ORIGINAL ARTICLE

How to select patients for antireflux surgery? The ICARUS guidelines (international consensus regarding preoperative examinations and clinical characteristics assessment to select adult patients for antireflux surgery)

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ABSTRACT

Objective Antireflux surgery can be proposed in patients with GORD, especially when proton pump inhibitor (PPI) use leads to incomplete symptom improvement. However, to date, international consensus guidelines on the clinical criteria and additional technical examinations used in patient selection for antireflux surgery are lacking. We aimed at generating key recommendations in the selection of patients for antireflux surgery.

Design We included 35 international experts (gastroenterologists, surgeons and physiologists) in a Delphi process and developed 37 statements that were revised by the Consensus Group, to start the Delphi process. Three voting rounds followed where each statement was presented with the evidence summary. The panel indicated the degree of agreement for the statement. When 80% of the Consensus Group agreed (A+/A) with a statement, this was defined as consensus. All votes were mutually anonymous.

Results Patients with heartburn with a satisfactory response to PPIs, patients with a hiatal hernia (HH), patients with oesophagitis Los Angeles (LA) grade B or higher and patients with Barrett's oesophagus are good candidates for antireflux surgery. An endoscopy prior to antireflux surgery is mandatory and a barium swallow should be performed in patients with suspicion of a HH or short oesophagus. Oesophageal manometry is mandatory to rule out major motility disorders. Finally, oesophageal pH (±impedance) monitoring of PPI is mandatory to select patients for antireflux surgery, if endoscopy is negative for unequivocal reflux oesophagitis.

Conclusion With the ICARUS guidelines, we generated key recommendations for selection of patients for antireflux surgery.

Significance of this study

What is already known on this subject?

- Anti-reflux surgery is suggested in a subgroup of patients having gastro-esophageal reflux disease.
- Selecting patients for anti-reflux surgery however is not straightforward.

What are the new findings?

- Based on several statements that generated consensus, a number of recommendations can be made for selecting patients for anti-reflux surgery.
- All patients require endoscopy, pH-monitoring off PPI and esophageal manometry.

How might it impact on clinical practice in the foreseeable future?

- Referring a patient for anti-reflux surgery has to be an informed decision process, based on both positive and negative supporting findings.

INTRODUCTION

GORD occurs when the reflux of (duodeno)-gastric contents into the oesophagus causes troublesome symptoms and/or tissue damage (oesophagitis, stricture, Barrett's oesophagus).[1] GORD is a very common condition with a prevalence of 20% in the Western population. It may present with a broad spectrum of symptoms, subdivided into typical, oesophageal manifestations (heartburn and regurgitation) and a variety of atypical, extra-oesophageal symptoms, such as chronic cough, wheezing and

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hoarseness. Typical and atypical symptoms can coexist in the same patient.[2–4]

Proton pump inhibitors (PPIs) are the first-line medical treatment for patients with GORD, and PPI therapy has proven to be highly effective in healing oesophagitis.[5 6] However, efficacy rates for symptom relief are significantly lower, with between 10% and 40% of patients with GORD failing to respond symptomatically, either partially or completely.[6] Underlying mechanisms behind symptom generation in refractory GORD are the presence of weakly acidic and bile reflux, residual acid reflux, oesophageal hypersensitivity and psychological comorbidities.[6]

When lifestyle modifications, dietary changes and especially when medical treatment (antacids, histamine 2 (H_2-) receptor antagonist and PPIs) for GORD fails, antireflux surgery can be proposed. Antireflux surgery can also be recommended in case of intolerance to PPIs or as an alternative in anticipated long-term medical therapy in young patients with GORD. While medical treatment is focused on reducing the acidity of the refluxate, classic antireflux surgery generates a mechanical and functional barrier preventing reflux from gastric contents into the oesophagus.

Several long-term follow-up studies looking at recurrence rates of reflux symptoms have been published over the last years. A recent Swedish study followed 2655 patients who underwent primary laparoscopic antireflux surgery for a mean of 5.1 years and demonstrated recurrence of reflux in 470 (17.7%) of patients. Risk factors for recurrence of reflux were female gender, older age and comorbidity.[7] A 5-year follow-up study, the LOTUS trial (Long-Term Usage of Esomeprazole vs Surgery for Treatment of Chronic Gastro-oesophageal Reflux Disease), demonstrated that a standardised laparoscopic Nissen fundoplication performed in expert centres and treatment with esomeprazole had similar outcome results concerning treatment failure rate, although that relief of heartburn was somewhat superior after surgery. The vast majority of patients achieved and remained in remission after 5 years, both in the surgical group as well as in the medical treatment group.[8] However, the LOTUS study only enrolled patients with complete symptom control on esomeprazole and the results are not necessarily applicable to the group of patients with insufficient symptom control on PPIs, which constitutes a risk factor for a poor outcome.[9]

Selection of patients for antireflux surgery is traditionally based on the symptom pattern (preferably typical GORD symptoms), on the response to PPIs (at least partial response) and on the result of oesophageal pH or pH-impedance monitoring (pathological acid exposure in the absence of acid suppressive therapy).[9 10] In 2013, a US-based consensus concerning preoperative diagnostic workup before antireflux surgery was published; however, this was a national consensus (the expert panel consisted of only American experts), achieved through informal voting.[11]

The literature reports that outcome of antireflux surgery is influenced not only by anatomical and technical aspects, as assessed by endoscopy, radiology, manometry and reflux monitoring, but also by demographic and comorbidity factors such as the presence of IBS, functional dyspepsia (FD), anxiety and depression. However, it is unclear to which extent these aspects should influence decisions to perform antireflux surgery, and to date, global consensus guidelines on the clinical criteria and additional technical examinations used in patient selection for antireflux surgery are lacking.

Therefore, the aim of this project was to develop a global and multidisciplinary consensus on patient characteristics and preoperative examinations that could offer the clinician guidance in selecting adult patients with GORD for classic antireflux surgery and possibly in adapting the technical aspects of the intervention in order to optimise clinical outcome.

METHODS

A Delphi process was started, with support from the International Society for Diseases of the Oesophagus (ISDE), to develop consensus statements for preoperative investigations and their results in the selection of adult patients for antireflux surgery. This approach combines the principles of evidence-based medicine, supported by systematic literature reviews and the use of a voting process. This method is increasingly used in healthcare as a rigorous means of determining consensus for complex problems in medicine for which evidence from controlled trials is lacking.[1 12–15]

The principal steps in the process were: (1) selection of an international Consensus Group consisting of several experts in GORD management with different clinical and scientific backgrounds to contribute to this expert panel; (2) development of draft statements by a Working Group composed of five Consensus Group experts with varied backgrounds; (3) systematic literature reviews to identify evidence to support each statement; (4) three rounds of repeated voting of the statements and voting discussion until a stable level of consensus voting was reached and (5) grading of the strength using accepted criteria.[16]

For the Consensus Group, which comprised the Working Group, 42 international experts with demonstrated knowledge/expertise were invited, and 35 from 15 countries (Australia, Belgium, Brazil, Canada, Denmark, France, Italy, Japan, Netherlands, Norway, Sweden, Switzerland, Turkey, UK and USA) agreed to participate. The group, consisting of gastroenterologists, surgeons and physiologists, combined a diversity of views and expertise related to GORD diagnosis and management.

