

Comparison of laparoscopic Nissen and Toupet fundoplication using a propensity score matching analysis

Masato Hoshino¹ · Nobuo Omura¹ · Fumiaki Yano¹ · Kazuto Tsuboi¹ ·
Se Ryung Yamamoto¹ · Shunsuke Akimoto¹ · Norio Mitsumori¹ ·
Hideyuki Kashiwagi¹ · Katsuhiko Yanaga¹

Received: 28 November 2016 / Accepted: 31 January 2017 / Published online: 1 March 2017
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Abstract

Purpose Laparoscopic fundoplication (LF) has become a standard operative procedure for GERD-related diseases in Japan, although meta-analyses have mainly evaluated findings from Western countries. The propensity score matching method was used to compare and investigate the treatment outcomes of two fundoplication procedures (the Nissen and Toupet methods).

Methods Among 474 patients who underwent initial LF from December 1994 to April 2016, we extracted 401 cases (Nissen: 92 cases, Toupet: 309 cases), excluding 73 patients in whom follow-up was insufficient. We then matched 126 of these patients (63 per group).

Results The esophageal acid reflux time (%) was 12.2:2.8, being higher in the Nissen group than in the Toupet group ($p < 0.001$). Regarding the surgical outcome, the amount of bleeding was higher in the Nissen group ($p = 0.001$), and the number of hospitalization days following surgery was longer ($p = 0.003$). Furthermore, a significantly rate of postoperative difficulty in swallowing (%) was observed in the Nissen group, at 13:0 ($p = 0.004$). The recurrence rate (%) was 8:3, with no difference between the two groups ($p = 0.243$).

Conclusions Although there was no marked difference in the recurrence rate between the two procedures, postoperative dysphagia was observed at a higher frequency with the Nissen method than the Toupet method.

Keywords Nissen fundoplication · Toupet fundoplication · Gastroesophageal reflux disease (GERD) · Propensity score matching analysis · Surgical outcomes

Introduction

In recent years, the number of patients suffering from gastroesophageal reflux disease (GERD) has been increasing in Japan, due largely to the effects of Westernized diets. In Western countries, laparoscopic fundoplication has become well-established as a surgical treatment for GERD in the late 1990s; however, in Japan, it has only recently started to become the standard treatment. Laparoscopic fundoplication is broadly divided into the Nissen method, in which circumferential wrapping is carried out, and the Toupet method, which is carried out 210°–270° posterior [1–4]. For the two procedures, randomized clinical trials (RCTs) and meta-analyses have been reported mainly from Western countries; however, while there were no marked differences between the two procedures with respect to backflow prevention, there have been many reports of high rates of postoperative difficulty in swallowing with the Nissen method [5, 6]. However, in Japan, the number of laparoscopic fundoplication cases is much smaller than that reported from Western countries, with no reports comparing the two procedures using a large number of cases. Furthermore, there have been no reports comparing cases with matching of patient background characteristics in Japan.

Accordingly, in this study, the propensity score matching method was used to reduce bias in patient background and pathophysiology as much as possible to compare the therapeutic outcomes of the Nissen method and Toupet method in Japan. This clinical investigation was approved by the

✉ Masato Hoshino
qq2w2yb9@mist.ocn.ne.jp

¹ Department of Surgery, The Jikei University School of Medicine, 3-25-8 Nishishinbashi, Minato-ku, Tokyo 105-8461, Japan

Jikei University School of Medicine University Hospital Ethics Committee; 28-047.

