
Surgical Treatment for Gastroesophageal Reflux Disease (GERD) in Asia

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Sally Wai Yin Luk and Philip W.Y. Chiu

Abstract

The incidence of gastroesophageal reflux disease (GERD) is increasing in Asia. The majority of the patients are treated by long-term usage of proton pump inhibitors (PPI). Anti-reflux surgery had been considered as an equivalent alternative to long-term PPI. However, few studies have investigated the performance of anti-reflux surgery for the treatment of GERD in Asia. In this chapter, we review the current evidence and application of anti-reflux surgery for the treatment of GERD in Asia.

Keywords

Gastroesophageal reflux disease • Anti-reflux surgery • Laparoscopic fundoplication

Introduction

Gastroesophageal reflux disease (GERD) is a disorder in which duodenogastric contents reflux recurrently into the esophagus, causing troublesome symptoms and/or complications [1, 2]. From the surgical perspective, this is the failure of the anti-reflux flap valve mechanism at the esophagogastric junction (OGJ) that allows the

S.W.Y. Luk • P.W.Y. Chiu (✉)

Division of Upper GI and Metabolic Surgery, Department of Surgery, Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong SAR, China

e-mail: philipchiu@surgery.cuhk.edu.hk

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backflow of gastric contents into the esophagus [3]. The symptoms are considered to be troublesome when they adversely affect one's quality of life (QOL) [1].

While GERD has long been a public concern in the West [4], this is an emerging disease entity in Asian countries over the past two decades. According to population-based studies, prevalence of GERD in East Asia ranges from 2.5 to 7.8% [5], and, interestingly, it is much higher in West Asia, with reported prevalence up to 50% [6, 7]. It is estimated that GERD affects up to 5% of the Chinese population [8]. In Singapore, a population survey found more than a sixfold increase in reporting reflux symptoms in a cohort of 237 community residents, rising from 1.6% to 9.9% from 1994 to 1999 [9].

Another study from a Japanese center reported that prevalence of reflux esophagitis on endoscopic examination has increased from 0.8% in 1975 to 2.3% in 1997 [10]. The apparent rising trend could partly be due to the low awareness of the disease in the past, together with an aging population [11]. Apart from racial difference, Asians share similar risk factors for GERD as Caucasians do, including age, male sex, smoking, increasing BMI, family history, and higher socioeconomic status [11, 12]. The Westernization of lifestyle and worldwide epidemic of obesity could be the attributing factors for the increasing prevalence. [11] As a result, there is a need for more comprehensive management of GERD in the Asia-Pacific region.

Asia-Pacific consensus on the management of GERD was first published in 2004 and updated in 2008 [13, 14]. However, there is still a paucity of literature on the indications and the type of anti-reflux surgery (ARS) performed in the Asian population. In this chapter, we will overview challenges in the management of GERD, in particular the role of surgical intervention, in Asian countries.

Diagnostic Challenges

GERD has a spectrum of clinical presentations, encompassing at least three broad groups of patients presenting with: (a) typical reflux symptoms, including heartburn and/or acid reflux, but without reflux esophagitis, so-called nonerosive reflux disease (NERD); (b) atypical reflux symptoms; (c) erosive esophagitis, i.e., erosive reflux disease (ERD), with or without complications. The expression of heartburn is less clear in most of the Asian languages, leading to difficulty in making a correct clinical diagnosis, which often overlaps with symptoms of dyspepsia [15]. Moreover, it is not uncommon for Asian patients to have atypical manifestations, such as non-cardiac chest pain, as the sole presenting feature of GERD [16–18]. It is the clinicians' responsibility to clarify the terms, together with the awareness of the diagnosis, in the context of atypical symptoms. The 24-h ambulatory pH study is currently regarded as the most objective investigation to establish the diagnosis of GERD. In the Western literature, the determination of excessive acid exposure would depend on esophageal acid exposure time (percentage of pH < 4 at 5 cm from LES) of more than 5%, or a composite score >14.72 according to the revised Johnson-DeMeester score [19]. However, these criteria for excessive acid exposure have not been validated in the Asian population. Furthermore, owing to the

relatively low prevalence of GERD in Asia, 24-h pH tests are usually limited to tertiary referral centers [14, 18].

It has been reported that up to 30% of patients with NERD have normal esophageal acid exposure time upon 24-h pH study [20, 21]. The exact pathophysiology in this subgroup is not well understood, yet the plausible visceral hypersensitivity to acid may play a role in causing symptoms [22].

