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Comparison of outcomes of per-oral endoscopic myotomy for primary achalasia among geriatric and younger patients: A single center study

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Abstract

Background: Geriatric patients with primary achalasia have high disease burden and are often left untreated. Locally, there is no existing study on the comparison of Per-oral Endoscopic Myotomy (POEM) outcomes in young versus older patients, hence the aim of this study to determine the success rate and safety of POEM in primary achalasia among younger patients versus geriatrics.

Methods: Records of all primary achalasia patients who underwent POEM at our institution between January 2015 to December 2021 were reviewed. Patients were categorized into two: group A (<65 years) and group B (>/= 65 years). Sample size was determined using equivalence test. Fisher's Exact Test or Pearson's Chi Square Test, and Mann Whitney U Test for independent samples were employed to analyze the difference of categorical and continuous variables, respectively, between the two age groups. A p-value <0.05 was considered as statistically significant.

Results: The study included 49 patients: group A (n=40) and group B (n=9). The technical success rate was 100% since all patients on both groups had complete myotomy without significant differences in operative time, submucosal tunnel length, esophageal and gastric myotomy, and number of endoscopic clips. Clinical success of POEM was similar for both groups, as all patients had an Eckardt score of 0 post-POEM. Adverse event rate was low and mild in in terms of severity, with no significant difference between the two age groups. The median length of hospital stay was 5 days for both age groups.

Conclusion: This study demonstrated high clinical and technical success rate as well as low complication rate of POEM among older patients with primary achalasia, similar to the results in the younger age group. With this, we recommend POEM as a safe and effective treatment option for elderly patients with primary achalasia.

Keywords: *POEM, Achalasia, Geriatrics*

Introduction

The impact of achalasia as a chronic esophageal motility disorder significantly affects the quality of life due to symptoms of occasional chest discomfort, dysphagia and regurgitation. Its pathology is secondary to inadequate relaxation of the lower esophageal sphincter (LES) due to progressive ganglion cell degeneration in the myenteric plexus.[1]

The effect of advancing age in esophageal motility among patients with achalasia is still unknown. What is known is that these symptoms cause greater impairment and debilitation among elderly.[1] It is noted that healthy older people have lower population of ganglion cells in the intramural myenteric plexus which is associated with decreased esophageal peristalsis.[5]

All available treatment options for achalasia are aimed at facilitating bolus transit across the LES which includes pharmacotherapy, chemical paralysis through botulinum toxin A (Botox) injection, mechanical dilation through pneumatic balloon dilation, and surgical dilation.[6]

Among younger patients with achalasia, Laparoscopic Heller myotomy (HM), albeit an invasive procedure, is considered as the treatment of choice due to high success rate.[7] Its safety among geriatric achalasia patients still needs further analysis. The high risk of perforation at 4-7% in interventions such as balloon dilation and laparoscopic HM is of concern among the geriatric population.[1,9] Other treatment options including pharmacologic regimen, most of the time, offer short-lived results and incomplete relief which wanes through time.[6]

The development of Per-oral Endoscopic Myotomy (POEM) by Dr. Inoue et al. in 2010 revolutionized the treatment strategies in achalasia. In a meta-analysis on the comparative efficacy of POEM and Heller myotomy by Park et al., it showed that when it comes to short-term efficacy, POEM was superior to HM. However, there was no noted difference in reflux symptoms and pH level monitoring.[7]

The disease burden of achalasia among geriatric patients remains as there is still controversy on the treatment recommendation in this particular subgroup, hence there is a large percentage of them left untreated.[8] Due to presence of comorbidities, treatment options offered to geriatrics include mechanical dilation, Botox injection and pharmacotherapy. Barriers to undergoing endoscopic or surgical interventions may be due to perceived risks and complications among elderlies.

In review of 148 achalasia patients who underwent POEM in Japan, 37% of which (n=55) were elderly (aged (≥ 65 years) while 63% were younger (<65 years), it showed evidence of safety and effectiveness of POEM for patients of advanced age. The operative details, outcomes and treatment success rates were comparable in the two groups. Since it was a minimally invasive approach, the findings in this study suggested that POEM, with its promising results, could be a preferred therapeutic intervention among geriatrics with achalasia.[8]

However, currently, there are insufficient studies regarding treatment options for primary achalasia in the local setting. In this study, we aim to compare the success rate and safety of POEM for primary achalasia among elderly versus younger patients with the hope to contribute to existing evidence on the clinical indication of POEM.