We conducted a systematic literature search using a number of relevant keywords (MeSH: antireflux surgery and manometry/endoscopy/pH-metry/gastric emptying/comorbidities/barium X-ray). A core panel of five members reviewed the list of publications and identified the ones relevant to the process. These were stored in PDF format on a central server to which Delphi panel members had access. The references cited in this chapter are only a selection of the articles reviewed in each area and were selected to clarify the discussion.

The Working Group developed an initial 27 statements and prepared and reviewed the evidence to support the statements that were presented to the Consensus Group. The Consensus Group subsequently revised, expanded and consolidated the statements, ultimately providing 37 statements to start the Delphi process. The experts were then allocated to groups of four and each member also functioned as lead expert for one statement. Each lead expert prepared a short summary of the available evidence (using the papers on the central server as literature source) for this statement, which was later further updated based on input from other members. Statements were revised by the Working Group based on the feedback from the Consensus Group before the start of the first voting round and based on additional literature reviews, but also after each voting round.

Three voting rounds followed where each statement was presented with the evidence summary, and then the entire panel indicated the degree of agreement for the statement using a six-point Likert scale (table 1). When 80% of the Consensus Group agreed (A+ or A) with a statement, this was defined as consensus. All votes were mutually anonymous. The strength of evidence for each statement was scored using the grading

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Table 1 Six-point Likert scale

Point	Description
A+	Agree strongly
A	Agree with minor reservation
A-	Agree with major reservation
D-	Disagree with major reservation
D	Disagree with minor reservation
D+	Disagree strongly

of recommendations assessment, development and evaluation (GRADE) system (table 2).[17] All statements with grading and references are found in table 3.

The following statements, on relevant aspects to consider adult patients for antireflux surgery, were composed by the Working Group and reviewed and adjusted as needed by the Consensus Group. All statements label patients with certain characteristics as 'good candidates for antireflux surgery'. This does not imply that surgery must be pursued in these patients, but it identifies them as potentially suitable for referral for surgery. Moreover, it is essential to understand that a decision for antireflux surgery based on a single characteristic (captured in a single statement) is also not appropriate. Referring a patient for antireflux surgery has to be an informed decision process, based on both positive and negative supporting findings.

RESULTS

Clinical presentation and comorbidities

Patients with heartburn as the main symptom who respond satisfactorily to PPIs are good candidates for antireflux surgery.

Statement endorsed, overall agreement 94.1%: A+ 67.6%, A 26.5%, A− 5.9%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE A.

The vast majority of presurgery and postsurgery studies in the literature enrol patients with 'typical' GORD symptoms which include both heartburn and regurgitation, as well as patients with GORD who have typical symptoms refractory to acid suppression therapy. Several peer-reviewed studies investigating patients who reported a complete or partial response to PPI therapy prior to antireflux surgery, showed a benefit of antireflux surgery.[18–21] Moreover, the response to PPI therapy, good compliance and objective preoperative evidence of acid reflux all predict a favourable outcome.[22] However, specific data on heartburn as the main symptom preoperatively and the response of heartburn symptoms to antireflux surgery were (often) not provided.

There is also the issue of the terminology 'satisfactorily', which is very subjective. It has indeed been shown that responses to satisfactorily relief could possibly be influenced by baseline severity.[23 24] However, this terminology is easy to understand by patients and it fits within the practice of medicine in the office setting. Furthermore, in IBS therapy trials, the usefulness of 'satisfactorily relief' as an outcome parameter was linked to its ability to integrate various symptoms and the impact of therapy on various symptoms.[25]

Table 2 Grading of recommendations assessment, development and evaluation system[16]

Code	Quality of evidence	Definition
A	High	Further research is very unlikely to change our confidence in the estimate of effect. ► Several high-quality studies with consistent results. ► In special cases: one large, high-quality multicentre trial.
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. ► One high-quality study. ► Several studies with some limitations.
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. ► One or more studies with severe limitations.
D	Very low	Any estimate of effect is very uncertain. ► Expert opinion. ► No direct research evidence. ► One or more studies with very severe limitations.

2. Patients with regurgitation as the main symptom are good candidates for antireflux surgery, regardless of the response pattern to PPI therapy.

Statement *not* endorsed, overall agreement 79.4%: A+ 14.7%, A 64.7%, A−- 11.8%, D− 5.9%, D 2.9%, D+ 0.0%; GRADE B.

The ability for PPIs to adequately improve regurgitation appears to be much less than their ability to improve heartburn.[26 27] In the literature, there is a lack of solid evidence to support the statement above. However, in a systematic analysis, surgery does appear to be superior to PPIs in alleviating symptomatic regurgitation, although dysphagia, rectal flatulence and the inability to belch or vomit were significantly more common in patients treated surgically.[8 28 29] Important to notice is that symptoms of regurgitation due to primary oesophageal motility disorders (eg, achalasia, rumination syndrome) have to be ruled out by means of oesophageal motility testing (preferably using high-resolution manometry (HRM)) before referring a patient for antireflux surgery.

3. Patients with reflux-hypersensitive oesophagus (normal acid exposure but positive symptom association with reflux events) are good candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 55.9%: A+ 5.9%, A 50.0%, A− 26.5%, D− 11.8%, D 2.9%, D+ 2.9%; GRADE C.

Reflux hypersensitivity is categorised as a functional disorder in the latest Rome IV criteria and defined as 'patients with oesophageal symptoms who lack evidence of reflux on endoscopy or abnormal acid burden on reflux monitoring, but show triggering of symptoms by physiological reflux'.[3] Symptoms in patients with reflux hypersensitivity are caused by reflux events (main difference with functional heartburn); therefore antireflux surgery can theoretically improve symptoms as it minimises oesophageal reflux. The majority of studies suggest that patients with a hypersensitive oesophagus are possibly good candidates for antireflux surgery,[4 30–34] while a few reports suggest the opposite.[35] More specifically, outcome in patients with hypersensitive oesophagus where reflux has been documented in the past (either by the presence of oesophagitis or a pathological acid exposure time) is similar as to patients with documented reflux without being hypersensitive.[31 32] However, a recent study by Patel *et al* showed that pure acid sensitivity was a negative predictor for symptom improvement with antireflux therapy, including surgical management.[35] Moreover, patients with reflux hypersensitivity often display a high level of anxiety. Blondeau *et al* demonstrated that psychosocial factors and somatisation might contribute to symptom perception in patients with reflux hypersensitivity.[36] This confounding factor has to be taken into consideration before referring these patients for antireflux surgery.

