

## Special Article



# Evidence-Based Practice Guideline for Surgical Treatment of Gastroesophageal Reflux Disease 2018

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## ABSTRACT

The prevalence of gastroesophageal reflux disease (GERD) is increasing in Korea, and physicians, including surgeons, have been focusing on its treatment. Indeed, in Korea, medical treatment using a proton pump inhibitor is the mainstream treatment for GERD, while awareness of surgical treatment is limited. Accordingly, to promote the understanding of surgical treatment for GERD, the Korean Anti-Reflux Surgery Study Group published the Evidence-Based Practice Guideline for the Surgical Treatment of GERD. The guideline consists of 2 sections: fundamental information such as the definition, symptoms, and diagnostic tools of GERD and a recommendation statement about its surgical treatment. The recommendations presented 5 debates regarding fundoplication: 1) comparison of the effectiveness of medical and surgical treatments, 2) effectiveness of surgical treatment in cases of refractory GERD, 3) effectiveness of surgical treatment of extraesophageal symptoms, 4) comparison of effectiveness between total and partial fundoplication, and 5) effectiveness of fundoplication in cases of hiatal hernia. The present guideline is the first to demonstrate the efficacy of the surgical treatment GERD in Korea.

**Keywords:** Fundoplication; Gastroesophageal reflux; Guideline; Systematic review; Treatment

## INTRODUCTION

### Background

Gastroesophageal reflux disease (GERD) is one of the most common benign diseases of the upper gastrointestinal tract [1-3]. The prevalence of GERD reached 7.3% in 2008, with a mean annual increase of 15.3% in Korea [4]. In Western countries, GERD is typically treated with a proton pump inhibitor (PPI) and fundoplication [5-11]. Despite numerous studies reporting the effectiveness of surgical treatment, medication-oriented treatment remains the mainstay

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#### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

because of a lack of awareness of surgical treatment in Korea. Although there are several guidelines for GERD worldwide, the surgical treatment of GERD in Korea has never been reported [5,6,12]. The only 2 guidelines for treating GERD in Korea did not focus on surgical treatment [13,14]. Therefore, the first Korean guideline for GERD was established to provide clear criteria for surgical treatment.

#### Scope

The present clinical practice guideline is based on the published literature and expert opinions when evidence is lacking. This guideline is specific and comprehensive for the surgical treatment of GERD; however, it does not address issues related to prevention, medical treatment, and postoperative follow-up.

This guideline is intended to help physicians and surgeons as well as endoscopists and radiologists making the diagnosis. It was also designed to allow patients and populations to provide medical information.

## METHODS

### Constitution of the project groups and review panels

The present guideline was initiated by the Korean Anti-Reflux Surgery (KARS) Study Group. Experts participated in the guideline development methodology (National Evidence-Based Healthcare Collaborating Agency). To develop this guideline, the KARS Study Group organized the guideline committee, which established the project working groups and review panels.

### Literature review method

A systematic literature search was performed of MEDLINE, EMBASE, and the Cochrane Library for articles published on or before February 2, 2018. Hand-searching was also performed to complement the results. Relevant studies were searched by pairs of clinical experts. Inclusion and exclusion criteria were predefined and tailored to key questions. Articles were screened by title and abstract and the full text was retrieved for review. Two reviewers performed each step and consensus was reached.

We critically appraised the quality of the selected studies using risk of bias tools. We used the Cochrane Risk of Bias for randomized controlled trials (RCTs) [15], risk of bias for nonrandomized studies for non-RCTs [16], quality assessment of diagnostic accuracy studies-2 for diagnostic studies [17], and a measurement tool to assess systematic reviews for systematic reviews/meta-analyses [18]. The panels independently assessed the studies and consensus was reached. Disagreements were resolved by discussion and a third reviewer.

We extracted the data using a pre-defined format and synthesized it qualitatively. Evidence tables were created according to key questions.

### Levels of evidence

Levels of evidence and grading of recommendations were modified based on Scottish Intercollegiate Guidelines Network [19] and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methods [20]. Level of evidence was classified as 4 levels; the main factors were study design and quality (Table 1). We also considered outcome consistency.

**Table 1.** Level of evidence

Class	Explanation
High	At least 1 RCT or SR/meta-analysis with no concerns of study quality
Moderate	At least 1 RCT or SR/meta-analysis with minor concerns of study quality or at least 1 cohort/case-control/diagnostic test design study with no concerns of study quality
Low	At least 1 cohort/case-control/diagnostic test study with minor concerns of study quality or at least 1 single arm before-after study, cross-sectional study with no concerns of study quality
Very low	At least 1 cohort/case-control/diagnostic test design study with serious concerns of study quality or at least 1 single arm before-after study, cross-sectional study with minor/severe concerns of study quality

RCT = randomized controlled trial; SR = systematic review.

