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Review Article

Non-achalasia esophageal motility disorders: Role of per-oral endoscopic myotomy

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A B S T R A C T

Major disorders of esophageal peristalsis other than achalasia include Jackhammer esophagus (JHE), distal esophageal spasm (DES), and esophago-gastric junction outflow obstruction (EGJOO). These disorders are rare, distinct from achalasia and characterized by high resolution manometry. Unlike achalasia, the treatment strategies are not well defined in these disorders. Therapies directed at lower esophageal sphincter may be inadequate in JHE and DES as a variable length of esophageal body is also involved in symptom generation. On the other hand, EGJOO is a more heterogeneous group and the decision for endoscopic treatment is based on comprehensive evaluation of the underlying etiology. A subset of patients with EGJOO without significant stasis may improve on conservative treatment. Per-oral endoscopic myotomy (POEM) is a newer endoscopic treatment modality that has established its role in the management of achalasia. Limited studies suggest the efficacy of POEM in non-achalasia esophageal motility disorders as well. The ability to perform long esophageal myotomies with POEM makes it an attractive management tool for these patients.

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Keywords: Endoscopy; Esophageal motility disorders; Esophageal spasm, diffuse; Myotomy

Introduction

Non-achalasia esophageal motility disorders include Jackhammer esophagus (JHE), distal esophageal spasm (DES), and esophagogastric junction outflow obstruction (EGJOO). These disorders are distinct from achalasia and have been classified as major disorders of peristalsis as per the Chicago classification v3.0.¹ Esophageal high resolution manometry (HRM) is useful in characterizing these disorders. The most common presenting symptom in these disorders is dysphagia. In addition, concomitant chest pain is noticed in patients with JHE and DES. In contrast to achalasia, these disorders are rare with unclear natural course of the disease. Consequently, there are no established guidelines for the management of non-achalasia motility disorders.

In the following section, we discuss the diagnostic criteria and the management of these motility disorders. In addition, the current evidence for the role of per-oral endoscopic myotomy (POEM) in these disorders will be elaborated.

Manometric Criteria for Non-Achalasia Esophageal Motility Disorders

HRM is paramount in classifying esophageal motility disorders including achalasia and other non-achalasia esophageal disorders of peristalsis (Table 1).¹ HRM allows for the diagnosis as well as selecting the appropriate management strategies in these esophageal motility disorders. The length of esophageal myotomy can be selected by reviewing the tracings on HRM.

Disorders of EGJOO are a broad category inclusive of achalasia and EGJOO. Both these disorders are characterized manometrically by an elevated integrated relaxation pressure (IRP > 15 mmHg). The distinguishing feature between achalasia and EGJOO is the presence of intact or weak peristalsis in the latter.

JHE or hypercontractile esophagus is defined by a distal contractile integral (DCI) of > 8,000 mmHg.s.cm in at least 20% of the swallows (Fig. 1A). In contrast to achalasia and EGJOO, IRP is normal in vast majority of patients. However, it is important to note that in a subgroup of JHE hypercontractility may also involve lower esophageal sphincter (LES) or even restricted to LES.¹ This may have therapeutic implications and justifies the inclusion

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Table 1 The Chicago Classification of Esophageal Motility Disorders v3.0

Motility disorder	Manometric criteria
Jackhammer esophagus	At least two swallows with DCI > 8,000 mmHg·s·cm; hypercontractility may involve, or even be localized to, the LES
Diffuse esophageal spasm	Normal median IRP, $\geq 20\%$ premature contractions with DCI > 450 mmHg·s·cm
Esophagogastric junction outflow obstruction	Elevated median IRP (> 15 mmHg), sufficient evidence of peristalsis such that criteria for types I–III achalasia are not met

Data from the article of Kahrilas et al (*Neurogastroenterol Motil.* 2015;27:160–74).¹

DCI, distal contractile integral; LES, lower esophageal sphincter; IRP, integrated relaxation pressure.