Materials and Methods

This was a retrospective, cross-sectional, analytical study conducted at De La Salle University Medical Center (DLSUMC), in Dasmariñas, Cavite, Philippines through chart review from the Medical Records Section. The Institutional Review Board and Ethics Committee approved the study. Admitted patients with primary achalasia who underwent POEM at DLSUMC from January 2015 to December 2021 were included. All patients diagnosed with primary achalasia who underwent POEM were included and analyzed into two groups: group A (<65 years) and group B (>/= 65 years). Inclusion Criteria included: 1) patients diagnosed with primary achalasia and underwent POEM; 2) patients might or might not have prior treatment for primary achalasia; 3) patient must be admitted at DLSUMC for POEM between January 2015 to December 2021. Patients diagnosed with other esophageal disorder such as Diffuse esophageal spasm, Barrett's esophagus etc. were excluded.

The computed sample size was 39 which was determined using Raosoft software equivalence test using 95% confidence interval. This was used as the minimum number of cases to be included in the study.

A total of 49 patients met the inclusion criteria and were included in the study analysis. Information gathered include clinicodemographic profile including age, gender, achalasia subtype, duration of symptoms, comorbidities and prior treatments received for primary achalasia. Data on assessing clinical success included pre and post POEM Eckardt score. Technical success data, on the other hand, included information on completion of myotomy, procedural time, and myotomy length (esophageal and gastric). The rate and severity of different adverse events were also included such as esophageal hemorrhage/perforation, hypotension, pleural effusion, lung infection, conversion to surgical procedure. Lastly, the length of hospital stay was also included in chart review.

Statistical Analysis

This study primarily aimed to determine if there was significant difference in the success rate and safety of POEM in primary achalasia among younger patients vs geriatrics. The outcome variables included clinical success, technical success, rate and severity of adverse events and length of hospital stay. Confounding variables included patient's coexisting comorbidities, prior treatments received for primary achalasia and the duration of achalasia symptoms. These confounders might be difficult to eliminate since there was a limited number of primary achalasia patients who underwent POEM in the institution and patient characteristics. Continuation of this study to include more subjects would help improve the effect of these confounders.

Distributions of continuous variables, such as the pre- and post-POEM Eckardt scores, procedural time, submucosal tunnel length, myotomy length, number of endoscopic clips and length of hospital stay, were presented using the median and the first and third quartiles. Meanwhile, categorical variables, such as age group, gender, achalasia subtype, comorbidities, prior treatments for primary achalasia, completion of myotomy and the presence and severity of adverse events were described using frequency counts and percentages.

Fisher's Exact Test or Pearson's Chi Square Test, and Mann Whitney U Test for independent samples were employed to analyze the difference of categorical and continuous variables, respectively, between the two age groups. Statistical analyses were conducted using SPSS v26. For this study, a p-value <0.05 was considered as statistically significant.

Results

The study included 49 patients divided into 2 groups: Group A young patients (n=40) and Group B geriatrics (n=9). Table 1 shows the demographics and baseline characteristics of primary achalasia patients. The median age of patients in the young age group was 31 years old (Q1-Q3: 29-58), while that in the geriatric age group was 72 years old (Q1-Q3: 67-73). No significant difference was found in the gender distribution and the percentage of patients with diabetes mellitus, respiratory disease and other comorbidities between the two age groups. However, there was a higher percentage of geriatric patients with hypertension compared to the young age group (55.6% vs. 10.0%, p = 0.006). Meanwhile, none of the patients had cerebrovascular or cardiovascular diseases.

No significant difference between the young and geriatric age groups was found in the distribution of achalasia subtypes and in the percentage of patients that underwent treatments prior to POEM. The severity of symptoms pre-POEM, as measured by the Eckardt score, was also similar between both groups (11.0 vs. 10.0, p = 0.533).

Table 1. Demographics and baseline characteristics

Variables	**All Patients n = 49** *n (%) or median (Q1, Q3)*		**Group A (<65 years old) n = 40** *n (%) or median (Q1, Q3)*		**Group B (>/=65 years old) n = 9** *n (%) or median (Q1, Q3)*		**p-value**
Age at POEM, in years	34.0	(29.0, 58.0)	31.0	(26.3, 45.8)	72.0	(67.0, 73.0)	**0.000** [a]
Gender							0.463 [b]
Male	25	(51.0%)	19	(47.5%)	6	(66.7%)	
Female	24	(49.0%)	21	(52.5%)	3	(33.3%)	
Achalasia subtype							0.130 [c]
Type I	12	(24.5%)	8	(20.0%)	4	(44.4%)	0.195 [b]
Type II	9	(18.4%)	8	(20.0%)	1	(11.1%)	1.000 [b]
Type III	1	(2.0%)	0	(0.0%)	1	(11.1%)	0.184 [b]
Unspecified	27	(55.1%)	24	(60.0%)	3	(33.3%)	0.266 [b]
Pre-POEM Eckardt Score	11.0	(9.0, 12.0)	11.0	(9.3, 12.0)	10.0	(8.5, 12.0)	0.533 [a]
Comorbidities							
Hypertension	9	(18.4%)	4	(10.0%)	5	(55.6%)	**0.006** [b]
Diabetes mellitus	3	(6.1%)	1	(2.5%)	2	(22.2%)	0.083 [b]
Respiratory disease	2	(4.1%)	2	(5.0%)	0	(0.0%)	1.000 [b]
Others	4	(8.2%)	2	(5.0%)	2	(22.2%)	0.149 [b]
None	35	(71.4%)	31	(77.5%)	4	(44.4%)	0.096 [b]
Prior treatments							
Botox	4	(8.2%)	3	(7.5%)	1	(11.1%)	0.569 [b]
Pneumatic dilation	10	(20.4%)	8	(20.0%)	2	(22.2%)	1.000 [b]
Botox and dilation	2	(4.1%)	1	(2.5%)	1	(11.1%)	0.337 [b]
None	37	(75.5%)	30	(75.0%)	7	(77.8%)	1.000 [b]

