REVIEW

POEM and the management of achalasia

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ABSTRACT

Achalasia is a rare oesophageal motility disorder predominantly causing dysphagia and regurgitation of food and fluids. Diagnosis is made typically after a combination of tests including endoscopy, barium swallow and oesophageal manometry. The advent of high-resolution manometry has led to the Chicago Classification which divided achalasia into three types. This improved the understanding of presentation, prognosis and might also help tailor therapy. Botulinum toxin has been shown to have good, but short-term efficacy. The predominant treatments include pneumatic balloon dilatation and laparoscopic Heller's myotomy, both of which have similar and durable outcomes, although the success of both reduces with time. Per-oral endoscopic myotomy (POEM) has been shown to be as effective, safe and durable as earlier treatments for achalasia; however, randomised controlled trials are lacking. Indications for POEM are expanding to other hypercontractile motility disorders of the oesophagus.

BACKGROUND

Achalasia is a rare, irreversible oesophageal motility disorder of unknown aetiology. Presentation can be varied and symptoms often intermittent rather than progressive, which can lead to a delay in diagnosis. Symptoms are typically characterised by dysphagia, chest pain, regurgitation of undigested foods and liquids and weight loss. Secondary symptoms can also include cough, recurrent chest infections, heartburn and choking.

Investigations

The Eckardt score is most commonly used to grade symptoms.¹ Each of the primary symptoms (dysphagia, regurgitation, chest pain and weight loss) is scored on a scale from 0 to 3. The maximum severity score is 12, while a score of ≤ 3 is commonly considered to be a satisfactory response. Primary investigations for achalasia

include endoscopy, barium swallow and oesophageal manometry. The primary aim of endoscopy is to exclude alternative pathology principally pseudo-achalasia and/or other causes of obstruction.

Standard manometry has been largely superseded by high-resolution manometry (HRM). A catheter with a maximum of 36 sensors is passed from the nares, through the oesophagus and across the lower oesophageal sphincter (LOS). Each sensor represents a pressure point. The software uses this information to reconstruct a visually intuitive spatiotemporal representation of oesophageal 'function' where changes in pressure are represented as changes in colour over time. The evolution of HRM has led to the development of a new classification of motor disorders, coined the Chicago Classification. This has also led to the subdivision of achalasia based on the combination of three important parameters, the first of which is mandatory:

1. Integrated relaxation pressure, a measure of impaired oesophago-gastric junction (OGJ) relaxation, defined as the lowest average relaxation pressure within the swallow relaxation window. In other words, this is a measure of resistance to flow across the OGJ.
2. Failed peristalsis for all swallows (with or without pressurisation throughout the oesophagus).
3. Premature contraction measured as a reduced time to deglutition, a new measure for spasm.

Thus, other than resistance at the OGJ, type I achalasia is typified by a dilated oesophagus with no measureable pressurisation. Type II exhibits pan-oesophageal (uniform) pressurisation throughout the tubular oesophagus and type III requires evidence of spastic contractions (figure 1).

A timed barium swallow (TBS) provides more information than a standard barium study. A larger volume of barium

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(up to 200 mL) is drunk in one go and the height/width of retained barium is measured at 1, 2 and 5 min. Typical standard barium appearances include a tapered OGJ and oesophageal dilatation; however, in addition, an objective measure of the barium height prior to and following therapy defines improvement in barium emptying as an objective predictor of long-term success. Furthermore, in asymptomatic patients following therapy, a lack of improvement in the barium height strongly predicted symptom recurrence at 1 year.²

Current treatments

Pharmacological treatment of achalasia includes nitrates, calcium channel blockers and botulinum toxin (BT).

BT blocks the release of acetylcholine which then fails to induce muscular contraction. BT was first used for the treatment of achalasia in 1994. Pasricha *et al*³ presented their results of a randomised controlled trial of 80 units of intersphincteric BT versus placebo. At 1 week, 90% of the BT injection group showed significant symptom reduction compared with the placebo group. The major limitation of BT is its short-term efficacy, with a decline in symptomatic response from 78.7% at 1 month decreasing to 70% at 3 months, 53.3% at 6 months and 40.6% at 1 year.⁴ The use of BT is therefore limited to patients where other treatments are contraindicated or considered to be too high risk.