Fig. 1. High resolution manometry in a case with Jackhammer esophagus. (A) Pre-POEM manometry revealing a high distal contractile integral (13,298 mmHg.s.cm). A normal relaxation of lower esophageal sphincter can be appreciated. (B) Post-POEM manometry in the same case revealing normalization of the distal contractile integral (866 mmHg.s.cm). POEM, per-oral endoscopic myotomy; UES, upper esophageal sphincter; LES, lower esophageal sphincter; CDP, contractile deceleration point.

of LES during POEM in this subgroup of patients with JHE.

DES is defined as premature contractions ($\geq 20\%$, distal latency < 4.5 sec) along with a normal relaxation of LES (IRP < 15 mmHg).¹ Reduced distal latency and normal IRP distinguish DES from JHE and disorders of EGJOO, respectively. The current classification using reduced distal latency has been found to be superior to the previous one which was based on conventional manometry and used contractile frontal velocity (> 8 cm/sec) as the diagnostic criteria. It is important to note that distal latency is also dependent on age and size. Therefore, the diagnosis of DES should be made with caution in pediatric age group.²

JHE

JHE is a rare esophageal motility disorder found in about 3%–4% of patients subjected to motility testing.³ Dysphagia is the most common presenting complaint followed by chest pain in cases with JHE.^{3–5} Interestingly, the severity of dysphagia but not chest pain has been found to be associated with DCI.^{5,6} Contrary to the popular belief, a subgroup of patients with JHE may have hypertensive LES pressures (> 40 mmHg) and impaired relaxation of LES (IRP > 15 mmHg).⁴ Consequently, these patients may benefit from LES targeted therapies like pneumatic dilatation. On the contrary, the response to dysphagia and chest pain may be sub-optimal in LES only therapies due to involvement of a long length of esophagus. Due to the rarity of this condition, there are limited studies on the impact of treatment modality on the clinical outcomes of JHE. POEM has been evaluated in several small studies including 4 to 18 patients with JHE.^{7–13} In these studies, POEM has been found to be a safe and effective treatment in patients with JHE with clinical success ranging from 70% to 100% (Table 2, Fig. 1).^{7–13} POEM has distinct advantages over Heller's myotomy in these cases as the entire esophagus is exposed and accessible

for carrying out a long myotomy. The length of esophageal myotomy can be determined by reviewing the tracings on HRM and proximal extent of spastic contractions on endoscopy (Fig. 1A).¹⁰ Whether LES should be included in the myotomy during POEM is debatable. The inclusion of LES appears logical in a subset of patients with JHE with high LES pressures and impaired relaxation of LES. Whereas, patients with normal LES metrics on manometry may not drive much benefit from LES myotomy. In addition, the risk of gastroesophageal reflux adds to the argument against the inclusion of LES during POEM in these patients. Experts believe that sparing LES may not be wise in the presence of an aperistaltic esophagus as a result of POEM.¹⁰ As a consequence, the propulsive force of esophagus may be inadequate to push the food bolus across a preserved LES.⁸ Moreover, a subset of patients with JHE may progress to achalasia with time. In a retrospective study, 3 of 12 patients with a diagnosis of JHE progressed to type III achalasia over a mean of 24 months (range, 19–31 months).¹⁴

However, there are no studies comparing these two approaches i.e., inclusion vs exclusion of LES during POEM in cases with JHE. Our approach remains the one to include LES during POEM and limit the gastric extent of myotomy to 2–3 cm. We also prefer to preserve oblique fibers during posterior POEM to minimize the risk of post-POEM reflux.

