 3473–3478.
10. Targarona EM, Grisales S, Uyanik O, Balague C, Pernas JC, Trias M: Long-term outcome and quality of life after laparoscopic treatment of large paraesophageal hernia. *World J Surg* 2013; 37: 1878–1882.
11. Prassas D, Rolfs TM, Schumacher FJ: Laparoscopic repair of giant hiatal hernia. A single center experience. *Int J Surg* 2015; 20: 149–152.
12. Kitano M, Yamashita Y, Hashidume M, Baodo T, Yanaga K, Watanabe M, Kitagawa Y, Takiguchi S, Endo S, Morikawa T, Tamaki Y, Matsumoto S, Yotsu R, Akira S, Terachi T, Hasegawa T, Onishi K: 12th Nationwide Survey of Endoscopic Surgery in Japan. *J Jpn Soc Endosc Surg* 2014; 19: 495–640.
13. Furukawa N, Iwakiri R, Koyama T, Okamoto K, Yoshida T, Kashiwagi Y, Ohya T, Noda T, Sakata H, Fujimoto K: Proportion of reflux esophagitis in 6010 Japanese adults: prospective evaluation by endoscopy. *J Gastroenterol* 1999; 34: 441–444.
14. Kusano M, Hosaka H, Kawamura O, Kawada A, Kuribayashi S, Shimoyama Y, Yasuoka H, Mizuide M, Tomizawa T, Sagawa T, Sato K, Yamada M: More severe upper gastrointestinal symptoms associated with non-erosive reflux disease than with erosive gastroesophageal reflux disease during maintenance proton pump inhibitor therapy. *J Gastroenterol* 2015; 50: 298–304.
15. Fujiwara Y, Higuchi K, Shiba M, Yamamori K, Watanabe Y, Sasaki E, Tominaga K, Watanabe T, Oshitani N, Arakawa T: Differences in clinical characteristics between patients with endoscopy-negative reflux disease and erosive esophagitis in Japan. *Am J Gastroenterol* 2005; 100: 754–758.
16. Matsuki N, Fujita T, Watanabe N, Sugahara A, Watanabe A, Ishida T, Morita Y, Yoshida M, Kutsumi H, Hayakumo T, Mukai H, Azuma T: Lifestyle factors associated with gastroesophageal reflux disease in the Japanese population. *J Gastroenterol* 2013; 48: 340–349.
17. Becher A, Dent J: Systematic review: ageing and gastro-oesophageal reflux disease symptoms, oesophageal function and reflux oesophagitis. *Aliment Pharmacol Ther* 2011; 33: 442–454.
18. Iwakiri K, Sano H, Tanaka Y, Kawami N, Umezawa M, Futagami S, Hoshihara Y, Nomura T, Miyashita M, Sakamoto C: Characteristics of symptomatic reflux episodes in patients with non-erosive reflux disease who have a positive symptom index on proton pump inhibitor therapy. *Digestion* 2010; 82: 156–161.
19. Corley DA, Kubo A: Body mass index and gastroesophageal reflux disease: a systematic review and meta-analysis. *Am J Gastroenterol* 2006; 101: 2619–2628.
20. Ayazi S, Hagen JA, Chan LS, DeMeester SR, Lin MW, Ayazi A, Leers JM, Oezcelik A, Banki F, Lipham JC, DeMeester TR, Crookes PF: Obesity and gastroesophageal reflux: quantifying the association between body mass index, esophageal acid exposure, and lower esophageal sphincter status in a large series of patients with reflux symptoms. *J Gastrointest Surg* 2009; 13: 1440–1447.
21. Luketich JD, Raja S, Fernando HC, Campbell W, Christie NA, Buenaventura PO, Weigel TL, Keenan RJ, Schauer PR: Laparoscopic repair of giant paraesophageal hernia: 100 consecutive cases. *Annals of surgery* 2000; 232: 608–618.
22. Dahlberg PS, Deschamps C, Miller DL, Allen MS, Nichols FC, Pairolero PC: Laparoscopic repair of large paraesophageal hiatal hernia. *Ann Thorac Surg* 2001; 72: 1125–1129.
23. Larusson HJ, Zingg U, Hahnloser D, Delpont K, Seifert B, Oertli D: Predictive factors for morbidity and mortality in patients undergoing laparoscopic paraesophageal hernia repair: age, ASA score and operation type influence morbidity. *World J Surg* 2009; 33: 980–985.
24. Swanson LL, Jobe BA, Kinzie LR, Horvath KD: Esophageal motility and outcomes following laparoscopic paraesophageal hernia repair and fundoplication. *Am J Surg* 1999; 177: 359–363.
25. Gupta A, Chang D, Steele KE, Schweitzer MA, Lyn-Sue J, Lidor AO: Looking beyond age and co-morbidities as predictors of outcomes in paraesophageal hernia repair. *J Gastrointest Surg* 2008; 12: 2119–2124.
26. Koch OO, Kaindlstorfer A, Antoniou SA, Asche KU, Granderath FA, Pointner R: Laparoscopic Nissen versus Toupet fundoplication: objective and subjective results of a prospective randomized trial. *Surg Endosc* 2012; 26: 413–422.
27. Tan G, Yang Z, Wang Z: Meta-analysis of laparoscopic total (Nissen) versus posterior (Toupet) fundoplication for gastro-oesophageal reflux disease based on randomized clinical trials. *ANZ J Surg* 2011; 81: 246–252.
28. Lodrup A, Pottegard A, Hallas J, Bytzer P: Use of proton pump inhibitors after antireflux surgery: a nationwide register-based follow-up study. *Gut* 2014; 63: 1544–1549.

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