Management of refractory heartburn: are we convinced that surgery is better than medical treatment?

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Title: Randomized trial of medical versus surgical treatment for refractory heartburn

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Summary

In a nutshell, this was a single centre, randomised-controlled trial comparing surgical vs medical modality in treating proton-pump inhibitor (PPI)-refractory heartburn; a common condition where optimal treatment approach is not known.[1]

All patients referred to the Veterans Affairs gastroenterology clinics for refractory heartburn were screened. Eligible patients would complete the gastro-oesophageal reflux disease (GORD) – Health Related Quality of Life (GORD-HRQL) questionnaire followed by 2-week trial of omeprazole at a dose of 20 mg twice daily, after which the GORD-HRQL was repeated. Patients who did not show improvement (i.e. decrease of >50% in the initial GORD-HRQL score) then underwent endoscopy with biopsies from the lower oesophagus, but also oesophageal manometry and intraluminal impedance–pH monitoring while continuing omeprazole at the same dose and frequency. Patients with severe reflux oesophagitis, non-GORD endoscopic abnormalities, oeosinophilic oesophagitis, achalasia or absent contractility were excluded. Other patient-reported outcomes included depression, anxiety and health function.

Eligible participants were subsequently randomised into surgical treatment (laparoscopic Nissen fundoplication), active medical treatment (omeprazole 20 mg twice daily plus titre-up doses of baclofen, and desipramine depending on symptoms) or control medical treatment (omeprazole 20 mg twice daily plus placebo). Heartburn medications were prohibited after fundoplication in the surgery group. Patients were followed up quarterly for a total of 1 year. Endpoint was treatment success, defined as a decrease of 50% or more in the GORD-HRQL score at 1 year.

A total of 366 patients were screened, 288 patients were excluded and remaining 78 patients then underwent randomisation. The baseline characteristics of study participants were similar between both treatment arms, with a male preponderance (82% males) and a mean age of 45 years old. The baseline GERD-HRQL scores, impedance–pH values and symptom association probability scores were comparable in all three groups.

Overall, the treatment success of surgery (18 out of 27 patients, 67%) was significantly superior to that of active medical treatment (eight out of 25 patients, 28%; $p = 0.007$) and of control medical treatment (three out of 26 patients, 12%; $p < 0.001$). The difference in treatment success rate between active and control medical therapy was 16% (95% confidence interval -5–38; $p = 0.17$). There were no reported deaths, only one patient required repeated surgery. In addition, surgery also benefitted patients with reflux hypersensitivity (71% improvement).

Opinion

Despite previous reports that antireflux surgery was equivalent to PPI in the control of GORD symptoms and improved cost effectiveness for as long as 5 years,[2,3] surgery is often regarded in many guidelines as the fail-safe approach rather than a first-line option.[4,5] However, there were studies

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that reported that surgical treatment is more effective than medical therapy with respect to patient-relevant outcomes in terms of short- and mid-term post surgery.[6] The decision for antireflux surgery requires an objective confirmation of GORD.[7] It is important to exclude other diagnoses of refractory heartburn prior to a decision of surgical or medical treatment plan. This was evidenced in the Spechler et al.[1] study where nearly 45% of total enrolled patients were excluded for either resolved symptoms or having another diagnosis. In addition to endoscopy, it is recommended that oesophageal manometry, impedance–pH monitoring and sometimes barium swallow are performed beforehand, but in real-life practice such investigations are not often available or accessible in certain countries.[5,6]

In the trial by Spechler et al.,[1] the total duration of heartburn symptoms prior to enrollment was not specified. The 2-week trial of omeprazole 20 mg twice daily seems a little too short a duration for a participant to be considered refractory heartburn. Some UK-based studies used 6–12 months of reflux symptoms as inclusion criteria.[8] Sandhu and Fass defined refractory heartburn as symptoms of reflux of gastric content that do not respond to a double dose of a PPI given for at least 8 weeks.[9] NICE has recommended a full-dose PPI for 4–8 weeks for initial treatment of GORD.[10] While the American College of Gastroenterology guidelines did not specify initial PPI treatment duration, they suggested steps for optimisation of PPI therapy including lifestyle modification, improvement of compliance, proper dosing time, split PPI dosing and switching to other PPIs.[11] All except proper dosing time was emphasised to participants in the current study by Spechler et al.[1] The short initial double-dose PPI 2-week trial in the study might lead to overdiagnosis of refractory heartburn and thus unnecessary invasive interventions.

It is not clear if the choice of omeprazole over newer PPIs would have made a difference in the results of the study by Spechler et al.[1] A meta-analysis in 2006 has shown that esomeprazole was significantly better than other PPIs (omeprazole, lansoprazole and pantoprazole) in the healing of erosive oesophagitis, although actual clinical benefits were only modest.[12] More recent network meta-analysis has concluded that compared to dexlansoprazole 60 mg, esomeprazole 20 mg, pantoprazole 40 mg, lansoprazole 30 mg, rabeprazole 20 mg and omeprazole 20 mg, esomeprazole 40 mg was superior in mucosal erosion healing and heartburn relief.[13] Even histamine 2-receptor antagonist could be of benefit for heartburn as long-term treatment despite having lower efficacy.[14] Furthermore, use of a single type of PPI for a short duration does not reflect real-life situations where other concomitant medications are commonly present.

In the study by Spechler et al.,[1] the treatment success of surgery is perhaps supported by a previous Cochrane review by Wileman et al.,[15] where four trials with a total of 1,232 randomised patients were analysed showing surgery was favoured over medical treatment in the outcome measure of health-related quality of life for a follow-up duration of 1–3 years, with maximum symptoms improvement at 3 months and 1 year after surgery. While surgery was effective, specific post-fundoplication complaints, such as dysphagia and bloating, remained a significant problem.[16] Previously, open surgery tended to have higher risks and costs, however, with the advancement of laparoscopic technique, some studies indicated that laparoscopic antireflux surgery is cost effective provided that its clinical benefits are sustained in the medium to long term.[3]

It is interesting that two-thirds of patients with reflux hypersensitivity responded to surgery in the Spechler et al. study.[1] While there are previous studies to support surgery for patients with hypersensitivity, there are also reports that indicate otherwise,[5] especially with pure acid sensitivity.[17] The present study was a carried out in a single centre and thus results are not generalisable to other centres owing to different skill sets and equipment. Therefore, a follow-up prospective study to assess medium- to long-term efficacy of surgery vs medical therapy appears to be the need of the hour.

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