**Table 2.** Grading of recommendations

Grade classification	Explanation
Strong for	The benefit of intervention is greater than the harm with a high or moderate level of evidence that can be strongly recommended in most clinical practices.
Weak for	The benefit and harm of the intervention may vary depending on the clinical situation or patient/social value. It is recommended conditionally according to the clinical situation.
Weak against	The benefit and harm of intervention may vary depending on the clinical situation or patient/social value. The intervention may not be recommended in clinical practice.
Strong against	The harm of intervention is greater than the benefit with a high or moderate level of evidence. The intervention should not be recommended in clinical practice.
No recommendation	It is impossible to determine the recommended direction owing to a lack of evidence or discrepancy in results. Thus, further evidence is needed.

Recommendation grades were classified into 5 levels using modified GRADE methodology: strong for, weak for, weak against, strong against, and no recommendation (**Table 2**). We considered evidence level, clinical applicability, benefit, and harm as recommendation factors. A committee reviewed the draft of the working group then discussed the grades until consensus was reached.

## RESULTS

### Definition

GERD is defined as the stomach contents refluxing into the esophagus and causing uncomfortable symptoms and complications with or without an esophageal mucosal break [21-24]. According to the Montreal Consensus, “GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications” [25]. Complications include esophagitis, asthma due to reflux, aspiration pneumonia, and laryngitis [26-28]. From the surgical point of view, GERD is mainly caused by the failure of anti-reflux barriers such as a defective lower esophagus sphincter (LES), a gastric emptying disorder, or failed esophageal peristalsis [29].

### Symptoms

Symptoms of GERD vary widely; esophageal symptoms such as heartburn and regurgitation are the most characteristic features, while gastrointestinal symptoms such as dyspepsia, epigastric pain, and somatoform disorder may also occur [30-43]. Extraesophageal symptoms include cough, hoarseness, globus, and shortness of breath, and they may be associated with reflux cough syndrome, reflux laryngitis syndrome, reflux asthma syndrome, and reflux dental erosion syndrome [28,44-52].

## Diagnosis and preoperative evaluation

An objective diagnosis of GERD before surgery is essential [53-55]. The purpose of the preoperative examination is to select patients who will benefit from surgical treatment. Controversy persists about the type and order of preoperative examinations [56-58].

### *Esophagogastroduodenoscopy (EGD)*

EGD is the most important diagnostic tool for confirming the diagnosis of GERD. The identification of Barrett's esophagus, mucosal breaks such as esophagitis, hiatal hernia, and biopsies to rule out of malignancy are allowed by EGD [59-65].

### *24-hour pH monitoring*

Another important diagnostic tool is 24-hour pH monitoring [66-68]. Due to the lack of evidence of GERD in EGD, 24-hour pH monitoring is required to distinguish between acid reflux and non-acid reflux [55,69,70]. It is also an important predictive factor of prognosis after surgical treatment [71,72]. This examination should be performed by interrupting the PPI or antisecretory agent [73]. Impedance pH monitoring, which has multiple channels for detecting acid reflux in the esophagus, was recently introduced [74]. However, the benefits of impedance pH monitoring compared with conventional 24-hour pH monitoring is controversial [73,75].

### *Esophageal manometry*

Esophageal manometry is not as important as EGD or pH monitoring, but it can provide important information for the diagnosis of LES [76-78]. Although there is little evidence of the preoperative necessity for esophageal manometry, it is important to identify otorhinolaryngologic problems and esophageal motility disorders including achalasia [79,80].

### *Barium swallow test*

The barium swallow test is less important than other tests but has the advantage of revealing the anatomical structure. Its use may be helpful in cases of a shortened esophagus due to a large hiatal hernia [5].

### *Further diagnostic tools*

Further diagnostic tools such as high-resolution manometry, planimetry, and scintigraphy have been introduced recently, but substantive evidence to support them is lacking [81-86].

## Operation indication and efficacy

*Medical versus surgical treatment: Is anti-reflux surgery more effective than PPI for treating GERD? (KQ1)*

Statement 1. Anti-reflux surgery is recommended to patients with GERD for its symptomatic relief, ability to increase quality of life, superior long-term outcomes, and cost-effectiveness. (level of evidence: high, strength of recommendation: strong for)

Anti-reflux surgery is considered an effective treatment option for GERD and is widely performed in Western countries. Many clinical trials comparing anti-reflux surgery and PPI for GERD were conducted, and these trials found anti-reflux surgery as effective as or more effective than PPI at controlling GERD symptoms over a follow-up period of 5 years [87-96]. In addition, several studies among them demonstrated that anti-reflux surgery was likely to be cost-effective compared to medical treatment [90,92,94]. From mid 2000s, clinical trials

of laparoscopic anti-reflux surgery versus PPI have reported similar outcomes to those of the open approach [90,91,93-95,97,98].

