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Title: **Clinical outcomes and safety of high resolution manometry guided superficial partial circular muscle myotomy in per-oral endoscopic myotomy for Jackhammer esophagus: A case series and literature review**

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Dear Editor and reviewers

I would like to thank the editor and reviewers of *World Journal of Clinical Cases* for their reviews of our article.

The reviewers' comments enabled us to revise and improve the manuscript. All changes are summarized below:

Response to reviewer's comment

Comment1.

Well written manuscript. i have some suggestions.

how is the follow up of patient?

Answer)

Outcome was measured as follows;

1) patients' symptom 2) result of high resolution manometry within 1 month after POEM

We are willing to add the sentences in OUTCOME and follow-up session (in red)

After the procedure, the patient's symptoms dramatically improved and post-POEM HRM was within the normal range. During a 1-year follow-up period, patients were in good health and remained symptom free.

Comment 2.

"Jackhammer esophagus is a severe disease."(<https://doi.org/10.1016/j.ijso.2018.04.037>) and (Am J Case Rep. 2014; 15: 168-171.) I suggest both of these up to date studies for the references.

Answer) We are willing to add those references in discussion session

Reference 1.

A survey of current approaches to thyroid nodules and thyroid operations

Ardalsik^a DenizFirat^b IsmayilYilmaz^b KemalPeker^b OguzIdiz^c BahriYilmaz^d
IsmailDemiryilmaz^b FehmiCelebi^b

<https://doi.org/10.1016/j.ijisu.2018.04.037>

reference 2.

Am J Case Rep. 2014; 15: 168-171.

Published online 2014 Apr 26. doi: 10.12659/AJCR.890260

PMCID: PMC4010621

PMID: 24803977

A case report of esophageal perforation: Complication of nasogastric tube placement

Arda Isik,^{A,B,C,D,E,F,1} Deniz Firat,^{B,C,D,F,1} Kemal Peker,^{A,D,E,F,1} Ilyas Sayar,^{A,E,F,2} Oguz Idiz,^{A,D,E,3} and Mehmet Soytürk^{B,D,4}

Response to Editor's comment

Comment 1. Please provide language certificate letter by professional English language editing companies (Classification of manuscript language quality evaluation is B).

For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies mentioned in 'The Revision Policies of BPG for Article'.

Response) Thank you very much for your concerns. The English in this document has beenchecked by at least two professional editors, both native speakers of English. For a certificate, please see:

<http://www.textcheck.com/certificate/9b3uMP>

Comment 2. Please provide the decomposable figure of Figures, whose parts are movable and editable. So you can put the original pictures in PPT and submit it in the system.

Response) Thank you very much for your comments. We uploaded original pictures in PPT files.

Comment 3. Your manuscript should be prepared with 1) Word-processing Software, using 2) 12 pt 3) Book Antiqua font and 4) 1.5 line spacing with ample margins.

Response) We appreciate your comments. We revised our manuscript as you recommended.

Comment 4.

Our policy for the Case Report manuscript requires the title to include the disease name, the number of cases, and the phrase "literature review". In addition, the **description of the paper as a literature review must be supported by the manuscript's content.** Please **update the reference list** and **add references with accompanying textual content** that will strengthen the manuscript as a literature review of the appropriate and up-to-date case-related information. Please note that if authors only add the words "literature review" to the title, but do not revise the textual content of the manuscript to provide a literature review, the manuscript will be rejected.

Response) Thank you very much for your valuable and important comments. We revised our manuscript (especially in discussion session) as below.

Discussion

We here report two patients with Jackhammer esophagus who were successfully treated with HRM-guided superficial partial circular muscle myotomy during POEM. After the procedures, both patients reported improve symptoms with no side effects. The current cases suggest that HRM-guided superficial partial circular muscle myotomy may be a potential treatment option for Jackhammer esophagus with a relatively low rate of post-procedure complications as compared to conventional POEM.

Jackhammer esophagus is rare and severe disease [2, 16, 17]. Jackhammer esophagus is extremely high amplitudes contractions and within normal limit of peristaltic contractions [4]. Treatment strategy for Jackhammer esophagus includes medication for smooth muscle relaxation (nifedipine), anti-reflex medication, and pneumatic dilatation of LES [4]. Because of the rare incidence of Jackhammer esophagus, proper evaluation of incidence is not easy, the medication refractory Jackhammer esophagus has been increasing. Recently for medical refractory Jackhammer esophagus, POEM was introduced^[11].