Pneumatic balloon dilatation (PD) ruptures the LOS by placing a polythene non-compliant balloon within the LOS and forcefully stretching the muscle by incremental increases in diameter and pressure. The balloon is passed over a guide wire (normally under fluoroscopic guidance) and positioned centrally within the LOS. The balloon is gradually inflated until the waist is flattened (usually at 10–15 psi). Sequential dilatation over an interval of 2–4 weeks beginning with a 30 mm balloon and followed by 35 mm and, if required, 40 mm improves outcomes.^{5 6} Initial symptom relief varies from 75% to 90% and improves with increased balloon size. At 2⁶ and 5 years,⁷ the success rates were 86% and 85%, respectively, and although not considered a failure of therapy, 25% patients require at least one repeat dilatation within the 5-year follow-up.⁷ Vela *et al*⁵ found the success of a single PD (defined as freedom from additional PDs) was 62% at 6 months and 28% at 6 years (with risk factors for failure including younger age of <40 years, male sex, a wider oesophagus and poor emptying following TBS; however, the recent long-term follow-up found no difference in outcome based on sex and age.⁷ The most common side effect of PD is gastro-oesophageal reflux, which affects 15%–35% of patients and can be managed with acid reducing therapy.⁷ The reported rate of perforation is variable and likely also highly associated with operator

experience and the size of the initial balloon; however, when sequential dilatations starting at 30 mm and increasing to at least 35 mm, the risk was found to be 1.8% per procedure and up to 5% overall when multiple dilatations are required over time. Furthermore, perforations are more likely with the first dilatation and in older patients.^{6 7}

First described in 1913, the Heller's myotomy which dissects the anterior circular muscle fibres has been modified to involve a laparoscopic approach. Furthermore, to reduce the likelihood and severity of reflux, a partial Dor (anterior) or Toupet (posterior) fundoplication almost always follows the myotomy. The procedure is safe, with a mortality rate of 0.1%. Success rates vary from 76% to 100%⁴ and the durability of Laparoscopic Heller's myotomy (LHM) declines with reported symptom success rates of 90% at 2 years and 84% at 5 years.⁷ Long-term evaluation demonstrates a further reduction in symptomatic success to 75% at 15 years.⁸ Success appears to be greater in patients younger than 40 years, those with type II achalasia and the absence of a mega-oesophagus.

A number of studies have compared the outcomes of PD with LHM. In a cohort cross-sectional follow-up study, Vela *et al*⁵ found that the success of graded PD and LHM was similar: 90% vs 89% at 6 months and 44% vs 57% at 6 years with no risk factors for failure identified. The largest randomised study to date comparing PD with LHM has also shown similar outcomes using symptom improvement score, TBS at 5 min and manometry-derived LOS pressure at both 2 years (86% vs 90%, respectively) and 5 years (85% vs 84%). Although not a predictor of clinical success for either treatment, patients younger than 40 years more often needed repeat pneumatic dilatations than did those older than 40 years.^{6 7}

RECENT DEVELOPMENTS IN THERAPY: PER-ORAL ENDOSCOPIC MYOTOMY

Per-oral endoscopic myotomy

The introduction of per-oral endoscopic myotomy (POEM) into the management options for achalasia has paralleled the paradigm shift from surgical to endoscopic treatment of gastrointestinal disorders and comes under the expanding umbrella of natural orifice transluminal endoscopic surgery. The technique involves four steps resulting in a myotomy of the LOS with access from the luminal side via a submucosal tunnel. Initially, a 1.5 cm mucosal incision is made approximately 13 cm above the OGJ with a needle knife, followed by a submucosal tunnel (often in the 3 o'clock position) passing through the OGJ and 2–3 cm into the gastric submucosal space. A proximal to distal myotomy, predominantly (but not always exclusively) of the circular muscle fibres with a needle knife, is performed from 2 to 3 cm distal to the mucosal incision, extending to the OGJ and at

Achalasia Subtypes

Integrated Relaxation Pressure (IRP)

- Most optimal measure for quantifying deglutitive relaxation
- Reports lowest mean LOS pressure for four continuous or non-continuous seconds within the relaxation window

Figure 1 Chicago Classification for achalasia. LOS, lower oesophageal sphincter.