A prospective randomized open parallel-group multicenter trial comparing the efficacy and safety of laparoscopic anti-reflux surgery with that of esomeprazole 20 or 40 mg/d over 5 years in patients with chronic GERD recently demonstrated that esophageal acid exposure was significantly reduced in the laparoscopic anti-reflux surgery group (n=116) compared with the PPI group (n=151) (baseline, 8.6% vs. 8.8%; after 6 months, 0.7% vs. 2.1%;  $P<0.001$ ; after 5 years, 0.7% vs. 1.9%;  $P<0.001$ ) [95]. In terms of cost efficacy of anti-reflux surgery, 1 study recently compared the cost-effectiveness of laparoscopic surgery (n=155) and medical management (n=104) using the data of a randomized multicenter trial (REFLUX). The results indicated that laparoscopic anti-reflux surgery is cost-effective provided that its clinical benefits are sustained in the medium to long-term [92]. Thus, anti-reflux surgery is an excellent treatment option with a better long-term effect and cost-effectiveness compared to PPI. In GERD patients, laparoscopic anti-reflux surgery is strongly recommended.

*Surgical treatment for refractory GERD: Is anti-reflux surgery more effective than PPI for treating refractory GERD? (KQ2)*

Statement 2. Anti-reflux surgery could be considered for a substantial proportion of patients showing an inadequate response to PPI therapy. Thorough examinations for the differential diagnosis and careful patient selection should be performed in those patients prior to the anti-reflux surgery. (level of evidence: moderate, strength of recommendation: weak for)

Surgery for GERD has been proven effective over long-term follow-up [87], but a concern remains about its indications for surgery to include patients who respond poorly to medical therapy. However, a few studies showed that patients with a poor response to PPI treatment can have good surgical outcomes [99-109].

Anvari and Allen [99] first showed that poor responders showed significant improvement in postoperative symptom scores and quality-of-life scores associated with significant reductions in lower esophageal acid exposure when anti-reflux surgery was performed in a specialized center on appropriately selected patients. Wilkerson et al. [100] also demonstrated a significant decrease in postoperative symptom scores in both good and poor responders; however, the poor responders tended to show a lower percentage of excellent or good surgical outcomes (Visick I or II: 94% vs. 87%, respectively;  $P=0.08$ ). In a recent prospective study, PPI responders and non-responders showed comparable anatomical and functional improvements, but PPI responders reported significant relief of both typical and atypical symptoms than PPI non-responders (heartburn: 93% vs. 73%,  $P=0.01$ ; regurgitation: 96% vs. 84%,  $P=0.04$ ; atypical symptoms (asthma/chest pain/cough): 96.6% vs. 83.9%,  $P=0.002$ ) [108].

*Surgical treatment for extraesophageal symptoms: Is anti-reflux surgery more effective than PPI for controlling extraesophageal symptoms? (KQ3)*

Statement 3. Anti-reflux surgery is recommended for gastroesophageal reflux patients with extraesophageal manifestations. (level of evidence: moderate, strength of recommendation: strong for)

GERD typically manifests as heartburn and regurgitation, but it can also present as extraesophageal manifestations such as asthma, chronic cough, laryngitis, hoarseness, and chronic sore throat. Despite a lack of well-designed RCTs in this area, some studies have shown that extraesophageal manifestations can be effectively managed by anti-reflux surgery. In incomplete clinical responses to medication, anti-reflux surgery augments the treatment of laryngopharyngeal reflux (LPR) in terms of the reflux symptom index (RSI) score, reflux finding score, and reflux-based specific quality of life scale [110]. Three years of follow-up after anti-reflux surgery showed that it effectively relieved the symptoms of LPR in selected populations. Benefits are seen within 1 month of surgery and persist for at least 3 years [111]. Long-term follow-up data (median follow-up, 91 months) have shown that 61% of patients reported no or mild reflux laryngitis symptoms postoperatively and that 69% of the patients evaluated their voice quality as improved after surgery. The majority of reflux laryngitis patients achieve long-term symptomatic benefit and satisfaction after surgery [112].

