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Peroral Endoscopic Myotomy as A Potential Alternative to Heller Myotomy and Pneumatic Dilation for the Treatment of Achalasia

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Abstract

Achalasia cardia is an esophageal motility disorder diagnosed with high-resolution manometry and categorized into type I, II and III. The mainstay treatment is laparoscopic Heller myotomy (LH), however many interventions have been introduced for achalasia management including pneumatic dilation (PD) and the newly emerging peroral endoscopic myotomy (POEM). In this review, we focus on the three main interventions that current guidelines suggest as safe and effective treatment options for achalasia; PD, LH and POEM. Both PD and LH are comparable for the management of achalasia type I and type II, while POEM utilizes natural orifice transluminal endoscopic surgery (NOTES) techniques and has gained increasing attention due to similar clinical success rates to those of the traditional interventions. However, an increased incidence of post-procedural gastroesophageal reflux (GERD) has been reported in the literature. Many studies have compared GERD between the different treatment modalities and the available antireflux interventions. Although the data are still conflicting, GERD can be prevented and, additionally, it seems to wane over time. This may make POEM potentially the optimal choice for the treatment of achalasia.

Keywords: Peroral Endoscopic Myotomy, Heller Myotomy, Pneumatic Dilation, Achalasia Cardia, Gastroesophageal Reflux Disease.

Introduction

Achalasia is an esophageal motor disorder that was first described by Willis in 1674, while the term "achalasia" was introduced by Hurst in 1927 [1, 2]. In fact, "achalasia" is a Greek word for "loss of relaxation". It affects males and females equally with an incidence of 0.3 to 1.63 per 100,000. However, in recent studies, the reported incidence is up to 26 per 100,00, probably due to more accurate diagnosis with advanced technology, such as high-resolution manometry (HRM) [3, 4]. Multiple causative factors have been studied, such as viral infections, autoimmune diseases or environmental factors, but the exact pathogenesis of achalasia remains unknown. Pathophysiologically, an initiating inflammatory process leads to loss of inhibitory ganglionic cells in the myenteric plexus of the esophagus and to an imbalance of excitatory and inhibitory neurotransmitters (NO and acetylcholine respectively) in the neuromuscular junction. This results in an increased muscle tone in the esophagogastric junction (EGJ), which is the cornerstone of achalasia diagnosis [5].

Based on distinct patterns in HRM, achalasia is categorized into 3 subtypes; Type I, type II and type III. Type I (classic achalasia) is characterized by low intraesophageal pressure, type II by pan-esophageal pressurization and type III by high-amplitude spastic contractions [6]. According to the American Society of

Gastrointestinal Endoscopy (ASGE), there are three feasible, efficacious and safe treatment choices today; Pneumatic dilation (PD), laparoscopic Heller myotomy (LH) and the recently emerging per-oral endoscopic myotomy (POEM). PD and laparoscopic Heller myotomy are both equally effective treatments for type I and type II achalasia, while for type III the POEM is the preferred treatment [4].

During PD a balloon dilator is positioned at the EGJ under fluoroscopic guidance and inflated to a certain pressure point. Balloons of 30 mm, 35 mm and 40 mm are used successively until the desired outcome is reached[7, 8]. This method is safe and effective and has comparable results with LH in terms of long-term clinical success and patient quality of life[4, 9]. LH, however, was for a long time the procedure of choice, mainly because a fundoplication was also feasible during the operation, which had been shown in clinical trials to decrease postoperative reflux from 47.6% to 9%[10–12]. The myotomy begins at 2 cm to 3 cm (extended myotomy) above the GEJ to the right of the anterior vagus nerve, the longitudinal muscle fibers are divided and the dissection continues down to the mucosa. The myotomy should extend about 6 cm proximally and 2-3 cm distally to the EGJ. It is considered complete when the "gun barrel view" is achieved through intraoperative endoscopy. To finish the reconstruction, a "Toupet" or "Dor" fundoplication is preferably performed, aiming to reduce the incidence of postoperative acid reflux and the formation of strictures[13–15]. The downside of LH is the incidence of postoperative dysphagia, which can manifest due to inadequate myotomy, GERD with strictures, fibrosis, or a herniated fundoplication. A longer myotomy on the other side could lead to increased postoperative GERD rates (up to 42%). Lastly, reported long-term failure rates of LH reach 35% in high-volume centers [16].

In 2010, Inoue et al. introduced POEM as a novel, safe and effective treatment for esophageal achalasia. They described the dissection of the circular muscle layer through a submucosal tunnel created endoscopically in 17 adult patients. The myotomy extended from about 7 cm proximally to the GEJ to 2 cm distally and no serious complications were described. Immediately after the procedure, a statistically significant decrease in resting pressure on manometry was reported and in the short follow-up of 5 months, no recurrence of dysphagia was present [17]. Since then, larger studies have shown that GERD, reflux esophagitis, or, rarely, recurrence of dysphagia could present in the long-term, but clinical success rates may be over 90% at 3 years and may decrease to 87.1% at 5 years [18–20].

Despite technical differences, both LH and PD and LH and POEM are comparable treatment options for the treatment of achalasia types I and II. For the management of type III achalasia there is a trend favoring POEM, but not enough data are yet available to be a strong guideline recommendation. In everyday practice, the choice of intervention is based on local expertise, achalasia type and, of course, patient preference and goals [4, 21].