DES

DES is an uncommon esophageal motility disorder of esophagus characterized manometrically by a short distal latency (< 4.5 sec) in the absence of impaired relaxation of LES (IRP < 15 mmHg).¹ The patients with DES typically present with intermittent chest pain and dysphagia. Due to intermittent nature of symptoms, manometry may be required on more than one occasion in cases with a high index of suspicion and normal manometry

Table 2 Studies Evaluating the Outcome of Per-Oral Endoscopic Myotomy in Non-Achalasia Esophageal Motility Disorders

Study	Type (n)	Length of myotomy (cm)*	Efficacy (%)	Follow-up
Khashab et al (2015) ⁷	DES: 9	16.6	100	234 days
	JHE: 10	14.3	70	
Bechara et al (2016) ⁸	JHE: 4	12–23	75	1 yr
Albers et al (2018) ⁹	DES: 1	12.5	100	1 yr
	JHE: 6		83.3	
Khashab et al (2018) ¹⁰	DES: 17	15.1	84.9	272 days
	JHE: 18		93.3	195 days
	EGJOO: 15			
Masadeh et al (2019) ¹³	DES: 3	NR	67	1 yr
	JHE: 5		100	
	EGJOO: 8		88	
Filicori et al (2019) ¹¹	DES: 11	13.0	80	48 mo
	JHE: 15	9.9		
	EGJOO: 14	7.4		
Bernardot et al (2020) ¹²	DES: 4	10 (esophageal)	80 (3 mo)	6 mo
	JHE: 13		63.2 (6 mo)	
	EGJOO: 7			
	Spastic: 6			

DES, distal esophageal spasm; JHE, Jackhammer esophagus; EGJOO, esophagogastric junction outflow obstruction; NR, not reported.

*Values are presented as mean or range.

tracings. Various treatment options have been utilized for DES including pharmacological (calcium channel blockers, sublingual nitroglycerin), botulinum toxin injection, and Heller's myotomy. However, ideal treatment option for DES remains unknown due to rarity of the condition and absence of quality data. More recently, POEM has emerged as an effective endoscopic treatment modality in these patients (Table 2).^{7–13} As mentioned above, the entire esophagus is exposed during POEM and therefore, it allows for myotomy of the entire diseased esophagus. The response to POEM has been found to range between 67%–100% in recently published studies.^{7,9–13} The technique of POEM in DES is essentially similar to that used in achalasia cardia. However, longer myotomy is required in these cases. HRM is useful in defining the diseased esophageal segment and deciding the length of myotomy. As with JHE, the inclusion of LES into myotomy remains controversial in patients with DES. There are few case reports where DES transformed into achalasia over a period of time. These reports formed the basis of the theory that both DES and achalasia may be the spectrums of same disease and therefore, LES should be included in the myotomy during POEM. We suggest a gastric myotomy of 2–3 cm and avoidance of oblique fibers during POEM. With this approach, the incidence of gastroesophageal reflux disease (GERD) as well as the probability of dysphagia in future is likely to be reduced.¹⁵

EGJOO

The potential etiologies for EGJOO are hiatal hernia, mechanical obstruction (infiltrative diseases or malignancies), and early or incompletely expressed achalasia.¹ Besides HRM, the diagnostic workup for EGJOO include gastroscopy and imaging like computed tomography or endosonography in addition to HRM.

The natural history of patients with EGJOO is unclear and a substantial proportion of patients may improve spontaneously on follow-up. Therefore, careful patient selection is important to avoid overtreatment in cases with functional EGJOO. Pérez-Fernández et al¹⁶ reported the outcomes in 28 patients with EGJOO. A structural cause of obstruction was detected in 29% of

patients. Majority of the patients presented with dysphagia (36%) and typical (25%) or atypical (21%) symptoms of GERD. Spontaneous resolution of symptoms was observed in 40% of patients during a follow-up of 6-months. The predictors of spontaneous resolution in this study included typical symptoms of GERD or epigastralgia as the main symptom and resting or basal pressure of the upper esophageal sphincter < 50 mmHg.¹⁶