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Table 3 All statements with grading and references

Statement	Grade of evidence	References
1. Patients with heartburn as the main symptom who respond satisfactorily to proton pump inhibitors (PPIs) are good candidates for antireflux surgery.	A	18–25
2. Patients with regurgitation as the main symptom are good candidates for antireflux surgery, regardless of the response pattern to PPI therapy.	B	8 26–29
3. Patients with reflux-hypersensitive oesophagus (normal acid exposure but positive symptom association with reflux events) are good candidates for antireflux surgery.	C	3 4 30–36
4. Patients with functional heartburn (Rome III/IV criteria, who have no association of symptoms with documented episodes of reflux events) are poor candidates for surgery.	B	3 34 37
5a. Patients with non-cardiac chest pain are good candidates for antireflux surgery only if symptoms can be attributed to reflux.	C	38–46
5b. Patients with extra-oesophageal syndromes (asthma, chronic cough or laryngitis) are good candidates for antireflux surgery only if symptoms can be attributed to reflux.	C	45 47–73
6. Patients with eosinophilic oesophagitis (EOO) on oesophageal biopsies are poor candidates for antireflux surgery.	C	74–78
7. Patients with scleroderma (and/or other severe smooth muscle disease) are poor candidates for antireflux surgery.	C	79–89
8. Patients with concomitant functional disorders such as dyspepsia and IBS are good candidates for antireflux surgery, only if symptoms can be attributed to reflux.	B	90–95
9. Patients with a body mass index >35 kg/m^2 are poor candidates for antireflux surgery.	B	96–102
10. Patients with psychiatric illness (major depression or anxiety disorder) are good candidates for antireflux surgery only if symptoms can be attributed to reflux.	C	103–106
11. Patients known with substance abuse (such as alcohol abuse and drug abuse) are poor candidates for antireflux surgery.	D	97 107–114
12. Patients with dental erosions related to documented reflux are good candidates for antireflux surgery.	D	115–123
13. Endoscopy is mandatory and has to be carried out in the last year prior to antireflux surgery.	B	8 28 123
14. There is no need to wean the patient off PPI for an endoscopy in the preoperative workup for antireflux surgery.	C	28 124–127
15. Patients with GORD symptoms and an endoscopic diagnosis of a hiatal hernia (HH) are good candidates for antireflux surgery.	B	10 128–133
16a. Patients with GORD symptoms and unequivocal presence of reflux oesophagitis Los Angeles (LA) grade A or higher off PPI are good candidates for antireflux surgery.	B	2 8 134–139
16b. Patients with GORD symptoms and unequivocal presence of reflux oesophagitis LA grade B or higher off PPI are good candidates for antireflux surgery.	B	
17. Patients with GORD symptoms without reflux oesophagitis during endoscopy performed off PPIs are poor candidates for antireflux surgery.	B	3 32 134 141–143
18. Patients with GORD symptoms and Barrett's oesophagus (non-dysplastic specialised intestinal metaplasia) on biopsies of the distal oesophagus are good candidates for antireflux surgery.	B	22 144–154
19. In patients considered for antireflux surgery, biopsies of the oesophageal body should be obtained during endoscopy.	C	75 77 155–161
20. In patients with suspicion of HH or short oesophagus, a barium swallow is mandatory in the preoperative workup for antireflux surgery.	B	162–167
21. Patients with GORD symptoms and a small or medium size sliding HH on barium swallow are good candidates for antireflux surgery.	B	58 133 168–170
22. Patients with GORD symptoms and a large sliding HH on barium swallow are good candidates for antireflux surgery in the absence of short oesophagus.	B	92 162 166 171 203 204
23. Symptomatic patients with a para-oesophageal hernia on barium swallow are good candidates for antireflux surgery in addition to para-oesophageal hernia repair.	C	172–176
24. Patients with GORD symptoms and a short oesophagus on barium swallow are poor candidates for antireflux surgery.	C	162 164 165
25. Oesophageal manometry is mandatory to select patients for antireflux surgery.	D	177–179
26. Patients with GERD symptoms and a hypercontractile oesophagus (Jackhammer and the previously described Nutcracker) oesophagus on manometry are good candidates for anti-reflux surgery if symptoms can be attributed to reflux.	D	180–182
27. Patients with GORD symptoms and distal oesophageal spasm on manometry are poor candidates for antireflux surgery.	D	183–185
28. In patients with GORD symptoms and hypocontractility of the oesophageal body on manometry, antireflux surgery should be tailored.	D	186–189
29. Patients with GORD symptoms and severe hypocontractility or failed peristalsis on manometry are poor candidates for antireflux surgery.	D	186 188 189
30. Oesophageal pH (±impedance) monitoring off therapy is mandatory to select patients with NERD for antireflux surgery.	B	22 33 190–194
31. Oesophageal pH (±impedance) monitoring off therapy should be performed for selection for antireflux surgery of patients who have short Barrett's oesophagus in the absence of erosive oesophagitis.	B	190
32. Patients with GORD symptoms and normal reflux exposure on pH (±impedance) monitoring off PPI therapy are poor candidates for antireflux surgery.	B	56
33a. Patients with GORD symptoms, a normal reflux exposure on pH (±impedance) monitoring off therapy and a positive symptom association are good candidates for antireflux surgery.	C	31 35 56 195
33b. Patients with GORD symptoms, a normal reflux exposure on pH (± impedance) monitoring off therapy and a positive reflux symptom association are good candidates for anti-reflux surgery, only if symptoms respond to PPI therapy.	B	
34a. Patients with GORD symptoms and pathological reflux exposure on pH (±impedance) monitoring off therapy and a negative reflux symptom association are eligible for antireflux surgery.	C	33 192 194
34b. Patients with GORD symptoms and pathological reflux exposure on pH (± impedance) monitoring off therapy and a negative reflux symptom association are eligible for antireflux surgery, only if symptoms respond to PPI therapy.	C	
35. Patients with pathological reflux exposure on pH (±impedance) monitoring on PPI who respond to baclofen therapy are good candidates for antireflux surgery.	D	196 197
36. A gastric emptying test for solid food is necessary to select patients with GORD with concomitant dyspeptic symptoms for antireflux surgery.	C	198–200
37. If the gastric emptying test is abnormal for solid food, patients should not undergo an antireflux surgery.	C	198 199 201 202

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4. Patients with functional heartburn (Rome III/IV criteria, who have no association of symptoms with documented episodes of reflux events) are poor candidates for surgery.

Statement endorsed, overall agreement 100%: A+ 91.2%, A 8.8%, A− 0.0%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE B.

Functional heartburn is defined according to the Rome IV criteria as 'a burning retrosternal discomfort or pain refractory to optimal antisecretory therapy in the absence of gastro-oesophageal acid reflux (GOR), histopathological mucosal abnormalities, major motor disorders or structural explanations'.[3] In other words, in functional heartburn, symptoms manifest themselves without association to reflux events. From the mechanistic point of view, it is therefore unlikely that functional heartburn would be improved by antireflux surgery. The few available studies do not support the efficacy of surgery.[34 37]

5a. Patients with non-cardiac chest pain (NCCP) are good candidates for antireflux surgery only if symptoms can be attributed to reflux.

Statement *not* endorsed, overall agreement 79.4%: A+ 14.7%, A 64.7%, A− 14.7%, D− 2.9%, D 2.9%, D+ 0.0%; GRADE C.

NCCP is a common condition, with a prevalence of up to 25% in the US adult population.[38] After excluding a cardiac cause, reflux is the most common underlying mechanism for this disorder. Patients with NCCP might be referred to antireflux surgery after ruling out oesophageal motility disorders such as hypercontractile oesophagus and functional chest pain.[39] Although literature on GORD-related NCCP as the sole indication for surgical treatment is non-existent, fundoplication has been performed in this patient group. Improvement after surgical treatment is better in patients with a clear correlation between reflux events and symptoms, in patients who also display typical reflux symptoms such as heartburn and third when there is a satisfactory response to PPIs prior to the surgery.[40–46]

5b. Patients with extra-oesophageal syndromes (asthma, chronic cough or laryngitis) are good candidates for antireflux surgery only if symptoms can be attributed to reflux.

Statement *not* endorsed, overall agreement 44.1%: A+ 8.8%, A 35.3%, A− 44.1%, D− 8.8%, D 2.9%, D+ 0.0%; GRADE C.