Methods

Study population

Among the 474 cases that underwent initial laparoscopic fundoplication from December 1994 to April 2016, 401 patients (Nissen: 92 patients, Toupet: 309 patients), excluding those for whom follow-up was insufficient, were extracted. Of these 401 extracted patients, 126 (63 patients each) were matched according to age, gender, body mass index (BMI), the degree of esophageal hiatal hernia, and the degree of reflux esophagitis (Fig. 1). There were 87 male patients, with a median age of 49 (interquartile range: 40–58). Their preoperative pathological conditions were evaluated based on the AFG classification [7, 8], i.e., the degree and type of esophageal hiatal hernia were determined as the *A* factor (four-stage evaluation from 0 to 3), while the degree of reflux esophagitis was determined as the *P* factor (four-stage evaluation from 0 to 3), and the looseness of the cardia was determined as the *V* factor (0–3). Recurrence was defined as when hernia recurrence of grade A1 or higher or erosive esophagitis of Los Angeles classification grade A or higher was observed upon upper esophagogastroduodenoscopy [9]. Postoperative difficulty in swallowing was defined by the number of extra-hospitalization days following surgery due to difficulty in swallowing, or when balloon dilatation was carried out under upper endoscopy during follow-up [10, 11].

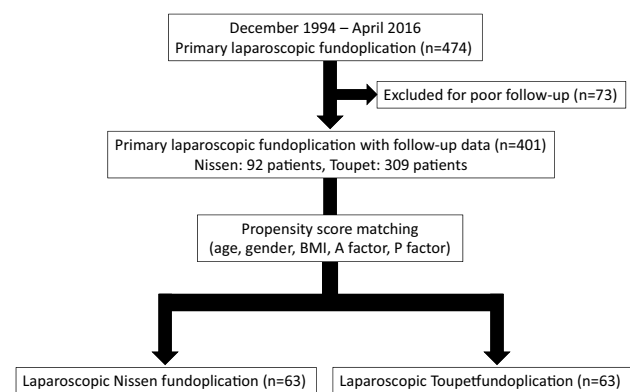


Fig. 1 Subject extraction method. A total of 73 among 474 patients who underwent initial laparoscopic fundoplication during the study period were excluded due to insufficient follow-up. The remaining 401 cases were extracted, and matching was carried out by calculating propensity scores. The Nissen group (63 cases) and Toupet group (63 cases) were the subjects of the present study

Twenty-four-hour esophageal pH monitoring

Intake of acid secretion-inhibiting drugs was discontinued from 1 week prior to the study. A Digitrapper MK-II or MK-III (Medtronic Inc., Minneapolis, MN, USA) was used for conventional pH monitoring, which was changed to multichannel intraluminal impedance pH (MII-pH) monitoring from June 2008 using Sleuth (Sandhill Scientific, Highlands Ranch, CO, USA), along with a catheter by the same company. Catheters were nasally inserted under radiology and left inside the body, so that the tip (distal sensor) stayed in the stomach and the proximal sensor stayed within 5 cm of the superior end of the LES [lower esophageal sphincter]. Patients ate only hospital food, three times a day, during the study; snacks were prohibited, water intake was allowed, and 24-h continuous monitoring was carried out. The data were automatically analyzed using a software program [12]. Intraesophageal pH <4 h was calculated as a parameter and regarded as the intraesophageal acid exposure time.

Surgical indications and procedures (Nissen or Toupet fundoplication)

We established surgical indications for the patients as follows: (1) PPI-resistant erosive GERD; (2) GERD with extra-esophageal manifestations; (3) giant esophageal hernia; (4) case requiring continued PPI therapy; and (5) a causal relationship between reflux and symptoms proven by MII-pH in cases of non-erosive reflux disease (NERD). The MII-pH results were included in the evaluation of surgical indications, and we consider understanding the MII-pH results for NERD to be of particular importance for the pathophysiology.

The details of the surgical procedure have been described previously [8]. Surgery was carried out using four-to-five trocars. Regarding the anterior stem of the vagal nerve, 4 cm of the abdominal esophagus was secured, with the posterior trunk separated from the posterior wall of the esophagus while attached to the anterior wall of the esophagus. All short gastric arteries and veins were resected to allow room for wrapping. With the Nissen method, an esophagus bougie of approximately 56–60 Fr was orally inserted, and floppy Nissen was carried out with the abdominal esophagus covered to the fundus of the stomach for approximately 2 cm circumferentially. With the Toupet method, the abdominal esophagus was coated from the dorsal side of the esophagus for approximately 4 cm non-circumferentially by approximately two-thirds of the circumference without inserting an esophagus bougie. The crura of the diaphragm and a fundic wrap on the same side were sutured to achieve deviation from the inside of the mediastinum during cardioplasty.