Comparing the 25 patients in the anti-reflux surgery group and 28 patients in the PPI group with extraesophageal manifestations, improvements in RSI score ( $P < 0.005$ ) and symptom scores of cough ( $P = 0.032$ ), mucus ( $P = 0.011$ ), and throat clearing ( $P = 0.022$ ) were significantly superior in the surgery group to those in the PPI group [9]. A systemic review and meta-analysis pooled data from 21 reports and reported GERD-related chronic laryngitis patients. The objective response rates were 80% for anti-reflux surgery (95% confidence interval [CI], 67%–93%; 3 studies, 123 patients) versus 64% for anti-reflux medicine (95% CI, 50%–77%; 18 studies, 2,741 patients). There was an increase in the effect among patients treated with surgery [113].

### Surgical technique

*Total versus partial fundoplication: Is partial fundoplication more effective than total fundoplication for treating GERD? (KQ4)*

Statement 4. Partial fundoplication and total fundoplication are comparably effective at treating GERD.  
(level of evidence: high, strength of recommendation: weak for)

The surgical treatment of choice for GERD is total or partial fundoplication [114]. Many studies that compared total and partial fundoplication for GERD proved the effects and side effects of both procedures [114-120]

A meta-analysis of 5 RCTs compared partial ( $n = 227$ ) and total ( $n = 231$ ) fundoplication and reported that esophageal acid exposure (standardized mean difference [SMD], 0.19;  $P = 0.15$ ), esophagitis (19% vs. 13%,  $P = 0.34$ ), heartburn score (SMD, 1.27,  $P = 0.13$ ), dilatation rate (1.4% vs. 2.8%,  $P = 0.39$ ), reoperation rate (5.7% vs. 2.8%,  $P = 0.13$ ), perioperative outcome, regurgitation, PPI use, lower esophageal sphincter pressure, and patient satisfaction with partial fundoplication were similar to that of total fundoplication at 1 year after surgery. In addition, the Dakkak dysphagia score (2.8 vs. 4.8, weighted mean difference:  $-2.25$ ,  $P < 0.001$ ), gas and bloating (11% vs. 18%,  $P = 0.04$ ), flatulence (14% vs. 25%,  $P = 0.02$ ), inability to belch (19% vs. 31%,  $P = 0.05$ ), and relief of bloating (34% vs. 44%,  $P = 0.04$ ) were lower after partial fundoplication. At 5 years post-surgery, the Dakkak dysphagia score, flatulence, inability to belch, and inability to relieve bloating were still lower after partial fundoplication, while heartburn score, dilatation rate, reoperation rate, PPI use, and patient satisfaction rates were similar [116].



A meta-analysis of 7 RCTs that compared anterior (n=345) and posterior (n=338) fundoplication reported that esophageal acid exposure (3.3% vs. 0.8%,  $P<0.001$ ), heartburn (21% vs. 8%,  $P<0.001$ ), and reoperation rate (8% vs. 4%,  $P=0.06$ ) were higher after anterior fundoplication in the short term. On the other hand, the Dakkak dysphagia score (2.5 vs. 5.7,  $P<0.001$ ) was lower after anterior fundoplication. Esophagitis, regurgitation, and perioperative outcomes were similar. In the long-term, heartburn (31% vs. 14%,  $P<0.001$ ), PPI use (25% vs. 10%,  $P=0.002$ ), and reoperation (10% vs. 5%,  $P=0.03$ ) rates were higher after anterior fundoplication, while the Dakkak dysphagia score and the inability to belch, gas and bloating, and patient satisfaction rates were similar [118].

### Hiatal hernia

*Fundoplication in hiatal hernia: Is fundoplication necessary for paraesophageal hernia (PEH)? (KQ5)*

Statement 5. Fundoplication in addition to PEH repair is recommended to decrease the risk of postoperative gastroesophageal reflux and esophagitis. (level of evidence: high, strength of recommendation: strong for)

PEH is defined as a defect in the diaphragmatic hiatus that can cause significant sequelae. For many years, the need for fundoplication at the time of laparoscopic repair of PEH has been controversial.

Some authors argue that postoperative gastroesophageal reflux is uncommon in patients without fundoplication. The risk of postoperative dysphagia can be reduced by not performing fundoplication [121,122]. In practice, however, most surgeons tend to perform fundoplication at the time of PEH repair [123,124]. Fundoplication can minimize the possibility of postoperative gastroesophageal reflux caused by disruption of the hiatus. In particular, some data support that fundoplication may anchor the cardia below the diaphragm, thereby decreasing the recurrence rate [124,125].

A recent pilot RCT showed that the routine addition of fundoplication to PEH repair is reasonable for decreasing postoperative reflux and concomitant esophagitis and that fundoplication-related side effects are not clinically significant [126].

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## SUPPLEMENTARY MATERIALS

### Supplementary Table 1

Quality assessment

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### Supplementary Table 2

Evidence profile

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### Supplementary Fig. 1

Flowcharts of the literature search and study selection process.

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