Upper endoscopy has low sensitivity as an objective diagnostic tool, as a majority of Asian patients do not have reflux esophagitis, not to mention the presence of its associated complications such as peptic stricture or Barrett's esophagus [23]. In a study from Hong Kong, only 631 out of 16,606 patients had endoscopic evidence of esophagitis; 14 of those had stricture, and 10 had Barrett's esophagus [24]. Interestingly, the endoscopic definition of esophagogastric junction in Japan is according to distal end of esophageal palisade vessels instead of proximal extent of the gastric fold [25]. Coupled with the high performance of endoscopy in Japan, these may account for more prevalence of Barrett's esophagus among Japanese than in other Asian countries. Nonetheless, most published data in the literature has revealed the low prevalence of Barrett's esophagus in Asia ranging from 0.06 to 0.22% [26, 27]. With the high prevalence of *Helicobacter pylori* (*H. pylori*) in Asia, esophagogastroscopy is usually performed to rule out peptic ulcer disease and gastric cancer before embarking on management of GERD [14, 28, 29].

Challenges in Surgical Management

Most patients in Asia with GERD can be symptomatically controlled by proton pump inhibitors (PPI) [30, 31]. This is partly due to the smaller parietal cell mass in Asians and a high prevalence of *H. pylori* infection [32]. However, PPI only alleviates GERD symptoms, without tackling the underlying mechanical problem. The anti-reflux flap valve created after fundoplication aims at restoring the LES pressure. Moreover, anti-reflux surgery (ARS) abolished the trigger to transient lower esophageal sphincter relaxations (TLESRs) [33]. The recent concern regarding the long-term effect of PPIs in inducing osteoporotic fracture, infection, and altering pharmacokinetics of concomitant drugs like clopidogrel further enhances the role of surgery in managing GERD [34].

Indications for surgical intervention in Asia should follow international guidelines when the diagnosis of GERD is confirmed with objective evidence. These include those who (1) opt for surgery despite successful medical management, or (2) failed medical treatment, or (3) have complication of GERD, e.g., Barrett's esophagus and peptic strictures [35]. As response to PPI therapy tends to be better in Asian countries, few patients are referred for consideration of ARS. In our center, more than 80% of patients who underwent ARS were those who opted not for life-long medication, while only 6% were having erosive esophagitis or Barrett's esophagus. As the average age for GERD occurrence ranged from 30 to 50 years, lifelong medication will pose a major impact on their quality of life and a significant burden of the medication cost.

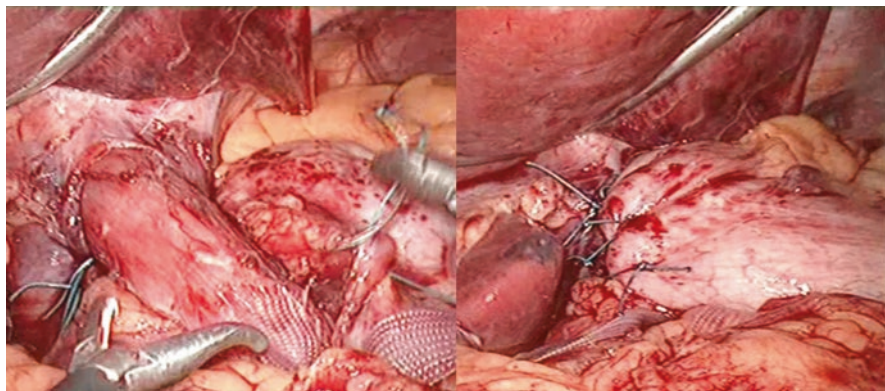
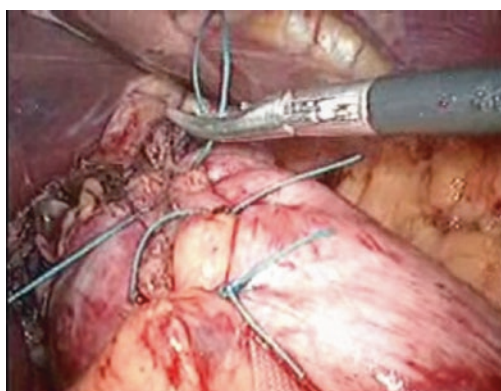


Fig. 9.1 Laparoscopic anterior partial fundoplication

Fig. 9.2 Laparoscopic Nissen fundoplication



Since the introduction of anti-reflux surgery by Dr. Rudolf Nissen in 1954, fundoplication has become widely adopted as an alternative surgical treatment for GERD in the Caucasian population [36]. There has been development of different types of fundoplication, including Nissen 360 degree fundoplication and anterior and posterior partial fundoplication (Figs. 9.1 and 9.2). Up to the early 1990s, there were more than 12,000 open operations performed. With the advent of the first laparoscopic fundoplication by Dallemagne et al. in 1991 [37], the awareness of surgical treatment for GERD began to increase in Asia. The first report of laparoscopic fundoplication in an adult from Korea was published in 1996 [38]. In Hong Kong, our unit has performed laparoscopic anti-reflux procedures since the early 2000s. Subsequently, there were case series published from Japan, Korea, Malaysia, and India reporting the early surgical outcomes of the laparoscopic fundoplication in their countries [39–41].

