Perspective

Perfect-results after laparoscopic surgery for gastroesophageal reflux - are they achievable?

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Abstract: In the quest for the perfect outcome following antireflux surgery, Nissen's original fundoplication has undergone many modifications. The original procedure achieved good reflux control, but this was offset by a relatively high incidence of troublesome side effects. The modifications which have been proposed as solutions to the problem of troublesome side effects have now all been tested in randomized trials. Outcomes from these suggest that division of the short gastric vessels during Nissen fundoplication is unnecessary, and that partial fundoplications are associated with less side effects. However, there is a trade-off between the risk of side-effects *vs*. the risk of recurrent reflux across the spectrum of antireflux procedures ranging from Nissen fundoplication at one end to lesser degrees of partial fundoplication at the other. Whilst a perfect outcome is almost certainly not achievable following antireflux surgery, the trade-off between the risk of reflux *vs*. the risk side effects needs to be considered during work-up, and the fundoplication can be tailored to the preoperative esophageal motility and individual patient preferences to achieve better outcomes.

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The era of surgery for gastro-esophageal reflux began in the 1950's following Nissen's original description of a 360 degree wrap of gastric fundus around the distal esophagus (1). In an earlier time when acid suppressing medication was not available, this procedure offered the only effective treatment opportunity for individuals who experienced significant symptoms of gastro-esophageal reflux. Nissen's original fundoplication entailed surgery via an open transthoracic approach with the construction of a 5 cm long, fairly tight circumferential wrap of gastric fundus around the distal esophagus. Both the anterior and posterior walls of the fundus were used for the fundoplication and the short gastric blood vessels were not divided. However, it soon became apparent that even though this operation controlled reflux well, in many individuals it was associated with troublesome side effects, such as dysphagia, abdominal bloating and flatulence, and in some individuals reflux returned later, even though the operation was initially effective.

Across the 1960's to 1980's, in an attempt to reduce the risk of side effects yet still control reflux, a range of modifications to Nissen's original procedure were proposed. Rossetti simplified the construction of the fundoplication so that only the anterior wall of the fundus was used for fundoplication (2). Donohue *et al.* (3) advocated division of the short gastric vessels to enable a very loose wrap to be constructed, and DeMeester *et al.* (4) also loosened the wrap and shortened its length progressively from 5 cm to 1-2 cm. Partial fundoplications, during which the fundus was wrapped only part way round the esophagus; e.g., Toupet -posterior placement (5), Dor or Belsey - anterior placement (6,7), were also devised. At the same time, to reduce the morbidity associated with surgical access, surgeons also moved from an open transthoracic approach via a left postero-lateral thoracotomy to an open abdominal approach via an upper midline incision, and then in the 1990's to the current laparoscopic approach (8).

The proponents of each of these technical variations all reported good outcomes, and surgeons in various parts of the world modified their techniques accordingly. However, until the late 1990's the quality of the evidence base underpinning these variations was poor, and the evidence predominantly entailed reports of good outcomes from retrospective case note reviews, or prospective studies without control groups. Furthermore, opinion was largely led by what the "experts" recommended, even when this conflicted with the evidence derived from well constructed randomised controlled clinical trials.

In considering how to best perform surgery for gastro-esophageal reflux disease, several questions should be asked:

- What is the "perfect" outcome following an intervention for reflux?
- Does high quality evidence inform the quest for a "perfect" outcome?
- Is a "perfect" outcome achievable?

What is the "perfect" outcome for the treatment of gastro-esophageal reflux?

Symptoms of gastro-esophageal reflux develop when excessive regurgitation of gastric contents into the esophagus occurs. This is a mechanical problem, and it only happens when the valve mechanism at the gastro-esophageal junction fails to prevent excessive regurgitation of gastric content. Medical therapy addresses the symptoms of gastro-esophageal reflux by blocking the production of acid in the stomach, and consequently reducing the amount of acid exposure which enters the esophageal lumen. However, it fails to physically stop reflux from occurring, and the physical reflux of gastric content continues. If this contains other substances such as bile salts and pancreatic secretions which can also injure the esophageal mucosa, then reflux symptoms may not be well controlled, as medication only suppresses acid production. Surgical fundoplication is effective as it reconstructs the valve mechanism at the gastro-esophageal junction, and physically stops gastric content from entering the esophageal lumen.

Arguably, the "perfect" treatment for gastro-esophageal reflux should meet the following criteria:

(I) The intervention is a "one-off" - i.e. a single treatment cures the patient;
(II) The treatment is 100% successful;
(III) The problem never returns - i.e. the cure is permanent;
(IV) There are no complications;
(V) There are no side effects;
(VI) Treatment does not require any surgical incisions;
(VII) Treatment can be performed on an outpatient basis - i.e. does not require hospital admission.