Note: p-values in bold are statistically significant
[a] Mann-Whitney U Test
[b] Fisher's Exact Test
[c] Pearson's Chi Square Test

Table 2 demonstrates the technical and the clinical outcomes of POEM among patients with primary achalasia. POEM peri-procedural analysis showed no significant differences in operative time (85 min vs. 95 min, p = 0.339), submucosal tunnel length (15.5 cm vs. 15.0 cm, p = 0.352), esophageal myotomy length (10 cm vs. 10 cm, p = 0.657), gastric myotomy length (3.0 vs. 3.0, p = 0.255), and number of endoscopic clips (8 vs 5, p = 0.909) between the young and geriatric patients, respectively. Thus, the technical success rate was 100% since all patients had complete myotomy. The median length of hospital stay was 5 days for both age groups (p=1.000).

Clinical success of POEM was similar for both groups, as all patients had an Eckardt score of 0 post-POEM. Moreover, a similar percentage of young and old patients did not report an AE within 24 to 48 hours post-POEM (87.5% vs. 88.9%, p = 1.000). For those with AE post-POEM, no significant difference between the two age groups was found in the percentage who had esophageal hemorrhage, lung infection and pneumoperitoneum or pneumomediastinum. In terms of severity, most had only developed a Grade 1 AE (10% vs. 11.1%, p = 1.000), while only one patient, belonging in the young age group, had a Grade 2 AE. Meanwhile, none of the patients had developed hypotension, esophageal perforation, pleural effusion, atelectasis, or had converted to a surgical procedure.

Table 2. Technical and Clinical Outcomes of POEM

Variables	All Patients n = 49 *n (%) or median (Q1, Q3)*		Group A (<65 years old) n = 40 *n (%) or median (Q1, Q3)*		Group B (>/=65 years old) n = 9 *n (%) or median (Q1, Q3)*		p-value	
Technical success								
Procedural time (minutes)	90.0	(67.0, 122.0)	85.0	(67.0, 114.3)	95.0	(63.5, 167.0)	0.339	[a]
Submucosal tunnel length (cm)	15.0	(13.0, 18.0)	15.5	(13.0, 18.0)	15.0	(12.5, 16.5)	0.352	[a]
Esophageal myotomy length (cm)	10.0	(10.0, 12.0)	10.0	(10.0, 11.8)	10.0	(9.0, 13.5)	0.657	[a]
Gastric myotomy length (cm)	3.0	(3.0, 3.0)	3.0	(3.0, 3.0)	3.0	(2.0, 3.0)	0.255	[a]
Number of endoscopic clips	7.0	(6.0, 8.5)	8.0	(6.0, 8.8)	7.0	(6.5, 9.5)	0.909	[a]
Duration of hospital stay (days)	5.0	(4.0, 6.0)	5.0	(4.0, 6.0)	5.0	(4.0, 5.5)	1.000	[a]
Adverse effects								
Esophageal hemorrhage	1	(2.0%)	1	(2.5%)	0	(0.0%)	1.000	[b]
Lung infection	4	(8.2%)	4	(10.0%)	0	(0.0%)	1.000	[b]
Pneumoperitoneum/Pneumomediastinum	2	(4.1%)	1	(2.5%)	1	(11.1%)	0.337	[b]
Presence and severity of adverse effect/s							0.889	[c]
No adverse effect	43	(87.8%)	35	(87.5%)	8	(88.9%)	1.000	[b]
Grade 1	5	(10.2%)	4	(10.0%)	1	(11.1%)	1.000	[b]
Grade 2	1	(2.0%)	1	(2.5%)	0	(0.0%)	1.000	[b]

[a] Mann-Whitney U Test
[b] Fisher's Exact Test
[c] Pearson's Chi Square Test

Discussion

This was the first local study comparing the outcomes of POEM among younger and elderly patients with primary achalasia. Based on the results, both age groups had similar and high clinical and technical success rates upon comparing the outcomes of POEM. Symptom relief post-POEM was remarkable correlating with the effectiveness of POEM for primary achalasia even for elderly patients. Low complications and severity were observed with no life-threatening conditions encountered.