Compared to Western countries, the development and performance of ARS have lagged behind in Asia due to low prevalence of GERD, surgical invasiveness compared to PPI, as well as patients' preference to medical therapy. Two meta-analyses

published comparing clinical and perioperative outcomes of open versus laparoscopic ARS showed that laparoscopic ARS is associated with significant shorter hospital stay, with earlier return to normal activities, and less morbidity [42–44]. All the cohort studies from Asia had been using laparoscopic ARS (LARS) with 0% conversion rate, despite the fact that most Asian surgeons have limited experience in the open approach.

A recent randomized control trial from China by Cao et al. compared laparoscopic anterior 180-degree (LAF) versus Nissen fundoplication (LNF) [45]. This is the only clinical trial from Asia included in the meta-analysis comparing LAF versus LNF. This study included a select group of patient with erosive GERD and high DeMeester score. There were significantly fewer patients in the LAF group with dysphagia and gas-related symptoms at 5 years, which was consistent with the meta-analysis results. In general, there is a tendency favor toward LAF worldwide, including the Asia-Pacific region. On the other hand, there are still debates on some of the technical aspects that may influence surgical outcomes in the West; these include the division of short gastric vessels, crural repair, and the use of bougie to gauge the warp [46]. Division of short gastric vessels is usually recommended for the formation of short floppy Nissen fundoplication, and these vessels were preserved in anterior partial fundoplication. Though intraoperative placement of bougie is essential to prevent postoperative dysphagia, non-forceful insertion under direct vision with laparoscopy is essential to prevent perforation. Compared to studies in the West, where 56–58-Fr bougies were commonly used, the size of bougie is usually smaller for Asian patients, ranging from 46 to 50 Fr.

Surgical Outcome in Asia-Pacific Region

From the reported Asian case series in the literature, the early postoperative recovery was satisfactory. Most patients could start to have an oral fluid diet immediately after the operation and resume a soft diet on postoperative day 2. In our center, the mean hospital length of stays is 3.6 ± 1.5 days. Early postoperative complications ranged from 4 to 16% [39–44]. Major complications reported were esophageal perforation associated with the bougie insertion [44] and gastric perforation [39]. Most patients experienced some sort of side effect during the early postoperative period. These symptoms were temporary dysphagia, bloating, and increased flatulence, which would often improve with time. Temporary transient postoperative dysphagia was common, ranging from 35 to 40%. Persistent dysphagia requiring endoscopic dilatation was 9–16%, and the dysphagia rate was higher after Nissen fundoplication than partial.

Owing to the short-term follow-up of the case series, there was a paucity of reports concerning the long-term surgical outcomes, and most of the reports in the literature were retrospective cohorts. The only published prospective 5-year surgical outcome in Asia was from China by Cao et al. [44]. According to their results, at 5 years the dysphagia score was significantly higher in LNF than LAF. The results of our center were consistent with this randomized study, with more patients

Table 9.1 Clinical outcomes of a retrospective comparison between laparoscopic Nissen fundoplication versus partial fundoplication at the Chinese University of Hong Kong

	LNF (39)	LPF (18)	P
Age	45.5	49.8	0.114
Gender (male:female)	25:14	13:5	
No of comorbidities	0.69	0.39	0.165
Esophagitis upon preoperative endoscopy	17 (43.6%)	11 (61.1%)	0.263
DeMeester score (preoperative)	21.1	39.6	0.07
Operative time (minutes)	129.8	152.7	0.114
Conversion	0	0	–
Hospital stay (days)	3.49	3.06	0.227
Reoperation	3 (7.7%)	1 (5.6%)	0.625
Recurrence of GERD	4 (10.5%)	5 (27.8%)	0.107
Dysphagia 4 weeks after surgery	11 (28.9%)	2 (11.1%)	0.126

LNF laparoscopic Nissen fundoplication; *LPF* laparoscopic partial fundoplication

developing dysphagia at the initial postoperative period after LNF. Out of the 60 patients who received LNF, 5 required endoscopic dilatation and subsequent redo fundoplication, while none of those after LAF developed persistent dysphagia.