The management of EGJOO is based on the severity of symptoms, etiology of outflow obstruction (functional vs organic), and objective evidence of stasis on timed barium esophagogram. Etiology specific treatment is required in cases with organic EGJOO due to a specific underlying cause like hiatal hernia, infiltrative esophageal disorders etc. Conservative management may suffice in cases with mild, intermittent symptoms, and in those without significant stasis. In cases planned for LES directed therapies, it may be useful to stratify patients based on criteria evaluated in previous studies. Several parameters have been evaluated to predict clinically relevant EGJOO requiring treatment. These include impaired relaxation of LES to amyl nitrite, IRP > 20 mmHg, presence of abnormal liquid bolus transit, compartmental pressurization on multichannel intraluminal impedance with HRM, and reduced EGJ distensibility index on functional luminal imaging probe (FLIP) panometry.^{17–20} In a recent study, FLIP was found to be useful in objectively selecting patients for treatment in cases with EGJOO.²⁰ In patients with a normal EGJ distensibility index (> 3 mm²/mmHg) on FLIP, improvement in Eckardt score was noticed in all with conservative management. Whereas, the response to achalasia type management was found in 78% cases with a low distensibility index i.e., < 2 mm²/mmHg.²⁰

Among the management modalities pneumatic dilatation, botulinum toxin injection, and POEM have been utilized in EGJOO with a reasonable degree of success. Limited data suggest that POEM may be effective in cases with EGJOO (Table 2).^{10–13} In a retrospective, multicenter study including 15 patients with EGJOO, clinical success was documented in 93% of patients.¹⁰ Similar response has been reciprocated in few other small studies (Table 2).

Technique of POEM in Non-Achalasia Esophageal Motility Disorders

POEM was initially described by Inoue et al²¹ in patients with achalasia cardia about a decade ago. Since then, the technique of POEM has largely remained unchanged for the management of achalasia cardia. Although, the steps of POEM procedure remain the same few technical modifications are required while performing POEM in non-achalasia motility disorders especially JHE and DES. POEM can be performed via an anterior (1–2 o'clock) or posterior (4–5 o'clock) route. Randomized studies comparing anterior and posterior POEM in patients with achalasia did not find any clinically relevant difference with respect to efficacy, complications, and incidence of GERD.²² However, these techniques have not been specifically compared in non-achalasia motility disorders. POEM may be more complex in these disorders in terms of pre-operative mapping of disease and subsequent myotomy. A longer length of esophageal myotomy is usually required in these cases as the spasticity involves a variable length of esophageal body. The length of esophageal myotomy is selected by reviewing the tracings of HRM and identifying the proximal border of high-pressure zone (Fig. 1). In addition, barium esophagogram and the endoscopic appearance of upper-border of spastic esophageal contractions are complementary to HRM in determining the diseased length of esophagus.

The inclusion of LES into POEM has been a subject of debate in cases with JHE and DES as mentioned before. LES myotomy should be performed in cases with EGJOO and JHE with concomitant hypercontractile LES or impaired relaxation of LES on HRM. The performance of LES myotomy is debatable in DES as well as JHE without involvement of LES. When performed, the risk of post-POEM reflux must be taken into account. POEM can be performed via an anterior or posterior approach. It may be useful to restrict the gastric length of myotomy to < 4 cm and preserve oblique fibers during posterior POEM to reduce the incidence of GERD.^{15,23} More recently, endoscopic fundoplication using the principles of NOTES (natural orifice transluminal endoscopic surgery) has been described.²⁴ However, prospective studies are required before incorporating NOTES fundoplication in clinical practice.

Summary

Non-achalasia esophageal motility disorders is a heterogeneous group of disorders including JHE, DES, and EGJOO. These disorders present with dysphagia and chest pain. These disorders are rare and there are no controlled trials evaluating different management strategies in these patients. Traditionally, these patients have been managed using pharmacotherapy including smooth muscle relaxants, botulinum toxin injection, dilatation, and Heller's myotomy. POEM has emerged as a minimally invasive endoscopic treatment for achalasia and has been shown to be efficacious in these non-achalasia motility disorders as well. However, majority of the data is marred with small sample size and retrospective design. In addition, the fluidity of these disorders suggests that the management strategies should be carefully selected. Nevertheless, POEM has the potential to be the treatment modality of choice in these disorders mainly due to its ability to cut long segments of diseased esophagus.

Conflicts of Interest

No potential conflict of interest relevant to this article was re-

ported.

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