The vast majority of data is reported in patients with typical GORD symptoms and coexisting extra-oesophageal symptoms that seem to respond to surgery. Varying degrees of symptom improvement has been shown mainly in case series in respiratory symptoms, asthma, cough and laryngopharyngeal symptoms.[43 47–69] Few data are available on the outcome of antireflux surgery for isolated atypical symptoms. Moreover, patient selection remains uncertain as there is no well-established method for demonstrating that these symptoms can be attributed to reflux. The use of symptom markers is valid for typical reflux symptoms; however, in case of extra-oesophageal symptoms, it has been subject of debate for a long time. An objective monitoring for chronic cough can be added through ambulatory manometry or acoustic monitoring.[70–73] Outcomes of Nissen fundoplication in patients with chronic cough attributable to reflux were good although in uncontrolled and often retrospective studies, but these were selected patients who also displayed a positive pH monitoring.[42 50–59 61–68] It has to be stressed out that none of the studies were placebo/sham controlled, which is pivotal in studying the exact effect of antireflux surgery in patients with chronic cough.

6. Patients with eosinophilic oesophagitis (EOO) on oesophageal biopsies are poor candidates for antireflux surgery.

Statement endorsed, overall agreement 88.2%: A+ 61.8%, A 26.5%, A− 8.8%, D− 2.9%, D 0.0%, D+ 0.0%. GRADE C

There is evidence in the literature that eosinophilic oesophagitis in children and adults does not respond to antireflux surgery.[74–77] Obtaining oesophageal biopsies in all patients evaluated for Nissen fundoplication is debatable, as reports suggest a low prevalence of eosinophilic oesophagitis in adults with refractory heartburn.[78]

7. Patients with scleroderma (and/or other severe smooth muscle disease) are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 64.7%: A+ 11.8%, A 52.9%, A− 26.5%, D− 5.9%, D 2.9%, D+ 0.0%; GRADE C.

Data on the outcome of antireflux surgery in patients with scleroderma (systemic sclerosis) is contradictory: there are a few non-randomised studies reporting (partial or full) resolution of reflux symptoms, while other studies suggest that surgery is of limited success in these patients.[79–84] Although the severity of reflux symptoms improved after Nissen fundoplication, postoperative dysphagia was present in 38%–71% of patients with scleroderma.[79 81 85] A retrospective study suggested laparoscopic Roux-en-Y gastric bypass might be a better option in patients with systemic sclerosis-associated reflux: less dysphagia and improved reflux control was seen after Roux-en-Y gastric bypass compared with fundoplication.[81 86] Although the oesophagus is not always affected in patients with systemic sclerosis, the majority of patients with oesophageal involvement is found to have aperistalsis, which is a risk factor for postoperative dysphagia also in patients without scleroderma.[87–89]

8. Patients with concomitant functional disorders such as dyspepsia and IBS are good candidates for antireflux surgery, only if symptoms can be attributed to reflux.

Statement *not* endorsed, overall agreement 64.7%: A+ 23.5%, A 41.2%, A− 26.5%, D− 8.8%, D 0.0%, D+ 0.0%; GRADE B.

According to Rome IV criteria, functional dyspepsia (FD) is defined as 'a medical condition that significantly impacts on the usual activities of a patient and is characterised by one of the following symptoms: postprandial fullness, early satiation, epigastric pain or epigastric burning that are unexplained after a routine clinical evaluation'.[90] Within patients with FD, a distinction between postprandial distress syndrome (PDS), with predominant postprandial fullness and early satiation and epigastric pain syndrome (EPS) characterised by epigastric pain or epigastric burning is made. There are currently no data about the influence of Rome III/IV FD comorbidity on the outcome of antireflux surgery, but it may parallel the inferior response to PPIs.[91] Studies suggest that antireflux surgery is not contraindicated in patients with dyspepsia comorbidity since these symptoms also tend to improve, but they do point out that the expected outcome is worse in patients with dyspepsia comorbidity.[92]

IBS is defined in the Rome IV criteria as 'recurrent abdominal pain associated with defaecation or a change in bowel habits'. Disordered bowel habits are typically present (ie, constipation, diarrhoea or a mix of constipation and diarrhoea), as are symptoms of abdominal bloating/distention. Symptom onset should occur at least 6 months before diagnosis and symptoms should be present during the last 3 months.[93] A study by Raftopoulos *et al* demonstrated that preoperative IBS is not a contraindication of antireflux surgery.[94] Although Axelrod *et al* do not state that IBS is a contraindication of antireflux surgery, they showed that patients with a diagnosis of functional bowel disease or with preoperative symptoms of functional bowel disease were more likely to have a poor outcome compared with patients without the diagnosis or symptoms of functional bowel disease.[95] The reported data—although scarce and variable in quality—indicate that neither FD nor IBS comorbidity

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is a contraindication for antireflux surgery because of a similar improvement of typical reflux symptoms. However, extensive counselling about the possibility of persistent functional GI symptoms and increased risk of gas-bloat syndrome postoperatively is warranted.

9. Patients with a body mass index >35 kg/m^2 are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 23.5%: A+ 2.9%, A 20.6%, A− 17.6%, D− 14.7%, D 38.2%, D+ 5.9%; GRADE B.

Obesity has been implicated as a major and independent risk factor for GORD by several mechanisms (increase of the intragastric pressure and of the abdominal–thoracic pressure gradient, increased gastric peptic secretion, abnormal gastric emptying).[96 97] Losing weight should be the first pillar in GORD treatment for obese patients. Although Perez *et al* demonstrated that there was a 31% occurrence rate of GORD after antireflux surgery in 48 obese patients, other more recent studies have shown that preoperative obesity was not associated with a poorer outcome following laparoscopic Nissen fundoplication.[98–102]

10. Patients with psychiatric illness (major depression or anxiety disorder) are good candidates for antireflux surgery only if symptoms can be attributed to reflux.

Statement *not* endorsed, overall agreement 32.4%: A+ 2.9%, A 29.4%, A− 29.4%, D− 20.6%, D 14.7%, D+ 2.9%; GRADE C.

Only few studies investigated the influence of psychiatric comorbidity on the outcome of antireflux surgery in patients with GORD. It has been demonstrated that patients with GORD and concomitant psychiatric disorders (major depression or anxiety as defined by the DSM-IV) have more severe symptoms and lower quality of life at baseline. Even if a 24 hours pH-monitoring is normal after surgery, these patients report less symptom relief and less quality of life improvement compared with patients without psychiatric comorbidity.[103–106]

11. Patients known with substance abuse (such as alcohol abuse and drug abuse) are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 26.5%: A+ 8.8%, A 17.6%, A− 50.0%, D− 5.9%, D 17.6%, D+ 0.0%; GRADE D.

Alcohol and smoking may induce GOR by decreasing lower oesophageal sphincter (LOS) pressure and disturbance of oesophageal motility, although there is no evidence that lifestyle and dietary changes, for example, stopping smoking will improve symptoms.[97 107–110] Impaired swallow-induced LOS relaxation and oesophageal body dysmotility were observed both in healthy volunteers and in symptomatic patients with dysphagia receiving opioids.[111 112] Additionally, there is no evidence in the literature that all these factors may have an impact on the results of antireflux surgery.[113 114]

12. Patients with dental erosions related to documented reflux are good candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 44.1%: A+ 0.0%, A 44.1%, A− 29.4%, D− 8.8%, D 5.9%, D+ 11.8%; GRADE D.