Unfortunately, no currently available treatment meets all of these criteria. Medication fails to meet the first 5 criteria, although side effects and complications are usually uncommon, and are reversible when medication is ceased. A range of transoral endoscopic antireflux procedures (9-12) were trialed in the late 1990's to mid 2000's, and do address criteria 6 and 7, but these have all failed to deliver reliable long term control of reflux, and have now been abandoned in many parts of the worlds. Surgical fundoplication also fails to meet all the criteria, but some of the modifications and variations to Nissen fundoplication arguably better meet the criteria for the "perfect" treatment, when compared to non-surgical options or Nissen's original procedure.

Assessing treatment outcomes

When considering outcomes following fundoplication, it is important to realize that surgeons, and patients often have different perspectives about what a good outcome actually is, for example, surgeons often focus on technical success following antireflux surgery, i.e. objective measures of reflux control and improvements in esophageal physiology. Normalization of objective measures of gastro-esophageal reflux such as endoscopic evidence of healing of esophagitis, normalization of intra-esophageal acid exposure measured by 24-hour ambulatory pH monitoring, or improvements in lower esophageal sphincter pressure measured using esophageal manometry are all issues surgeons focus on, and provide objective evidence of reflux control.

However, patients are usually more concerned about subjective outcomes, i.e. symptoms, and less concerned about objective outcomes which demonstrate reflux has been prevented. For the individual patient the issue of importance is long term symptom control with minimal side effects. They tend to look at the overall outcome following antireflux surgery, and hope to be better off after surgery. In assessing outcome from this perspective, there is often a balance between the control of reflux symptoms *vs.* the risk of post-fundoplication side effects. This balance can lead to patients reporting good or bad outcomes which don't make sense to the operating surgeon. For example, a patient can develop recurrent reflux following antireflux surgery, yet still consider the operation to be a success! This may occur when surgery is performed in individuals with symptoms

of gastro-esophageal reflux that are poorly controlled by proton pump inhibitor medication before surgery, but in whom some reflux symptoms return at a later stage. If these recurrent post-operative reflux symptoms are fully controlled by a proton pump inhibitor then the patient might still be happy with the outcome following surgery, as the patient is effectively symptom free. Other scenarios which can be acceptable, include full control of reflux symptoms following a fundoplication, but with the patient needing to modify his diet to some extent to avoid post-fundoplication dysphagia. If the original reflux symptoms were particularly troublesome, then some individuals might consider a trade-off such as mild dysphagia for solid food to be very acceptable.

In determining the overall outcome, individuals who undergo fundoplication will often balance the efficacy of reflux control against side effects, and consider this balance in the context of the extent of the preoperative problem to determine whether the overall outcome is acceptable or not. Hence, to measure outcome from the individual patient's perspective, global satisfaction measures that integrate the overall balance of symptom control *vs.* side effects are arguably more important than apparent technical success measured by objective tests.

What evidence is available to determine the best way to deliver a "perfect" outcome?

Since the 1990's a range of prospective randomised controlled clinical trials have been reported evaluating outcomes following antireflux surgery. Collectively these trials address technical issues and provide a good evidence base to determine how to best perform antireflux surgery.

Laparoscopic versus open fundoplication

Ten prospective randomised trials have been reported which compare laparoscopic versus open fundoplication, 9 evaluating Nissen fundoplication and one evaluating laparoscopic *vs.* open posterior partial fundoplication (13-17) and follow-up has been reported at up to 10-15 years in some trials. These trials enrolled between 40 and 192 patients and in general have shown benefits for the laparoscopic approach over the open approach. Early outcomes at follow-up up to 12 months demonstrate advantages for the laparoscopic approach, with shorter postoperative stays (3 *vs.* 4 days median), and less postoperative complications following laparoscopic fundoplication. Reoperation rates for reflux and side effects such as dysphagia were similar for both procedures, although there was a higher incidence of late incisional hernia formation following open surgery in some trials (14). However, in these trials these advantages of the laparoscopic approach were offset by somewhat longer operating times (approximately 30 minutes).

Division of short gastric vessels during Nissen fundoplication

Originally Nissen's fundoplication entailed a 360° fundoplication during which the short gastric blood vessels were left intact (1). However, following reports of troublesome postoperative dysphagia, routine division of these vessels to better mobilize the fundus and ensure a loose fundoplication, was promoted in the 1970's and 1980's by Donahue (3) and DeMeester (4), and this maneuver has entered common practice. The evidence supporting this was based on outcomes from case series. More recently, 6 randomised trials have been reported that enrolled a total of 438 patients and compared Nissen fundoplication with *vs.* without division of the short gastric blood vessels (18-21). The results of these studies have been remarkably consistent, and have shown no difference in reflux control or post-operative dysphagia for division *vs.* no division of the short gastric vessels. However, the larger trials demonstrated that division of the short gastric blood vessels during Nissen fundoplication is associated with an increased risk of flatulence and gas bloat-type symptoms, and more difficulty with belching. A recent meta-analysis which combined data for 201 patients from Australia and Sweden confirmed this analysis and the finding of more abdominal bloating after division of the short gastric vessels (22). The randomized trials do not support the widely held belief that dividing the short gastric vessels improves the outcome following Nissen fundoplication. Further, these trials actually suggest that dividing the vessels leads to a poorer outcome.