Gastroesophageal Reflux Disease after Treatment for Achalasia

Pneumatic dilation, LH and POEM are considered safe and effective treatment options for patients with achalasia, with exceptional results as was previously discussed. However, postoperative gastric acid reflux is, reportedly, a common adverse event among all interventions that can significantly affect the quality of life of the patients and could even require a second additional antireflux reintervention [15].

Torressan et al. used PD to treat 72 patients with achalasia type I and type II. In a median follow-up of 56 months, 7 patients presented with relapse and 5 of them were referred for either LH or POEM due to ineffectiveness of redilation. Furthermore, 27.7% presented with symptomatic GERD and needed therapy with proton pump inhibitors (PPI) [9]. Similarly, in the study of Chan et al. 26% of patients (6 individuals) who underwent LH and Dor fundoplication and 15.2% of patients (5 individuals) who underwent POEM for achalasia presented with GERD symptoms after the procedure and 3 in each group required PPIs. Symptomatic GERD between the groups and the need for PPIs was not statistically significantly different (p=0.311) [22]. Teh et al. prospectively studied the outcomes of 58 patients who underwent POEM. Twenty-five of them (43.1%) had symptomatic reflux at 1-year follow-up. Fourteen of them had increased acid exposure as found at 24-hour pH-impedance, but only 16% of the episodes were acidic, while 77.3% were weakly acidic [23]. It is noteworthy that heartburn symptoms could be caused by a fermentation-induced acidic environment, which is food stasis in the esophagus, and not true GERD. Fermentation is differentiated from true reflux by pHmetry.

Therefore, its role is substantial in the follow-up of patients treated for achalasia [24]. Unfortunately, not all patients with reflux will develop symptoms, making them inadvertently subjected to the risks of esophageal gastric acid exposure, such as erosive esophagitis, Barrett's esophagus and even cancer [25–27]. Hopefully, even though POEM may have a higher GERD incidence in the early postoperative period, it seems that reflux wanes over time both after POEM and after LH regardless of the utilization of PPIs [28].

Published an interesting paper on the management of gastric reflux after POEM in which the authors outline the risk factors leading to GERD after POEM, the optimal tools for the evaluation and the management of acid reflux, as well as the current and most effective techniques for reflux prevention. Specifically, age, BMI, female gender, GEJ pressure below 45 mmHg, previous treatments, the presence of hiatal hernia, as well as technical aspects of the procedure such as long, posterior myotomy and full thickness myotomy have been shown to increase the risk for post-POEM acid reflux. The importance of manual pH tracing is highlighted in order to differentiate fermentation-induced acidification due to food stasis, from true reflux. Together with clinical evaluation and endoscopy the clinician could accurately identify patients with GERD and initiate traditional treatment with PPIs or one of the emerging strategies of electrical stimulation or device-assisted endoscopic fundoplication. However, the most significant aspect is the prevention of GERD after POEM. Many measures have been proposed, such as the preservation of sling fibers which reinforce the natural anti-reflux barrier or the constitution of per-oral fundoplication after performing an anterior myotomy incorporating natural orifice transluminal endoscopic surgery (NOTES). A debate regarding the length of the myotomy is going on, as a shorter myotomy may decrease the incidence of acid reflux, but a longer one could provide better

symptom relief. This is also prevalent in the literature, as many systematic reviews have studied the effects of different myotomy lengths on post-procedural reflux incidence. For instance, Zhang et al. in their meta-analysis showed that a shorter myotomy leads to a significantly lower abnormal acid reflux by pH monitoring and a significantly less operative time than a longer one [30]. On the other hand, Weng et al. did not find any difference regarding acid reflux between shorter and longer myotomy groups [31]. Despite these conflicting data, most of the studies agree that a shorter myotomy length reduces the operative time and offers similar clinical success rates to a longer myotomy[31–33].

Finally, extended research has also been conducted as to whether anterior or posterior myotomy during POEM would have better results. Nabi et al. mentioned in their review that no substantial differences have been reported for these two variations. This is in agreement with other meta-analyses that showed that anterior and posterior myotomies are comparable in terms of clinical success and GERD occurrence at 2-year follow-up [34-36].

Clinical Considerations

Per-oral endoscopic myotomy is a major advancement in achalasia treatment as it incorporates NOTES, it is minimally invasive and has similar or superior results to the traditional techniques. However, it requires expertise, with a learning curve of approximately 40-60 cases for non-experts in endoscopic submucosal dissection to be able to perform it fluently [37]. Therefore, it is important for doctors to get special training to safely perform POEM on patients in their home institutions. Whatsmore, according to a meta-analysis by Zhong et al., this technique offers significant improvement in the quality of life of patients and in addition to high clinical success rates in the general population, it can be a safe and effective treatment modality both for geriatric and obese patients [38, 39].

Conclusion

Per-oral endoscopic myotomy is an emerging minimally invasive technique that incorporates NOTES, for the treatment of achalasia cardia. It has been compared with many interventions, including PD and the traditional gold standard LH, and the results show no significant differences in terms of postoperative complications, length of hospital stay or pain. Data are conflicting in terms of postoperative gastric acid reflux incidence, as some authors report increased reflux after POEM, however, this finding has been associated with food stasis and fermentation and not necessarily true reflux. Current guidelines suggest that either POEM or LH are comparable treatment options for patients with achalasia type I and II. Also, POEM is suggested as the preferred treatment for achalasia type III, but the quality of the data are still low. Nevertheless, the choice of treatment should be based on local expertise and on a shared decision-making between the patient and the health care provider.

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