The literature on dental erosions related to GORD is limited. Most studies indicate an increased prevalence of dental erosions in patients with GORD.[115] On average, 17%–68% with GORD have dental erosions.[116–122] A study by Wilder-Smith *et al* showed that esomeprazole 20 mg twice a day significantly reduced the decrease in enamel thickness compared with placebo, suggesting that treatment of GORD may reduce the development of dental erosions.[119] In a 1-year follow-up study, the same group described no further progression in erosive tooth wear in 74% of the patients.[123] However, to date, there are no studies available evaluating the effect of antireflux surgery on dental erosions.

Oesophagogastroduodenoscopy

13. Endoscopy is mandatory and has to be carried out in the last year prior to antireflux surgery.

Statement endorsed, overall agreement 94.1%: A+ 82.4%, A 11.8%, A− 5.9%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE B.

The literature on the use of and diagnostic output from endoscopy in the preoperative workup of patients with GORD before antireflux surgery is very extensive. Although there is no solid evidence that endoscopy is mandatory prior to antireflux surgery, there seems to be a general consensus that endoscopy shall be performed before antireflux surgery. The proper timing for endoscopy has not been studied so far and is therefore not well defined and the voting outcome reflects the opinion and clinical experience of the experts of the panel.

14. There is no need to wean the patient off PPI for an endoscopy in the preoperative workup for antireflux surgery.

Statement endorsed, overall agreement 88.2%: A+ 41.2%, A 47.1%, A− 2.9%, D− 5.9%, D 0.0%, D+ 2.9%; GRADE C.

The literature to support a decision on whether there is greater value of maintaining or for stopping PPI therapy before making a decision regarding selection of a patient for antireflux surgery is scarce. Standard current practice seems to either perform endoscopy on PPI or not to specify.[28 124 125] The information gained by preoperative endoscopy relates to the need to assess and grade dysplasia in Barrett's oesophagus, identify the possibility of a short oesophagus and assess the size and configuration of hiatal hernia (HH).[126 127] As interrupting PPI therapy for these assessments is unnecessary and unhelpful, patients can therefore continue their PPI treatment regimen for endoscopic assessment of reflux prior to a decision regarding the potential value of antireflux surgery.

15. Patients with GORD symptoms and an endoscopic diagnosis of a HH are good candidates for antireflux surgery.

Statement endorsed, overall agreement 82.4%: A+ 20.6%, A 61.8%, A− 14.7%, D− 2.9%, D 0.0%, D+ 0.0%; GRADE B.

A HH disrupts the anatomy and physiology of the normal antireflux mechanism (reducing the LOS length and LOS-pressure, impairing augmentation of the LOS by the right crus, impairing oesophageal peristalsis, increasing cross-sectional area of the oesophago-gastric junction (OGJ)). The herniated stomach acts as a reservoir allowing reflux into the lower oesophagus during swallowing. The presence of a HH is associated with increased symptoms of reflux, increased prevalence and severity of reflux oesophagitis, Barrett's oesophagus, oesophageal adenocarcinoma and reduced efficacy of PPI.[128 129] The severity of oesophagitis is best predicted by size of HH, followed by LOS pressure, in that order.[130] Although patients with a large HH are more prone to have pathological reflux and more symptoms, not all patients with a HH have GORD.[131]

Up to date, there are no prospective studies reporting the influence of HH in recommending antireflux surgery. The Canadian Consensus Conference on the management of GORD in adults did suggest that a significant HH, because of its likely contribution to reflux in an individual patient, may tip the balance towards surgery.[132] Most series looking for independent predictors of success for antireflux surgery did not find presence of HH to be significant in multivariate analysis.[10 133]

16a. Patients with GORD symptoms and unequivocal presence of reflux oesophagitis Los Angeles (LA) grade A or higher off PPI are good candidates for antireflux surgery.

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Statement *not* endorsed, overall agreement 50.0%: A+ 17.6%, A 32.4%, A− 47.1%, D− 2.9%, D 0.0%, D+ 0.0%; GRADE B.

16b. Patients with GORD symptoms and unequivocal presence of reflux oesophagitis LA grade B or higher off PPI are good candidates for antireflux surgery.

Statement endorsed, overall agreement 91.2%: A+ 47.1%, A 44.1%, A− 8.8%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE B.

Patients with GORD can be subdivided into those with erosive reflux disease (ERD, the presence of mucosal breaks) and those with non-erosive reflux disease (NERD, the absence of mucosal breaks) based on upper GI endoscopy findings.[134] It has been demonstrated that progression from NERD to erosive oesophagitis occurs while regression from ERD to NERD is rare.[135 136] The diminished response to medical treatment in patients with NERD would support a greater role for surgery in NERD than in ERD. It has been demonstrated that subjective and objective long-term outcomes of Nissen fundoplication were similar in ERD and NERD and results were sustained for up to 5 years after surgery.[137] Moreover, in terms of symptoms and signs of erosive oesophagitis, a long-term study reported that surgery was superior to conservative management with modified lifestyle and medication.[136]

Historically, reflux oesophagitis off PPI was considered a good selection criterion, usually in combination with abnormal pH metry, for patient selection for an antireflux surgery. Active oesophagitis is a definite sign of ongoing pathological reflux and may help to select patients for surgery. More than 85% of the patients with documented oesophagitis were satisfied with the results of surgery (laparoscopic or open).[138] However, previous studies demonstrated that up to 15% of the general population have oesophagitis LA grade A or higher. Almost half of these patients, in particular those with LA grade A are asymptomatic.[2 139]

Patient selection though remains mostly based on symptoms, as indicated by the recent LOTUS trial.[8 140]

17. Patients with GORD symptoms without reflux oesophagitis during endoscopy performed off PPIs are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 2.9%: A+ 0.0%, A 2.9%, A− 2.9%, D− 23.5%, D 44.1%, D+ 26.5%; GRADE C.

The diagnosis of NERD is based on upper GI endoscopy findings and a positive pH or pH-impedance study.[3 134] Impairment of quality of life, however, and severity of symptoms are similar as for ERD.[141 142] In theory, the diminished response to medical treatment in patients with NERD could support a greater role for surgery in NERD than in ERD. When comparing long-term outcome results of antireflux surgery in patients with PPI-refractory NERD and ERD, it was demonstrated that both subjective and objective long-term outcomes were similar in ERD and NERD and results were sustained for up to 5 years after surgery.[32 143]

18. Patients with GORD symptoms and Barrett's oesophagus (non-dysplastic specialised intestinal metaplasia) on biopsies of the distal oesophagus are good candidates for antireflux surgery.

Statement endorsed, overall agreement 82.4%: A+ 17.6%, A 64.7%, A− 14.7%, D− 2.9%, D 0.0%, D +0.0%; GRADE B.

The presence of Barrett's oesophagus can be considered proof of the presence of GORD. Many studies confirm that antireflux procedures in patients with Barrett's oesophagus effectively reduce reflux-related symptoms and that uncomplicated Barrett's oesophagus does not influence outcome of antireflux surgery.[22 144–153] A meta-analysis found no evidence that antireflux surgery prevents the progression to carcinoma of the oesophagus; therefore, postoperative endoscopic follow-up should be maintained.[154] In patients with refractory GORD eligible for antireflux surgery, the presence of Barrett's oesophagus should not be a contraindication. On the other hand, antireflux surgery should not be suggested to asymptomatic patients with Barrett's oesophagus or to patients with short segment Barrett's oesophagus to prevent evolution to dysplasia or adenocarcinoma.