Statistical analyses

The statistical analyses were carried out using the SPSS software program (SPSS Inc version 23.0, Chicago, IL, USA). All data are presented as the median and interquartile range (IQR), with $p < 0.05$ by a Mann–Whitney test and Chi-squared test regarded as indicating a statistical difference. The reoccurrence rate was calculated by the Kaplan–Meier method and compared using the log rank test. $p < 0.05$ was considered statistically significant. One-to-one propensity score matching was adopted to overcome bias arising from the lack of randomization as a consequence of the different co-variable distributions among patients. Matching was performed by calculating propensity scores using the following predictors: age, gender, BMI, A factor, and P factor.

Results

Patients' background and pathophysiology

There were no significant differences in the age, gender, BMI, A factor, or P factor on propensity score matching. However, the rate of esophageal pH < 4 h was significantly lower in the Toupet group than in the Nissen group (Tables 1, 2).

Surgical and postoperative outcomes

A tendency towards an extended surgery time was observed in the Nissen group ($p = 0.060$). The median amount of bleeding during surgery was almost none in both groups but was significantly higher in the Nissen group ($p = 0.001$). There was no marked difference between the two groups in terms of intraoperative complications, such as esophageal or gastric mucosal injuries and bleeding ≥ 200 ml. The length of hospitalization was 7 days in both groups, which was significantly shorter in the Toupet group ($p = 0.003$). As postoperative complications, no cases of difficulty in swallowing were observed in the Toupet group, compared to eight cases (13%)

Table 1 Demographic data of the two groups

	Nissen ($n = 63$)	Toupet ($n = 63$)	p value
Age (years)	49 (39–59)	48 (40–57)	N/A
Gender (M:F)	41:22	46:17	N/A
Body Mass Index (kg/m ²)	23.7 (22.2–26.0)	23.4 (21.8–26.3)	N/A
Duration of illness (months)	24 (12–60)	36 (8–60)	0.776

observed in the Nissen group ($p = 0.004$). The follow-up period was significantly shorter in the Toupet group ($p = 0.019$); however, there was no marked difference in the recurrence rate between the groups, with five cases in the Nissen group (8%) and two in the Toupet group (3%) (Table 3); the median follow-up period until recurrence was 35 months in the Nissen group (3, 25, 35, 61, and 77 months), 48 months in the Toupet group (22 and 74 months, respectively), and 35 months overall (Fig. 2). Esophageal hiatal hernia recurred in all cases in the Nissen group, with reflux esophagitis observed in two cases (40%). Esophageal hiatal hernia also recurred in both cases in the Toupet group, with reflux esophagitis observed in 1 (50%).

Discussion

Until the 1980s, when laparotomy or thoracotomy approaches were first introduced, including the Nissen method, Hill method, Belsey Mark IV method, and the Menguy method, all represented the mainstream procedures for GERD-related diseases. Following the

Table 2 Preoperative AFP classification and 24-h pH monitoring findings of the two groups

	Nissen ($n = 63$)	Toupet ($n = 63$)	p value
A factor	1 (1–2)	2 (1–2)	N/A
P factor	1	1 (0–1)	N/A
24-h pH < 4 holding time (%)	12.2 (5.7–27.9)	2.8 (1.1–5.4)	< 0.001

Table 3 Surgical findings and postoperative outcomes of the two groups

	Nissen ($n = 63$)	Toupet ($n = 63$)	p value
Operative time (min)	145 (120–179)	125 (105–170)	0.060
Estimated blood loss (ml)	0 (0–10)	0	0.001
Intraoperative complications	8 (13%)	3 (5%)	0.115
Mucosal injury	1	0	0.315
Bleeding (over 200 ml)	5 (8%)	1 (2%)	0.094
Others	2	2	1
Hospital days (day)	7 (7–8)	7	0.003
Postoperative complications	9 (14%)	0	0.002
Dysphagia	8 (13%)	0	0.004
Others	1	0	0.315
Follow-up (months)	80 (24–126)	22 (6–64)	0.019
Recurrence	5 (8%)	2 (3%)	0.243