Most studies defined recurrence of gastroesophageal reflux as need of redo fundoplication surgery or requirement of maintenance PPI. Recurrence of GERD 20–30 years was reported as 20–30% after open fundoplication, while recurrence at 5 years was around 5–15% for laparoscopic fundoplication [42]. The cause of recurrence was attributed to wrap disruption or migration. Cao et al. showed recurrence of GERD at 5 years was 15.63% (15 out of 96 patients, 8 in LAF, and 7 in LNF arms). Seven of them have undergone revision fundoplication, and GERD recurrence was confirmed with objective assessments including endoscopic examination and pH studies. Hence, laparoscopic fundoplication can achieve good reflux control among Chinese patients with erosive esophagitis. To note, the recurrence of reflux symptoms in Asian patients postoperatively needs particular attention, as this might not solely be caused by the recurrence of GERD. Owing to the high prevalence of *H. pylori* and risk of gastric cancer, further investigation including upper endoscopy is necessary prior to the prescription of maintenance PPI.

Our center conducted a retrospective comparison on the outcomes between laparoscopic Nissen fundoplication versus laparoscopic partial fundoplication in 57 patients in Hong Kong. There was no difference in the mean age and gender distribution between the two groups (Table 9.1). More than half of the patients who received fundoplication had endoscopic evidence of esophagitis (LNF group, 43.6%; LPF group, 61.1%; $p = 0.263$). There was no difference in the operative time between LNF and LPF. A total of four patients required reoperation, three in the LNF group and one in the LPF group. The reasons for reoperation in the LNF group were related to symptoms of dysphagia, while the reason for reoperation in the LPF group was due to recurrence of GERD. The overall rate of symptomatic control after laparoscopic fundoplication was 84.2%. There was a trend toward higher risks

of symptom recurrence for laparoscopic partial fundoplication when compared to laparoscopic Nissen fundoplication, though not statistically significant.

Learning Curve and Training in Asian Countries

With the standardization of surgical techniques for LNF in Western countries [47], the acquisition of the skills becomes generally easier to follow for Asian surgeons who have limited experience in open fundoplication. Commonly, LNF is performed with the patient in lithotomy position and five-port technique—including two 10 mm ports and three 5 mm ports with one of them tailored for liver retraction. The learning curve was well documented in the literature, reporting increased failure rates, complications, reoperations, operative time, and hospital length of stay for less experienced surgeons [48–50]. Interestingly, the learning curve for laparoscopic fundoplication is comparable to the West. In the era of minimal invasive surgery, laparoscopic techniques could be acquired without the prerequisite of open experience. Furthermore, under the laparoscopic view, the individual's anatomy is magnified, and details are more clearly demonstrated than in the open approach. In our center, the mean operative time for the first 10 LNF was 150 min, with gradual improvement to 90 min after 50 procedures. Over the past 20 years, the experience of LNF is getting mature rapidly within the Asia-Pacific region, and there is a trend toward laparoscopic partial fundoplication [51]. According to the international guidelines, it is recommended that young upper gastrointestinal surgeons have proctorship during their first 15–20 laparoscopic fundoplications [49].

Conclusion

It is now recognized that GERD is an emerging disease entity in Asia. It is foreseeable that the number of patients suffering from the disease will continue to increase in the Asia-Pacific region, and this poses a significant burden to the healthcare system. The particular diagnostic challenges could be overcome by means of improving awareness of the disease. It might be prudent to have regional validation for the use of the DeMeester score and symptom index, as the disease severity tends to be less with nonerosive GERD, yet patients' QOL are affected.

The majority of GERD patients are relatively young, and long-term acid suppressive therapy is usually required for symptomatic control. With the advancement in laparoscopic surgery, anti-reflux procedures become less invasive, with low perioperative morbidity and without mortality. Laparoscopic fundoplication, either complete or partial wrap, has become the alternative gold-standard treatment to medical therapy. More and more Asian gastrointestinal surgeons are competent in ARS, leading to an increasing tendency to offer this to patients, with higher acceptance. Although Asian countries have limited experience when compared to the Western countries, the overall surgical results from the East are encouraging. Training opportunities of the young surgeons are of paramount importance to meet the increasing

need. Asia-Pacific consensus and recommendations concerning the surgical management of reflux disease are warranted to improve the overall surgical outcomes and patients' quality of life in the long run.

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