Nissen versus posterior partial fundoplication

Eleven prospective randomised trials have compared Nissen *vs.* posterior partial fundoplication (23-26). Study size has ranged up to 200 patients, with 6 trials enrolling more than 100. The larger studies have all demonstrated that posterior partial fundoplication achieves equivalent reflux control, but with a reduced incidence of flatulence and

bloating. Dysphagia was less common following posterior fundoplication in 2 of the larger studies. Meta-analyses have confirmed the reduction in wind-related side effects and dysphagia following posterior partial fundoplication, and also confirm equivalent reflux control (27).

Arguably the most informative study was conducted by Lundell and colleagues (23). They reported the outcomes of a randomized trial of Nissen *vs.* posterior partial fundoplication in a series of publications detailing follow-up across nearly 2 decades (23). 137 patients were enrolled. Reflux control and dysphagia symptoms were similar, but flatulence was commoner after Nissen fundoplication at early to medium-term follow-up. At 18 years follow-up outcomes were similar in terms of reflux control, side effects and overall outcome, with success rates of more than 80% were reported for both procedures. This trial suggested that the earlier side effects that occur more often following Nissen fundoplication actually improve with very long term follow-up, although the outcomes across the first 5 years were in favour of posterior partial fundoplication.

Anterior versus Nissen fundoplication

Six prospective randomised trials have been reported that compare an anterior partial fundoplication variant *vs.* Nissen fundoplication. Four evaluated an anterior 180° partial fundoplication *vs.* Nissen fundoplication (28,29), and two an anterior 90° partial fundoplication (30,31). These studies all demonstrated a reduced risk of post-operative side effects (dysphagia and wind related problems) following anterior partial fundoplication. In addition, in these trials anterior 180° partial fundoplication achieved equivalent control of reflux symptoms, whereas anterior 90° partial fundoplication was associated with a slightly higher incidence of recurrent reflux at up to 5 years follow-up. Overall satisfaction with the outcome in these trials was similar for all fundoplication types. A recently reported meta-analysis confirms these conclusions (32). The trial of anterior 180° partial *vs.* Nissen fundoplication from Watson and colleagues has reported longer term follow-up at up to 10 years (29), and at late follow-up the earlier outcome differences for the two procedures disappeared, due to a progressive decline in the prevalence of dysphagia following Nissen fundoplication across the first decade of follow-up.

Anterior versus posterior partial fundoplication

Two trials have compared anterior *vs.* posterior partial fundoplication (32,33). Both report better reflux control following posterior partial fundoplication, less side effects after anterior partial fundoplication and similar outcomes for overall satisfaction. The overall results from the randomized trials comparing Nissen *vs.* posterior, Nissen *vs.* anterior and posterior *vs.* anterior partial fundoplication demonstrated similar overall satisfaction as measured by global outcome score, but a trade-off between the risk of troublesome side-effects *vs.* the risk of recurrent reflux symptoms across the spectrum of procedures ranging from Nissen fundoplication at one end to anterior 900 partial fundoplication at the other.

Is a "perfect" outcome following surgery for reflux achievable?

The short answer to the question posed is that a perfect outcome is actually not achievable following surgery for reflux. The trade-off between the risk of recurrent gastro-esophageal reflux *vs.* the risk of post-fundoplication side effects needs to be considered during the work-up and planning for antireflux surgery. However, the data from the randomised trials does suggest that at up to five years follow-up partial fundoplication variants generally achieve a better outcome, with less side effects and better satisfaction measures following partial fundoplication in many of the trials. However, the two trials reporting data beyond ten years (23,29) suggest equivalent outcomes for Nissen versus partial fundoplication of whatever type are eventually achieved, but this can take up to 10 years!

A pragmatic approach to surgery for gastro-esophageal reflux

In the clinical practice in my Department we never divide the short gastric blood vessels and we currently construct a partial fundoplication in approximately 80% of the patients who undergo antireflux surgery (34). Our standard approach is to dissect the esophagus and the esophageal hiatus, followed by routine posterior hiatal repair irrespective of whether or not a hiatus hernia is evident, and then we construct a fundoplication. In patients with disordered or poor esophageal motility demonstrated at preoperative esophageal manometry, we always construct an anterior 180° partial fundoplication, whereas in patients with adequate esophageal motility we discuss the advantages and disadvantages of Nissen *vs.* partial fundoplication with each patient and offer a choice between the Nissen

fundoplication with a lower risk of recurrent reflux *vs.* partial (usually anterior 180°) fundoplication with a lower risk of side effects, and the patient is encouraged to make a choice. Following this discussion, approximately 2/3's choose to undergo an anterior 180° partial fundoplication.

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