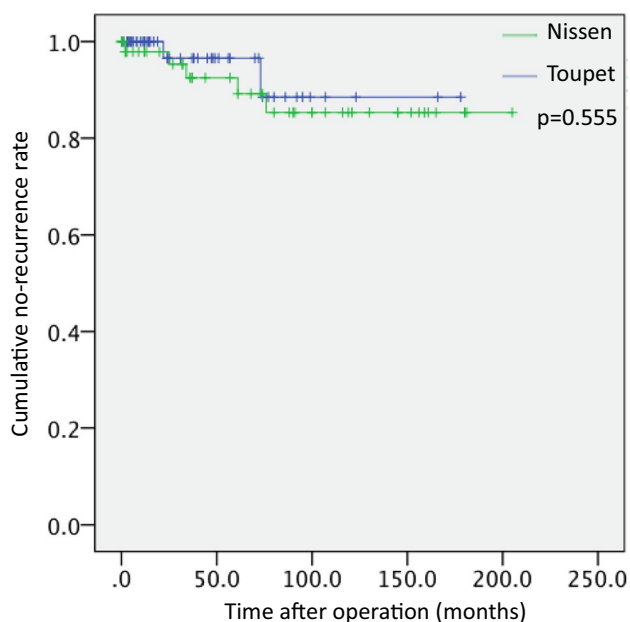


Fig. 2 Recurrence rate of the two procedures. The Kaplan–Meier estimates of the Nissen and Toupet methods with respect to recurrence are shown. No marked differences were observed between the procedures ($p=0.555$)

introduction of laparoscopic Nissen fundoplication in 1991 by Dallemagne et al. [13], laparoscopic fundoplication spreads instantly; the procedures that are currently carried out include the Nissen method, which is a circumferential fundoplication, and the Toupet method, which is a non-circumferential posterior fundoplication [1–4].

Both the Nissen and Toupet method are performed in Japan, but there is no consensus opinion regarding the indications for each procedure. The Nissen method was mainly performed at our institute when laparoscopic fundoplication was first introduced, due to the need for calibration of the esophagus by inserting an esophagus bougie during cardioplasty and the relative difficulty of suturing upon esophagus bougie insertion. In recent years, however, the Toupet method is mainly selected. Reports comparing the Nissen and Toupet methods have mainly evaluated the results of procedures performed in Western countries, with very few reports concerning Japan. For this reason, we conducted the present study [14].

In our study, we matched patient background characteristics as much as possible using the propensity score matching method; however, the esophageal acid reflux time was not matched, because this would have led to a decline in the number of subjects. As a result, the acid reflux time was lower in the Toupet group. The evaluation of acid reflux was carried out mainly using a Digitrapper MK-II or MK-III in the Nissen group, while many cases were evaluated by a Sleuth device in the Toupet group; therefore, the effect

of the evaluation modality should be considered when comparing the differences in acid reflux time. Han et al. used the MII-pH method and Bravo® System (Wireless pH monitoring) to investigate the difference in the acid reflux time by modality in 66 patients with GERD; they found that the acid reflux time was 0.85% using the MII-pH method, versus 7% on the first day and 8.4% on the second day using the Bravo® System [15]. Hila et al. reported that the acid reflux time was 2.7 and 5.8%, respectively, on comparing the findings with the MII-pH method and absolute pH monitoring in 60 patients with GERD [16]. Taken together, these previous findings suggest that there is a higher chance of the acid reflux time being reduced with the MII-pH method than with the conventional pH monitoring. It may, therefore, be surmised that our outcome was due to using this modality.