POEM is the first clinically efficacious natural orifice transluminal endoscopic

surgery (NOTES) with an endoscopic safety profile [1, 15, 18, 19]. However, despite its safety profile, post-POEM complications are not rare [6, 7, 9, 20]. Conventional POEM for Jackhammer esophagus is associated with several side effects including post-procedure sigmoid esophagus and ineffective esophageal motility^[14, 19]. It remains debated whether the lower esophageal sphincter should be cut to prevent symptom development after the procedure [7, 14, 18]. Recent systemic review showed that the pooled rate of clinical success in patients of Jackhammer esophagus for POEM was 89.6%^[21]. The success rates of both the length >10cms, and the length<10cms were 91.1% and 89.1%, respectively [21]. There are several researches on the symptom in patients with Jackhammer esophagus and the pre-peak and post-peak phase of contraction^[3, 22]. In these regards, to distinguish the contractile integral components of pre-peak and post peak phase contractile activity is important to treat Jack hammer disease [3, 22]. However, there are still concerns regarding post-POEM complications for medication refractory Jackhammer esophagus after POEM, such as passage disturbance and sigmoid esophagus^[2, 11-14].

To improve treatment efficacies and reduce the complications in the treatment of Jack hammer esophagus after POEM, we focused two issues; 1) to measure the accurate segments which are hypercontractile in the esophagus, 2) to conserve the esophageal motility after POEM procedures. HRM-guided superficial partial circular muscle myotomy which we introduced is a modified type of conventional POEM, and this method is expected to reduce side effects and increase treatment efficacy^[5, 11, 14]. Because partial circular myotomy during POEM involves cutting only the superficial layer of the circular esophageal muscle and not the full thickness of the muscle nor the full circular muscle layer, even after POEM, the previously diagnosed Jackhammer esophagus consists circular and longitudinal layer of muscle with its nature but reduced hypercontractile movements [11, 14, 19]. Moreover, in addition to region-targeted therapy, partial circular muscle myotomy was performed under HRM guidance to selectively detect hypercontractile segments. Therefore, decreased esophageal motility after the procedure are prevented. **Moreover, it is not necessary to cut the lower**

esophageal sphincter in a partial circular myotomy when low esophageal sphincter is not involved [23]. This method not only reduces the occurrence of side effects associated with conventional POEM, including partial or full thickness POEM, but also improves treatment efficacy.

批注 [오전1]: LES 를 involve 하지 않은경우에

In conclusion, HRM-guided superficial partial circular muscle myotomy during POEM may be a promising alternative to conventional POEM for the treatment of patients with Jackhammer esophagus who are refractory to conventional medical therapy, which is associated with improved efficacy and safety profile.

Comment 5.

Abstract:

The structured abstract should be at least 250 words. The abstract subsections will include background, case summary, and conclusion, written as:

BACKGROUND (no more than 80 words)

What does this case report add to the medical literature? Why did you write it up?

CASE SUMMARY (no more than 150 words)

What were the chief complaints, diagnoses, interventions, and outcomes?

CONCLUSION (no more than 20 words)

What is the main "take-away" lesson from this case?

<Before revision>

Jack hammer esophagus is a relatively rare disease and to date, there is no dramatic treatment option. Recently, conventional per-oral endoscopic myotomy (POEM) have expanded their area into Jackhammer esophagus. However, several complications such as post procedure motility disorders (ex. passage disturbance) are issues after POEM. To

overcome these issues, we here introduced high-resolution manometry (HRM)-guided superficial partial circular muscle myotomy, which involves cutting only the superficial layer of the esophageal circular muscle. Therefore, the circular and longitudinal muscle layers are preserved but hypercontractile movements are reduced, even after POEM. Herein, we report two cases of patients with Jackhammer esophagus who were treated with HRM-guided extremely superficial partial circular muscle myotomy during POEM. Case 1 was a 53-year-old female with medication-refractory odynophagia and case 2 was a 47-year-old man who presented with chest pain. They were diagnosed with Jackhammer esophagus using HRM, and the hypercontractile segments of the esophagus were identified. HRM-guided extremely superficial partial circular muscle myotomy was performed while preserving the lower esophageal sphincter, and clinical symptoms responded to this therapy. During a 1-year follow-up period, patients were in good health and remained symptom free.