Figure 2 The steps required for per-oral endoscopic myotomy (POEM).

least 2 cm into the stomach. Finally, the mucosal incision is closed with clips⁹ (see [figure 2](#)).

Pasricha *et al* first described the feasibility of endoscopic submucosal oesophageal myotomy in pigs in 2007. Inoue performed the first POEM in 17 humans in 2010, demonstrating excellent short-term success.⁹

Since then numerous series have been published and a recent meta-analysis of 551 patients resulted in a pooled rate of clinical success rate of 93%, with an overall mean Eckardt score reduced from 7 to 1 ($p < 0.001$), although the follow-up period varied from 3 to 36 months.

The safety profile of POEM is presumed to be at least comparable to LHM or PD.^{10 11} In a large retrospective analysis of 1680 patients over 5 years, only 55 patients (3.3%) experienced major adverse incidents (mAEs) including delayed mucosal barrier failure (0.8%), delayed bleeding (0.2%), hydrothorax (0.5%) and pneumothorax (1.5%). 0.2% required intensive care unit admission. No patients required surgical conversion. Multivariate regression demonstrated that institution experience of <1 year (OR 3.85), air insufflation (OR 3.41) and mucosal oedema (OR 2.01) were identified as related risk factors for complications. After introducing CO₂ insufflation, the mAE rate declined to 1.9%.¹²

To date, there are no randomised controlled studies comparing POEM with either LHM or PD. A pooled analysis of three cohort studies comparing POEM and LHM showed similar outcomes. In particular, the total adverse events, perforation rate and operative time were similar. There was however a non-significant trend towards reduced hospital stay in the POEM group.^{13–15}

Acid reflux is the most common complication of POEM occurring in 20%–46% of patients measured by objective means including erosive oesophagitis and abnormal pH. This is comparable to reflux rates after LHM with fundoplication with rates from 21% to 42%. The numerical composite score for pH measurements, the Demeester is the same for both groups after 6 months.¹³

POEM also appears to be durable with success rates varying from 78.5% to 100% after follow-up periods of 24–36 months.^{10 16} The number of cases studied ranged from 45 to 500.¹⁰ Eight of the 18 case failures described by Werner and colleagues were found to have been among the first 10 cases of each of the three units that contributed to the data, thus suggesting an early learning curve. Hungness *et al*¹⁷ however presented their experience of 115 POEM cases while excluding the first 15 cases (to reduce the learning curve artefact) and found that the outcomes were comparable to data from other therapeutic modalities with an overall success rate 92% and 94% in patients with types I and II achalasia and 90% with type III achalasia.

POEM appears to be superior to LHM for type III achalasia, with success rates of 98% vs 80% respectively, along with lower complications rates and a reduced operative period.¹⁸

FUTURE POTENTIAL

An accurate predictor to guide treatment choice and also extent of myotomy would improve outcomes as many patients require retreatment. An inflatable balloon branded EndoFLIP (Crospon Medical Devices, Galway, Ireland) assesses distensibility across the LOS and also LOS length.¹⁹ There is promise in its use as a predictor of treatment outcome and also

the extent of myotomy for both POEM and LHM; however, more studies are required to explore the utility of this device.

Recent studies have suggested that POEM may be effective for motility disorders other than achalasia, such as diffuse oesophageal spasm and jackhammer oesophagus. Khasab and colleagues demonstrated a significant decrease in Eckardt scores after POEM (6.71 vs 1.13; $p=0.0001$). Overall, clinical response was observed in 93% of patients during a mean follow-up of 234 days. Chest pain significantly improved in 87% of patients who reported chest pain before POEM. Repeat manometry after POEM was available in 44 patients and showed resolution of initial manometric abnormalities in all cases.²⁰ The results are encouraging, but more studies are needed to determine where POEM fits in the therapeutic decision making for these patients.

Contributors Both authors contributed equally to the review.

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