Regarding the therapeutic outcomes of the Nissen and Toupet methods, Shaw et al. conducted an RCT comparing the two methods in 50 cases and reported that there was no marked difference in the backflow prevention effect or postoperative difficulty in swallowing between the two groups and that the presence of dysmotility prior to surgery did not affect the outcome [3]. Mickevičius et al. conducted a similar report [17]. Qin et al. reported that the incidence of dysphagia in the short term was significantly lower after Toupet fundoplication than after that using the Nissen method, but the difference decreased significantly with extension of the postoperative recovery period [18]. Zornig et al. carried out a prospective comparison between four groups with respect to the differences in the Nissen and Toupet methods according to the presence of preoperative esophageal motility disorder and reported that while preoperative esophageal motility disorder did not affect the rate of postoperative difficulty in swallowing, the rate was significantly higher in the Nissen group than in the Toupet group [1]. Furthermore, according to the outcome of a meta-analysis, while no marked difference in the backflow prevention effect was observed, the incidence of postoperative difficulty in swallowing was higher in the Nissen group than in the Toupet group.

Varin et al. extracted 11 RCTs comparing the Nissen and Toupet methods, and their meta-analysis of their findings showed that difficulty in swallowing in the Nissen group had an odds ratio of 1.82–3.93 ($p < 0.001$), and gas-bloating had an odds ratio of 1.07–2.56 ($p = 0.02$), both of which were higher than in the Toupet group [5]. In addition, Tian et al. also carried out a meta-analysis of 13 RCTs comparing the Nissen method (814 cases) and the Toupet method (750 cases) and reported that the rate of repeat surgery accompanying gas-bloating and difficulty swallowing was higher with the Nissen method than with the Toupet method [6]. Although the follow-up period differed between the procedures, there was no marked difference in

the recurrence rate in the present study. However, we did observe a higher incidence of postoperative difficulty in swallowing in the Nissen group than in the Toupet group, which was the same as reported in the previous meta-analyses consisting largely of reports from Western countries.

Granderath et al. reported the outcomes of 33 cases that underwent surgery, reporting that the time from initial surgery to repeat surgery was 3.1 years [19]. Similarly, Iqbal et al. reported that the time until repeat surgery in 104 cases was 38 months [20]. These findings suggest that most postoperative recurrence occurs within 3 years following surgery. In the present study, the time until recurrence was 35 months—almost 3 years. The postoperative follow-up period was 22 months in the Toupet group, which was shorter than in the Nissen group. However, the Toupet group included only two cases of recurrence compared to five in the Nissen group, and it is difficult to believe that the recurrence rate in the Toupet group would become significantly higher than in the Nissen group over a median follow-up period of 3 years.

Several limitations associated with the present study warrant mention. First, it was not a prospective comparison study, and the number of cases was small compared to the previous studies in Western countries. Second, the postoperative follow-up period for the Toupet group was shorter than that for the Nissen group. However, this is the first report in Japan that reduced potential bias as much as possible by carrying out propensity score matching. In addition, according to a recent report on GERD-related diseases from 2009 to 2013 in Japan, the average number of such surgeries in Japan was only 185 annually; as such, the present study is actually an investigation of a relatively large number of cases and should, therefore, be considered a significant addition to our current knowledge [21].

Conclusions

In our comparison of the Nissen and Toupet methods for treating GERD-related diseases with a propensity score matching analysis among Japanese patients, the efficiency of both procedures was 90% or more, with no marked differences in the recurrence rate. In addition, both were good in terms of their backflow prevention effect, although the incidence of postoperative difficulty in swallowing was significantly lower in the Toupet group than in the Nissen group.

Compliance with ethical standards

Conflict of interest Drs. Masato Hoshino, Nobuo Omura, Fumiaki Yano, Kazuto Tsuboi, Se Ryung Yamamoto, Shunsuke Akimoto, Norio Mitsumori, Hideyuki Kashiwagi, and Katsuhiko Yanaga have no conflicts of interest or financial ties to disclose.

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