19. In patients considered for antireflux surgery, biopsies of the oesophageal body should be obtained during endoscopy.

Statement *not* endorsed, overall agreement 73.5%: A+ 58.8%, A 14.7%, A− 11.8%, D− 2.9%, D 2.9%, D+ 8.8%; GRADE C.

EOO and GORD are distinct clinical entities, theoretically with different pathophysiology and treatment. However, their differentiation may sometimes be problematic and disease previously thought to be associated with GORD may really be manifestations of EOO.[155 156] Additionally, there may be a benefit of treatment of GORD in EOO, particularly in paediatric patients.[157 158] Further confounding this issue of distinction is that patients not suspected of having EOO (those not undergoing preoperative biopsy) who receive antireflux surgery, have been reported to have poor outcomes.[75 77] The finding of eosinophils on biopsy does not necessarily confirm the diagnosis of EOO or exclude other oesophageal diseases, therefore rendering the need for mandatory biopsies questionable.[159 160] It has been shown that cost–benefit is only present when the prevalence of abnormal findings is expected to be 8% or more.[161]

Barium swallow

20. In patients with suspicion of HH or short oesophagus, a barium swallow is mandatory in the preoperative workup for antireflux surgery.

Statement endorsed, overall agreement 88.2%: A+ 44.1%, A 44.1%, A− 5.9%, D− 2.9%, D 2.9%, D+ 0.0%; GRADE B.

It is commonly accepted that 2.5 cm of intra-abdominal oesophagus is necessary to perform an effective antireflux procedure. Today, most antireflux operations are performed laparoscopically. The pneumoperitoneum necessary to perform laparoscopy elevates the diaphragm into the mediastinum and appears to 'lengthen' the oesophagus. Failure to recognise that the oesophagus is shortened may result in an inadequate length of intra-abdominal oesophagus at surgery. If a HH repair is constructed under tension on a short oesophagus, the hernia is reduced below the diaphragm at surgery and then retracts into the chest over time. The fundoplication may or may not remain subdiaphragmatically or it may disrupt or 'slip' onto the stomach. Slipped Nissen fundoplications may therefore result from the failure to recognise a shortened oesophagus before surgery. The occurrence of the true short oesophagus is indeed thought to be responsible for 20%–33% of the surgical failures after open or laparoscopic fundoplication.[162] A study by Mattioli *et al* demonstrated that short oesophagus is present in about 20% of patients undergoing routine antireflux surgery, highlighting the importance of performing adequate testing.[163]

If the hernia is identified in the upright position, it is assumed that there is oesophageal shortening. In addition, the oesophagus is probably shortened when the HH length is 5 cm or greater alone or in combination with a stricture or a long segment (>3 cm) Barrett's oesophagus.[162 164] Other radiological findings that suggest a short oesophagus include severe extensive ulcerative oesophagitis, straightening or loss of the angle of His, the presence of a stricture alone and type III mixed or complex para-oesophageal hernias.[165]

In summary, if endoscopy reveals the presence of a large hernia and/or the presence of severe oesophagitis or long

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segment Barrett's oesophagus, a barium swallow performed by a dedicated upper GI radiologist is strongly recommended before surgical intervention. This will allow to better plan the technical details of the surgery in order to eventually reduce the risk of anatomical and/or symptomatic recurrence.[166 167]

21. Patients with GORD symptoms and a small or medium size sliding HH on barium swallow are good candidates for antireflux surgery.

Statement endorsed, overall agreement 82.4%: A+ 20.6%, A 61.8%, A− 8.8%, D− 8.8%, D 0.0%, D+ 0.0%; GRADE B.

Very few studies have examined the effect of a HH on the outcome of antireflux surgery. A study by Power *et al* defined a HH size >3 cm at the time of the surgery as a predictor of failure.[133] However, the presence and the size of a HH had no relationship with outcome according to several other studies.[168–170]

22. Patients with GORD symptoms and a large sliding HH on barium swallow are good candidates for antireflux surgery in the absence of short oesophagus.

Statement endorsed, overall agreement 85.3%: A+ 50%, A 35.3%, A− 8.8%, D− 2.9%, D 0.0%, D+2.9%; GRADE B.

Upper endoscopy and barium swallow are commonly used to diagnose short sliding HH. It has been demonstrated that in morbidly obese patients, barium swallow is superior to endoscopy in diagnosing sliding HH.[171] Preoperative barium swallow can reveal more details on the sliding HH and contribute to better tailoring the antireflux surgery.[166] Although there is currently no consensus on the definition for small, medium and large HH, often the cut-off of >3 cm or hernias belonging to categories II–IV have been used to define a large HH.[94 172 173] As 2.5 cm of intra-abdominal oesophagus is mandatory to offer effective antireflux surgery, in large sliding HHs (larger intrathoracic component), a more comprehensive dissection is needed.[164]

23. Symptomatic patients with a para-oesophageal hernia on barium swallow are good candidates for antireflux surgery in addition to para-esophageal hernia repair.

Statement endorsed, overall agreement 97.1%: A+ 44.1%, A 52.9%, A− 2.9%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE C.

Para-oesophageal hernias (POH) are subtypes of HH, defined as a herniation of the peritoneal cavity into the chest through the diaphragmatic hiatus.

Given the difficulty of distinguishing if reflux symptoms are from POH alone or independent of the POH, most surgeons routinely add an antireflux procedure (fundoplication) after POH repair in elective situations.[174] A recent pilot trial by Muller-Stich *et al* showed a lesser degree of reflux and a less oesophagitis in patients where a fundoplication was added to the POH repair compared with those with a POH repair only.[172]

Some authors advocate a selective approach to antireflux procedures, with preoperative testing (including manometry, pH-metry or endoscopy) and patient symptoms determining whether or not to add a fundoplication.[173] Others suggest always performing an antireflux procedure, but tailoring the type of fundoplication (eg, full or partial) depending on the patient.[175] A minority suggest that fundoplication should be avoided due to the increased risk of dysphagia with antireflux procedures after POH repair.[176] None of these approaches however have been proven superior to others in a prospective trial.

24. Patients with GORD symptoms and a short oesophagus on barium swallow are poor candidates for antireflux surgery.

Statement not endorsed, overall agreement 17.6%: A+ 2.9%, A 14.7%, A− 23.5%, D− 41.2%, D 11.8%, D+ 5.9%; GRADE C.

In the absence of adequate comparative studies, the question of the short oesophagus remains controversial, and there is insufficient evidence to preclude patients with radiological suspicion of a short oesophagus from antireflux surgery. If patients progress to surgery, there is also insufficient evidence to define the best surgical procedure in this scenario. Well-designed case–control or randomised clinical trials are needed to provide an evidence base to address this question.

Oesophageal manometry

25. Oesophageal manometry is mandatory to select patients for antireflux surgery.

Statement endorsed, overall agreement 94.1%: A+ 82.4%, A 11.8%, A− 5.9%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE D.

Oesophageal manometry should be performed prior to antireflux surgery to rule out a major motor disorder, such as achalasia, OGJ outflow obstruction or absent contractility.[177 178] There is no data to support that the manometric finding of distal oesophageal spasm (DOS), Jackhammer oesophagus or minor disorders of peristalsis, such as fragmented peristalsis predicts postoperative dysphagia. Incorporating HRM and impedance into pressure flow parameters might be helpful in predicting outcome since the dysphagia risk index appeared to be helpful in identifying patients at risk for post-fundoplication dysphagia.[179]

26. Patients with GORD symptoms and a hypercontractile oesophagus (Jackhammer and the previously described Nutcracker) oesophagus on manometry are good candidates for antireflux surgery if symptoms can be attributed to reflux.

