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Review

Is the Stretta procedure as effective as the best medical and surgical treatments for gastro-oesophageal reflux disease? A best evidence topic

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ABSTRACT

A best evidence topic in surgery was written according to a structured protocol. The question addressed whether the Stretta® procedure is as effective as the best medical and surgical treatments for patients with symptoms of gastro-oesophageal reflux disease (GORD). One hundred and forty Stretta-related papers were identified using the reported search, of which five represented the best evidence to answer the clinical question. The authors, journal, date and country of publication, patient group, study type, relevant outcomes and results of these papers are tabulated. One study was a randomised controlled trial comparing Stretta with proton pump inhibitors (PPIs), and four were prospective observational studies that compared Stretta with laparoscopic fundoplication. These studies provide limited evidence that Stretta is as effective as medical therapy at controlling symptoms of GORD and may allow some patients to reduce their PPI use, but laparoscopic fundoplication appears to be more effective than Stretta though with a higher rate of adverse events. Further studies are required to determine the long-term efficacy of Stretta compared to the current best medical and surgical treatments.

1. Introduction

Gastro-oesophageal reflux disease (GORD) is a chronic condition involving the reflux of stomach contents into the oesophagus, leading to symptoms of heartburn, regurgitation, dysphagia and asthma, as well as being a predisposing factor for adenocarcinoma [1]. Currently, the best treatments for GORD are long-term acid suppression with proton pump inhibitors (PPIs) [2] or surgery in the form of laparoscopic fundoplication (LF) [3].

Although PPIs are effective inhibitors of acid secretion, they do not treat the cause of reflux and up to 58% of patients may not be satisfied with therapy [4]. Prolonged PPI therapy is associated with a number of adverse effects such as osteoporosis [5], *Clostridium difficile* infection [6] and community-acquired pneumonia [7], and up to 40% of patients have symptoms that are refractory to standard dose PPI therapy [8].

Surgery in the form of laparoscopic fundoplication (LF) is recommended by NICE in the UK for patients with a confirmed diagnosis of GORD and adequate symptom control with acid suppression therapy, but who do not wish to continue with this therapy long term [9]. Laparoscopic Nissen fundoplication (LNF), consisting of a total (360°) wrap is commonly performed, although other methods such as the laparoscopic Toupet fundoplication (LTF), which involves a partial (270°) posterior wrap, may be equally effective and carry a lower rate of post-operative dysphagia [10]. While LF is considered the 'gold standard' surgical treatment for GORD [11], it is an invasive procedure which is associated with a number of long-term side effects such as recurrence of disease, dysphagia and gas bloat syndrome [12]. Furthermore, while initial trials suggested that LF was more effective than medical management for the treatment of GORD [13], a new Cochrane review has found considerable uncertainty in the balance of benefits versus harms of LF compared to long-term medical treatment with PPIs [14].

In recent years, a number of new treatments for GORD have also been developed as alternatives to conventional surgery [15]. The new endoscopic treatments target the lower oesophageal sphincter (LOS) and reduce oesophageal acid exposure through 3 main methods: plication (e.g. Bard® EndoCinch™, CR Bard, Murray Hill,

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NJ, USA), bulking of the LOS with inert biopolymers (e.g. Enteryx®, Boston Scientific, Natick, MA, USA) and thermal ablation (e.g. Stretta®, Mederi Therapeutics Inc, Norwalk, CT, USA). Endoscopic plication, however, has been plagued by long-term failures [16] and injectable treatments continue to be investigated due to serious adverse events [17]. The LINX® procedure (Torax Medical Inc, Shoreview, MN, USA) is a new laparoscopic procedure that attempts to strengthen the LOS with magnets, and a recent BET in this journal has shown that this may be a safe and efficacious procedure for GORD procedures [18]. This is, however, still an invasive procedure with the inherent risks of laparoscopic surgery. In evaluating these new therapies for GORD, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) consortium strongly recommended the use of Stretta as an alternative to surgical management for GORD [19].