<After revision>

Background: Jack hammer esophagus is a relatively rare disease and to date, there is no dramatic treatment option. Recently, conventional per-oral endoscopic myotomy (POEM) have expanded their area into Jackhammer esophagus. However, several complications such as post procedure motility disorders (ex. passage disturbance) are issues after POEM. To overcome these issues, we here introduced high-resolution manometry (HRM)-guided superficial partial circular muscle myotomy, which involves cutting only the superficial layer of the esophageal circular muscle.

Case Summary: We report two cases of patients with Jackhammer esophagus who were treated with HRM-guided extremely superficial partial circular muscle myotomy during POEM. Case 1 was a 53-year-old female with medication-refractory odynophagia and case 2 was a 47-year-old man who presented with chest pain. They were diagnosed with Jackhammer esophagus using HRM, and the hypercontractile segments of the esophagus were identified. HRM-guided extremely superficial partial circular muscle myotomy was performed while preserving the lower esophageal sphincter. Therefore, the circular and longitudinal muscle layers are preserved but hypercontractile movements are reduced, even

after POEM. Patients' clinical symptoms dramatically improved right after POEM, and 6 month-follow up HRM revealed completely resolved status. During a 1-year follow-up period, patients were still in good health and remained symptom free.

Conclusion: HRM-guided superficial partial circular muscle myotomy may be a promising alternative to conventional POEM for treating Jackhammer esophagus with improved efficacy.

Comment 6. Please change the main body of the case report to the following format. CASE PRESENTATION

Under the heading of Case Presentation, the following seven aspects must be presented in this order: 1) Chief complaints; 2) History of present illness; 3) History of past illness; 4) Personal and family history; 5) Physical examination upon admission; 6) Laboratory examinations—e.g., routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests and occult blood test, blood biochemistry, immune indexes, and infection indexes; and 7) Imaging examinations—e.g., ultrasound, plain abdominal and pelvic CT scan, high-resolution chest CT scan, and head MRI. The patient case presentation should be descriptive, organized chronologically, accurate, salient, and presented in a narrative form.

<Before revision>

Case 1.

A 53-year-old woman was referred to our hospital for odynophagia and regurgitation. She had no known medical or surgical history. She had previously presented to a local hospital and had been prescribed oral proton pump inhibitors and nitroglycerin for several months, but her symptoms did not improve. There were no abnormal findings on electrocardiogram, and laboratory tests including total blood count, liver function, renal function, and other basic chemical tests were normal. On upper endoscopy, no abnormal findings were reported.

Esophagography (barium radiography) showed spasmodic contraction of the distal esophagus and a narrowing of the esophageal cavity (Figure1). HRM showed high-amplitude distal esophageal contractions with a DCI value $> 8,000$ mmHg.s.cm for 6 of a total of 10 swallows. The highest DCI value was 13,553 mmHg.s.cm (Figure1). The patient underwent POEM on June 18, 2017 (Figure3). HRM showed high-amplitude distal esophageal contractions located 25–38 cm from the incisors according to the distance gauge of the pressure measuring tubes. Therefore, we performed partial circular muscle myotomy of the esophageal muscle on the right side (Figure 3). We preserved the lower esophageal sphincter. After the procedure, the patient's symptoms dramatically improved and post-POEM HRM was within the normal range.

Case 2.

A 47-year-old man was referred to the gastrointestinal department from the cardiovascular department for atypical chest pain even after stent angiography and administration of anti-angina medications. He had two-vessel cardiovascular disease with angina and a stent was inserted. Despite use of a patent stent, cardiovascular medications including nitrates, and a 3-month trial of proton pump inhibitors, atypical squeezing pain in the epigastric region remained. Laboratory tests were normal, including total blood count, liver function, renal function, and other basic chemical tests. On upper endoscopy, no abnormal findings were reported. Barium radiography showed spasmodic contractions of the distal esophagus and a narrow esophageal cavity. HRM showed high-amplitude distal esophageal contractions with a DCI value $> 8,000$ mmHg.s.cm for 8 of a total of 10 swallows (Figure 2). The highest DCI value was 21,024 mmHg.s.cm. POEM was performed on September 20, 2018. HRM showed high-amplitude distal esophageal contractions located 28–39 cm from the incisors according to the distance gauge of the pressure measuring tubes. We

performed partial circular muscle myotomy of the esophageal muscle at this site and preserved the lower esophageal sphincter. After the procedure, the patient's symptoms dramatically improved and post-POEM HRM was within the normal range.