Statement *not* endorsed, overall agreement 64.7%: A+ 11.8%, A 52.9%, A− 29.4%, D− 2.9%, D 2.9%, D+ 0.0%; GRADE D.

Data on outcome of antireflux surgery of patients with a hypercontractile oesophagus is scarce: there are no randomised, controlled trials available in literature. However, retrospective data on outcome of patients with nutcracker oesophagus (although no longer defined in the Chicago classification V.3.0) undergoing antireflux surgery show no difference compared with patients with a normal oesophageal motility pattern.[180] Manometric abnormalities after a Nissen fundoplication were even improved in two patients with a Jackhammer oesophagus.[181] Hypertensive oesophageal contraction patterns are not a contraindication for antireflux surgery; however, patients and clinicians should be aware of the risk of developing chest pain after the surgery.[182]

27. Patients with GORD symptoms and distal oesophageal spasm on manometry are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 64.7%: A+ 26.5%, A 38.2%, A− 20.6%, D− 11.8%, D 0.0%, D+ 0.0%; GRADE D.

Patients with DOS are poor candidates for antireflux surgery, provided that the motor disorder has been well characterised, preferably using HRM. Therapeutic approaches indicated for patients with DOS include medicines such as sildenafil, as well as endoscopic injection of botulin toxin and surgical myotomy.[183–185] Although some patients may benefit from acid-suppressive therapy, antireflux surgery as the unique treatment should be avoided in patients with DOS.

28. In patients with GORD symptoms and hypocontractility of the oesophageal body on manometry, antireflux surgery should be tailored.

Statement *not* endorsed, overall agreement 47.1%: A+ 5.9%, A 41.2%, A− 41.2%, D− 0.0%, D 5.9%, D+ 5.9%; GRADE D.

There are no good data to suggest tailoring of antireflux surgery to oesophageal body hypomotility or hypocontractility.[186 187]

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Provocative manoeuvres during manometry could in the future identify patients where peristaltic performance following fundoplication can modify the risk for postoperative dysphagia. Multiple rapid swallows (MRS) are often added to the manometric protocol as a marker for esophageal body peristaltic reserve. It has been shown that MRS testing before laparoscopic antireflux surgery is able to help predict late postoperative dysphagia.[188 189]

29. Patients with GORD symptoms and severe hypocontractility or failed peristalsis on manometry are poor candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 64.7%: A+ 8.8%, A 55.9%, A− 23.5%, D− 2.9%, D 8.8%, D+ 0.0%; GRADE D.

Hypocontractility is not a contraindication for antireflux surgery, since surgery more often than not improved these manometric abnormalities.[186] Further research is warranted since very little data exists on outcome of patients with the most severe hypocontractility or aperistalsis. Similar as described above (statement 28) is the importance of adding MRS during a manometric protocol, which is a marker of contractile reserve of the oesophagus.[188 189] In addition, antireflux surgery can be tailored to each individual patient.

It has to be repeated that the main indication for manometry in patients with GORD considered for antireflux surgery is to identify patients with aperistalsis due to achalasia, who are candidates for fundoplication only when combined with myotomy of the LOS.

Reflux monitoring

30. Oesophageal pH (±impedance) monitoring off therapy is mandatory to select patients with NERD for antireflux surgery

Statement endorsed, overall agreement 97.1%: A+ 91.2%, A 5.9%, A− 0.0%, D− 2.9%, D 0.0%, D+ 0.0%; GRADE B.

In the absence of oesophagitis (ie, presence of mucosal breaks), pathological GOR and/or positive reflux symptom association 'off' therapy should be documented before embarking to antireflux surgery.[22 33 190–193] In the preoperative setting, the added value of impedance in patients 'off' therapy remains to be determined.

Data on preoperative assessment 'on' PPIs are scarce. Few uncontrolled and short studies suggest that good postoperative outcomes can be achieved in patients who are refractory to PPIs in whom pH-impedance monitoring demonstrated either an abnormal number of reflux episodes or positive symptom association analysis.[33 194]

31. Oesophageal pH (±impedance) monitoring off therapy should be performed for selection for antireflux surgery of patients who have short Barrett's oesophagus in the absence of erosive oesophagitis.

Statement endorsed, overall agreement 88.2%: A+ 41.2%, A 47.1%, A− 5.9%, D− 0.0%, D 5.9%, D+ 0.0%; GRADE B.

Oesophageal (impedance-) pH-monitoring off therapy should be performed in patients with short segment Barrett's oesophagus as it provides an objective quantification of patient's GOR.[190] This evaluation of PPI therapy would provide a baseline comparator in assessing the efficacy of acid-suppressive therapy and/or reflux-reducing therapy.

32. Patients with GORD symptoms and normal reflux exposure on pH (±impedance) monitoring off PPI therapy are poor candidates for antireflux surgery.

Statement endorsed, overall agreement 82.4%: A+ 17.6%, A 64.7%, A− 17.6%, D− 0.0%, D 0.0%, D+ 0.0%; GRADE B.

There is very limited data examining the outcomes of surgery in patients with normal reflux monitoring. This is in large part due to the fact that most of the studies evaluating outcomes of antireflux surgery require abnormal reflux monitoring as a criteria to be eligible for surgery.[56] Based on the available evidence, it would appear that patients with normal reflux exposure on pH (±impedance) monitoring off therapy are indeed poor candidates for antireflux surgery.

33a. Patients with GORD symptoms, a normal reflux exposure on pH (±impedance) monitoring off therapy and a positive symptom association are good candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 58.8%: A+ 14.7%, A 44.1%, A− 23.5%, D− 17.6%, D 0.0%, D+ 0.0%.

33b. Patients with GORD symptoms, a normal reflux exposure on pH (±impedance) monitoring off therapy and a positive reflux symptom association are good candidates for antireflux surgery, only if symptoms respond to PPI therapy.

Statement *not* endorsed, overall agreement 73.5%: A+ 11.8%, A 61.8%, A− 14.7%, D− 5.9%, D 5.9%, D+ 0.0%.

There is a very limited data examining the outcomes of surgery in patients with normal reflux monitoring. This is in large part due to the fact that most of the studies evaluating outcomes of antireflux surgery require abnormal reflux monitoring as a criteria to be eligible for surgery.[56] Some studies do suggest that reflux-hypersensitive patients with typical symptoms and an unsatisfactory response to PPIs may benefit from antireflux surgery with an outcome similar to the one of patients with pathological reflux.[31 195] However, as mentioned above (statement 3), a recent study by Patel *et al* showed that pure acid sensitivity was a negative predictor for symptom improvement with antireflux therapy, including surgical management.[35] Results should therefore be interpreted with caution.

34a. Patients with GORD symptoms and pathological reflux exposure on pH (±impedance) monitoring off therapy and a negative reflux symptom association are eligible for antireflux surgery.

Statement *not* endorsed, overall agreement 58.8%: A+ 5.9%, A 52.9%, A− 29.4%, D− 8.8%, D 2.9%, D+ 0.0%.