The Stretta procedure involves delivering radiofrequency energy to several points along the gastro-oesophageal junction (GOJ) via an endoscopically-placed catheter. It was developed as a minimally invasive alternative treatment for GORD, which could obviate the need for long term PPI therapy without bearing the inherent risks of surgery. The proposed mechanism of action is twofold: the radiofrequency energy may mechanically alter the GOJ as well as modulate neural pathways in order to reduce the frequency of transient lower oesophageal relaxations [20,21]. The most recent meta-analysis of Stretta studied the 3 sham-controlled trials and 1 trial comparing Stretta with PPIs and found no benefit of Stretta in reducing PPI use or improving quality of life [22]. The outcome of this meta-analysis was contested by SAGES [23] due to the small number of trials included in the study and the exclusion of two long-term studies suggesting durability of Stretta on symptoms over 10 years [24,25]. Although there have been several studies assessing outcomes after Stretta alone and trials involving sham procedures, there have been few studies comparing Stretta with PPI therapy and/or LF. In addition, none of the previously published systematic reviews [26,27], include the most recent studies comparing Stretta with LF.

We conducted a best evidence search according to a structured protocol [28] to determine how the Stretta procedure compares with the current best medical and surgical treatments for GORD.

2. Clinical scenario

In clinic, you are reviewing a 22-year-old man with severe symptoms of reflux, which are only controlled with high-dose PPI treatment. He has had no previous abdominal surgery and his investigations have revealed uncomplicated GORD without hiatus hernia. He has read about the Stretta procedure as an alternative to long term PPI therapy and laparoscopic fundoplication, and asks you whether this treatment modality would be appropriate.

3. Three part question

In patients with GORD, is the Stretta procedure as effective as the best medical or best surgical treatments?

4. Search strategy

A standardised literature search of the Medline database was conducted using the PubMed interface. The search terms were as follows: (Stretta OR radiofrequency) AND (reflux OR GERD OR GORD). The search was current as of 10th February 2016.

5. Search outcome

The search strategy identified 334 papers. Of these, 140 were related to the Stretta procedure. The following papers were excluded: 71 review articles of Stretta and/or endoscopic treatments for GORD, 37 studies of Stretta alone, 10 comment articles, 3 studies on animals, 3 cost analyses, 3 sham-controlled trials, 3 systematic reviews, 2 studies comparing endoluminal plication with Stretta, 1 responder subgroup analysis, 1 review of adverse events and 1 case report. This left 4 prospective observational studies that compared Stretta with laparoscopic fundoplication and 1 randomised-controlled trial (RCT) that compared Stretta with PPI treatment (see Table 1). These 5 papers were selected as representing the best evidence to answer this clinical question.

6. Results

The results from the 5 papers are summarised in Table 1.

7. Discussion

The best evidence comparing Stretta with the best medical and surgical treatments for GORD comprises 5 studies – 1 RCT comparing Stretta with PPI therapy alone, and 4 prospective observational studies comparing Stretta with laparoscopic fundoplication. There are currently no three-arm trials comparing Stretta, LF and PPI therapy together. All 5 studies included adult patients (aged 18 years or older) with GORD diagnosed through a combination of 24-h oesophageal pH monitoring, manometry and/or endoscopy.

7.1. Stretta vs. PPI therapy

Coron et al. [29] performed the only multicentre RCT comparing Stretta with best medical therapy. They selected 54 patients from 8 centres in France and randomised 43 to either Stretta or PPI-therapy alone. The participants in this trial underwent a pre-randomisation workup to define a group of patients with 'PPI-dependent' GORD. In contrast to the sham-controlled trial published by Corley et al. [30] where the percentage of patients using PPI at baseline was 88% in the Stretta group and 72% in the sham-treated group, all patients in this trial required at least a standard dose PPI regimen to achieve adequate symptom control. This allowed the authors to exclude a group of patients who achieved adequate symptom control with half-dose PPI regimen prior to randomisation, meaning that overall, these patients may have had more severe reflux disease than the sham trial.

Although there was a significant difference in the primary endpoint at 6 months with 78% of participants reducing or stopping PPI use compared to 40% in the control group ($p = 0.01$), there was no significant difference at 12 months with both intention-to-treat ($p = 0.16$) and per protocol analysis ($p = 0.10$). Secondary endpoints were analysed using per protocol analysis, and there were no significant differences in either quality of life outcomes at 12 months or acid exposure and endoscopic findings at 6 months. The main limitation of this trial was that it was significantly underpowered because Curon Medical decided to stop the development of the radiofrequency system during the trial. The authors' own power calculation stated that a sample size of 100 patients was required to detect a difference of 30% between the control and Stretta groups on the primary endpoint with a two-sided test with a type 1 error of 5% and a power of 80%, however, only 43 patients were randomised in the study. Despite the small sample size, a trend towards significance was found at 12 months for the primary endpoint.

7.2. Stretta vs. laparoscopic fundoplication

Liang et al. performed two prospective observational studies