Abstract and Introduction

Abstract


Context

Gastro-oesophageal reflux disease (GERD) is a chronic, relapsing condition – manifesting mostly with heartburn and acid regurgitation – that negatively affects daily quality of life. The two main treatments for GERD are medical – proton pump inhibitors (PPIs) and laparoscopic antireflux surgery (LARS). Both treatments have advantages and side effects that continue to be debated. On one hand, medical therapy may be associated with residual regurgitation and the potential long-term side effects of PPI (eg, osteoporotic fractures, drug–drug interaction). On the other hand, LARS may be associated with technical failures, dysphagia and bloating.

Methods

Under the acronym LOTUS, this 5-year randomised study compared efficacy and safety of LARS with ‘optimised’ PPI/oral esomeprazole (ESO) therapy for the long-term management of GERD. LOTUS is an open, parallel group, multicentre, randomised, controlled trial undertaken in expert and dedicated centres in 11 European countries. LARS was performed with a standardised protocol, incorporating a total fundoplication and a crural repair. Medical treatment involved oral ESO 20 mg once daily, which could be increased stepwise to 40 mg once daily and then 20 mg twice daily in the case of incomplete GERD control. A total of 372 patients (ESO, n=192; LARS, n=180) completed 5-year follow-up. Two hundred sixty-six patients were randomly assigned to receive ‘optimised’ ESO, 20–40 mg/day, allowing for dose adjustments; 288 were randomly assigned to undergo LARS, of whom 248 actually underwent the operation. Its main outcome measure was time-to-treatment failure (for LARS, defined as need for acid suppressive therapy; for ESO, inadequate symptom control after dose adjustment), expressed as estimated remission rates and analysed using the Kaplan–Meier method.

Findings

Estimated remission rates at 5 years were 92% (95% CI 89% to 96%) in the ESO group and 85% (95% CI 81% to 90%) in the LARS group (log-rank p=0.048). The difference between groups was not statistically significant following best-case scenario modelling of the effects of study dropout. The prevalence and severity of symptoms at 5 years in the ESO and LARS groups, respectively, were 16% and 8% for heartburn (p=0.14), 13% and 2% for acid regurgitation (p<0.001), 5% and 11% for dysphagia (p<0.001), 28% and 40% for bloating (p<0.001) and 40% and 57% for flatulence (p<0.001). Mortality during the study was low (four deaths in the ESO group and one death in the...
LARS group) and not attributed to treatment, and the percentages of patients reporting serious adverse events were similar in the ESO group (24.1%) and in the LARS group (28.6%). In conclusion, this multicentre clinical trial demonstrates that, either by drug-induced acid suppression with ESO or by LARS, most patients achieve and remain in symptomatic remission at 5 years.

Commentary

It is essential that this monumental, non-equivalence, non-superiority, exploratory study is dissected carefully, and its findings and conclusions are not misinterpreted or overstated. To this end, several important points need to be considered. First, the participating patients were responders to medical therapy (except for mild symptoms), not partial or complete non-responders. As such, the evidence provided by LOTUS would help the decision about proceeding with the alternative of surgery in those patients who are doing well on PPI but do not wish to take daily PPI with their associated, hitherto theoretical, long-term risks. Hence, these patients and their physicians will have to balance the gains (ie, equal benefits of surgery) with the risks – all nuisance symptoms such as bloating, flatulence and dysphagia – that may happen in the operated patients twice as frequently and may require visits and further interventions. LOTUS’s results will not apply to patients with complex, poorly responsive GERD, those with large hiatal hernias and ongoing regurgitation despite PPI or even those patients with heartburn and regurgitation, proven by extensive functional assessment with endoscopy/biopsies, pH monitoring and motility studies to have clear-cut GERD but with grades C or D oesophagitis at baseline. The study would not be applicable to most patients who require ESO 40 mg taken twice daily for symptom control.

Second, this multicentre study was performed in very carefully selected patients who were operated on by expert surgeons at large, academic centres. The results with patients operated on in the community setting or the results among poorly evaluated patients may not be similar, and the success/complication rates of LARS may be inferior to those seen in LOTUS. Numerous studies of long-term outcomes of LARS ranging from 5 to 12 years of follow-up suggest that the percentage of patients experiencing new, recurrent or persistent GERD-related symptoms after primary surgery ranges from 2% to 30%. Between 3% and 10% of these patients with a failed primary surgery undergo a revision, certainly less favourable than that in LOTUS.

What is the take-home message of this study and how do its results fit in with what is currently known in the field? LARS and dose-adjusted ESO are equally effective at 5 years if patients are carefully selected PPI responders and operated on by experts at large centres.

Competing interests
None.