34b. Patients with GORD symptoms and pathological reflux exposure on pH (±impedance) monitoring off therapy and a negative reflux symptom association are eligible for antireflux surgery, only if symptoms respond to PPI therapy.

Statement *not* endorsed, overall agreement 66.7%: A+ 6.1%, A 60.6%, A− 9.1%, D− 6.1%, D 18.2%, D+ 0.0%.

The literature available suggests that patients with proven pathological acid exposure who do not experience symptoms during pH (±impedance) monitoring or presenting a negative symptom–reflux association may still obtain good results from anti-reflux surgery.[33 192] Moreover, there is a subgroup of patients that is truly refractory to PPIs, with ongoing acid secretion.[193]

35. Patients with pathological reflux exposure on pH (±impedance) monitoring on PPI who respond to baclofen therapy are good candidates for antireflux surgery.

Statement *not* endorsed, overall agreement 20.6%: A+ 5.9%, A 14.7%, A− 61.8%, D− 2.9%, D 11.8%, D+ 2.9%.

Baclofen, a GABA B-agonist, is known to reduce the number of transient LOS relaxations and subsequently, it reduces all types of reflux, including weakly acidic reflux.[196] To date, there are no studies comparing baclofen with antireflux surgery, therefore it would be too speculative to say that patients responding to baclofen are good candidates for antireflux surgery. In the very recently published paediatric GOR clinical guidelines, the use of baclofen prior to antireflux surgery can be considered in

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children in whom other pharmacological treatments have failed (weak recommendation).[197]

Gastric emptying

36. A gastric emptying test for solid food is necessary to select patients with GORD with concomitant dyspeptic symptoms for antireflux surgery.

Statement *not* endorsed, overall agreement 5.9%: A+ 2.9%, A 2.9%, A− 8.8%, D− 5.9%, D 67.6%, D+ 11.8%; GRADE C.

Studies performed to assess the role of a preoperative gastric emptying test in antireflux surgery have generated controversial results: some studies have shown that this evaluation is useful to select the best type of surgery and to avoid surgical failures, while others have denied the validity of such an approach.[198–200] However, so far no study has been performed to establish whether the assessment of gastric emptying is relevant or not to favour success of surgery in patients with GORD with concomitant dyspepsia symptoms.

37. If the gastric emptying test is abnormal for solid food, patients should not undergo an antireflux surgery.

Statement *not* endorsed, overall agreement 2.9%: A+ 0.0%, A 2.9%, A− 0.0%, D− 20.6%, D 67.6%, D+ 8.8%; GRADE C.

Literature shows that there is no evidence to suggest that preoperative slow gastric emptying for solids is associated with a poor outcome after surgery with regard to reflux parameters.[201 202] A study by Lundell *et al* suggests that a slow preoperative gastric emptying for solids is weakly associated with symptoms of bloating.[202] However, two other studies investigating the relationship between gastric emptying rates before and outcome after antireflux surgery could not confirm this.[198 199] There is insufficient evidence to support the statement.

Recommendations

Based on the statements that generated consensus, a number of recommendations can be made for selecting patients for antireflux surgery. These are summarised in table 4.

The Delphi process also identified several areas of uncertainty, requiring further research. It is unclear whether patients with regurgitation as a main symptom, patients with NCCP, patients with extra-oesophageal manifestations of reflux and patients with dental erosions are good candidates for anti-reflux surgery (statements 2, 5 and 12). There is a lack of prospective controlled trials to support these statements. Patients with reflux hypersensitivity, patients with concomitant FD and IBS and patients with major psychiatric comorbidity are not considered good candidates for antireflux surgery (statements 3, 8 and 10). There is a need for additional markers of beneficial outcome of antireflux surgery in these patients, given the frequent overlap of GORD with FD and IBS symptoms. There is no consensus that patients with scleroderma are poor candidates for antireflux surgery (statement 7). It is unclear to which extent patients with Jackhammer (or Nutcracker) oesophagus or spasm on manometry are eligible for antireflux surgery (statements 26 and 27). The impact of oesophageal hypocontractility on the eligibility or type of antireflux surgery is unclear (statements 28 and 29). It is unclear whether patients with reflux hypersensitivity are eligible for antireflux surgery (statement 33). Finally, it is unclear whether patients with pathological reflux monitoring but negative symptom association are good candidates for antireflux surgery (statement 34).

It is important to stress that the decision of referring a patient for antireflux surgery has to take into account all positive as well as all negative support findings. Selecting patients suitable for antireflux surgery cannot be captured by one single statement and remains subject to guided clinical judgement and patient preference.

Table 4 Summary of the ICARUS guidelines

Recommendations	Based on statement(s)
Antireflux surgery can be considered for patients with typical symptoms of heartburn, with a good response to proton pump inhibitors (PPIs).	1
Patients with functional heartburn and patients with eosinophilic oesophagitis are poor candidates for antireflux surgery.	4, 6
Patients with morbid obesity and patients with substance abuse are not excluded from antireflux surgery.	9, 11
Endoscopy (during the last year) is mandatory prior to referral for antireflux surgery. There is no need to wean the patient off PPI for endoscopy.	13, 14
Patients with GORD symptoms and a hiatal hernia, Barrett's oesophagus or erosive oesophagitis grade B or higher at endoscopy are good candidates for antireflux surgery.	15, 16b, 18
Patients without erosive oesophagitis are not excluded from antireflux surgery.	17
There is no need to obtain routine biopsies of the distal oesophagus in patients considered for antireflux surgery.	19
A barium X-ray should be obtained in patients with suspicion of a hiatal hernia or short oesophagus when considered for antireflux surgery.	20
Patients with GORD symptoms and a hiatal hernia on X-ray are good candidates for antireflux surgery.	21, 22
Patients with GORD symptoms and a para-oesophageal hernia on X-ray are good candidates for antireflux surgery in addition to para-oesophageal hernia repair.	23
A short oesophagus on barium X-ray does not exclude the patient from antireflux surgery.	24
Oesophageal manometry and oesophageal pH monitoring (±impedance) are mandatory prior to referral for antireflux surgery. The latter is preferentially done off PPI and in patients with NERD.	25, 30, 31
Patients with normal pH-monitoring off PPI are poor candidates for antireflux surgery.	32
Response to baclofen does not enhance patient eligibility for antireflux surgery.	35
There is no need to assess gastric emptying rate in patients considered for antireflux surgery.	36, 37

CONCLUSION

GORD, often accompanied by the typical reflux symptoms heartburn and regurgitation or by atypical reflux symptoms such as chronic cough and wheezing, is very common in the Western World.[1 2] The first-line treatment for GORD is acid suppressive therapy, most often by PPI intake. PPIs have shown to be very effective in healing oesophagitis, however up to 40% of patients with GORD remain symptomatic while on an adequate dose of PPIs.[5 6] Antireflux surgery is often recommended for patients with insufficient relief of symptoms during PPI intake, in case of intolerance to or anticipated long-term use of PPIs. However, to date, consensus guidelines defining clinical criteria and additional technical examinations that need to be performed for patient selection for antireflux surgery are lacking. Therefore, we aimed to develop the ICARUS guidelines using a Delphi process.

The Consensus Group defined several statements that may guide clinicians and surgeons in their decision to select patients for antireflux surgery. All patients require endoscopy, pH-monitoring off PPI and oesophageal manometry. The consensus

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process also identified areas of uncertainty and some patient groups in whom referral for surgery should be avoided, such as functional heartburn.

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