<After Revision>

Case 1.

Chief complaints

A 53-year-old woman was referred to our hospital for odynophagia and regurgitation.

History of present illness

She had previously presented to a local hospital and had been prescribed oral proton pump inhibitors and nitroglycerin for several months, but her symptoms did not improve.

History of past illness/ Personal and family history

She had no known medical or surgical history. Her family history was negative.

Physical examination upon admission

Physical examination on admission revealed no abnormal palpable mass on head and neck area.

Laboratory examinations

There were no abnormal findings on electrocardiogram, and laboratory tests including total blood count, liver function, renal function, and other basic chemical tests were normal.

Imaging examinations

Esophagography (barium radiography) showed spasmodic contraction of the distal esophagus and a narrowing of the esophageal cavity (Figure1). HRM showed high-amplitude distal esophageal contractions with a DCI value > 8,000 mmHg.s.cm for 6 of a total of 10 swallows. The highest DCI value was 13,553 mmHg.s.cm (Figure1). HRM showed high-amplitude distal esophageal contractions located 25–38 cm from the incisors according to the distance gauge of the pressure measuring tubes.

Final diagnosis

The final diagnosis was medication refractory Jack hammer esophagus without involvement of low esophageal sphincter.

Treatment

The patient underwent HRM-guided superficial partial circular muscle myotomy (Figure3). Since HRM showed high-amplitude distal esophageal contractions located 25–38 cm from the incisors, we performed partial circular muscle myotomy of the esophageal muscle on the right side (Figure 3). We preserved the lower esophageal sphincter.

Outcome and follow up

After the procedure, the patient's symptoms dramatically improved and post-POEM HRM was within the normal range. During a 1-year follow-up period, patients were in good health and remained symptom free.

Case 2.

Chief complaints

A 47-year-old man was referred to the gastrointestinal department for atypical chest pain for 6 month

History of present illness

He was previously presented to the cardiovascular department for atypical chest pain.

However his symptom was not improved even after stent angiography and administration of anti-angina medications and oral proton pump inhibitors for several months. After then he was referred to the gastrointestinal department.

History of past illness/ Personal and family history

He had two-vessel cardiovascular disease with angina and a stent was inserted 5 years ago. Despite use of a patent stent, cardiovascular medications including nitrates, and a 3-month trial of proton pump inhibitors, atypical squeezing pain in the epigastric region remained. His family history was negative.

Physical examination upon admission

Physical examination on admission revealed no abnormal findings.

Laboratory examinations

Laboratory tests were normal, including total blood count, liver function, renal function, and other basic chemical tests.

Imaging examinations

On upper endoscopy, no abnormal findings were reported. Barium radiography showed spasmodic contractions of the distal esophagus and a narrow esophageal cavity (Figure 2). HRM showed high-amplitude distal esophageal contractions with a DCI value $> 8,000$ mmHg.s.cm for 8 of a total of 10 swallows (Figure 2 B). The highest DCI value was 21,024 mmHg.s.cm. POEM was performed. HRM showed high-amplitude distal esophageal contractions located 28–39 cm from the incisors according to the distance gauge of the pressure measuring tubes.

Final diagnosis

The final diagnosis was medication refractory Jack hammer esophagus without involvement of low esophageal sphincter.

Treatment

The patient underwent HRM-guided superficial partial circular muscle myotomy (Figure 3). Since HRM showed high-amplitude distal esophageal contractions located 25–38 cm from the incisors, we performed partial circular muscle myotomy of the esophageal muscle on the right side (Figure 3). We preserved the lower esophageal sphincter.

We performed HRM-guided superficial partial circular muscle myotomy of the esophageal muscle. Since HRM showed high-amplitude distal esophageal contractions located 28–39 cm from the incisors, we performed partial circular muscle myotomy of the esophageal muscle on the right side (Figure 3) and preserved the lower esophageal sphincter.

Outcome and follow up

After the procedure, the patient's symptoms dramatically improved and post-POEM HRM was within the normal range (Figure 2C). During a 6 month follow-up period, patients were in good health and remained symptom free.

Comment 6. Please check and confirm that there are no repeated references!

Answer) Thank you for your careful comments. We thoroughly rechecked the references.

Comment 7. Please provide the decomposable figure of Figures, whose parts are movable and editable. So you can put the original pictures in **PPT** and submit it in the system.

Answer) We are willing to put the original pictures in PPT and submitted. Thank you.