Primary achalasia peaks during the third to fourth decade of life and later after the sixth decade of life which coincides with the mean age at POEM of the patients in this study, 31 and 72 years old, respectively.[2] The disease burden among geriatric patients remains due to presence of comorbidities, perceived risks and complications of definitive surgical intervention and controversy on the treatment recommendation for the advanced age group.[8] Majority of the patients on both age groups, more than 75%, were treatment-naive prior to POEM. This coincides with previous findings that about 60% of achalasia patients older than 75 years old were left untreated.[5,8] Among the elderly patients with previous treatment, botox injection (11%) and pneumatic dilation (22%) or the combination of both (11%) were documented. No patient underwent Heller's myotomy which is considered as the definitive treatment for primary achalasia.[7]

The presence of comorbidities among patients with primary achalasia is associated with several challenges in performing complex procedures such that they have less physiological reserve on top of underlying comorbidities, making them at higher risk for surgical procedures and anesthesia.[8,9] In terms of comorbidities, there is a significantly higher percentage of elderly patients with hypertension ($p = 0.006$) and 22.2% of them had diabetes mellitus. No patients reported to have cardiovascular or cerebrovascular disease. Despite having comorbidities, only 11.1% of the elderly age group developed AE, specifically pneumomediastinum post-POEM with low severity (grade 1). In the young age group, only one patient developed grade 2 AE with lung infection. In an international multicenter study by Chen et al. in 2017, they evaluated the clinical efficacy and safety of POEM in 76 octogenarians which showed adverse event in 14.5% of patients in which majority were graded as mild and only one event graded as severe.[9]

In terms of duration of hospitalization, this study noted no significant difference on the days of hospital stay of patients with a median of 5 days ($p=1.000$). This however was relatively longer in comparison to the median length of stay of patients of 1 day for both age groups who underwent POEM in a study by Sanaka et al.[8]

Clinical success defined as Eckardt score of ≤ 3 post-POEM was achieved such that all patients in both age groups had a score of 0. The pre-POEM Eckardt score was not statistically significant ($p=0.533$). Moreover, technical success defined as completion of myotomy was observed in all patients also on both age groups. Its variables such as procedural time, submucosal tunnel length, esophageal and gastric myotomy length and, number of endoscopic clips showed no significant difference between the two age groups. The study by Sanaka et al. in 2020 on POEM for geriatric patients with achalasia showed similar treatment success rates between the two groups (94.9% young vs 94.7% in old patients).[8] This was also consistent with the results of the multicenter study of Chen et al., the technical and clinical success rates were 93.4% and 90.8%, respectively.[9]

Our study had several limitations which could be improved with subsequent follow-up studies. First, this was a retrospective study such that follow-up period of at least 6 months and long-term outcomes were not included. The number of patients included in the study was not well distributed in between the two age groups despite including all patients who underwent POEM during the specified study period. Lastly, clinical success was best documented using high resolution esophageal manometry which however was not performed in all included patients since it was expensive and was not readily available in the institution where the study was conducted.

Conclusion

This study demonstrates high clinical and technical success rate, as well as low complication rate of POEM among older patients with primary achalasia, similar to the results in the younger age group. Hence, to answer the research question, we accept the null hypothesis that there is no significant difference in the success rate and safety of POEM for both younger and older age groups. With this, we recommend POEM as a safe and effective treatment option for elderly patients with primary achalasia. With the perceived limitations, subsequent follow-up study is recommended.

References

1. Vaezi M, Pandolfino J, Yadlapati R et. al. ACG Clinical Guidelines: Diagnosis and Management of Achalasia. American Journal of Gastroenterology. 115:1393-1411. August 2020. doi:10.14309/ajg.0000000000000731

2. Nijhuis R, Zaninotto G, Roman S, et. al. European guidelines on achalasia: United European Gastroenterology and European Society of Neurogastroenterology and Motility recommendations. United European Gastroenterology Journal Vol. 8 (1) 13-33. 2020. doi: 10.1177/2050640620903213

3. Spechler SJ. Achalasia: Pathogenesis, clinical manifestations, and diagnosis. UptoDate. January 2021

4. Khashab MA. Peroral endoscopic myotomy (POEM). UptoDate. December 2019

5. Schechter R, Lemme E, Novais P et al. Achalasia in the elderly patient: a comparative study. Arq Gastroenterology. Jan-Mar 2011;48(1):19-23. doi.org/10.1590/S0004-280320110 00100005

6. Craft R, Aguilar B, Flahive C et al. Outcomes of Minimally Invasive Myotomy for the Treatment of Achalasia in the Elderly. JSLS. 2010 Jul-Sep; 14(3): 342–347
doi: 10.4293/108680810X12924466007368.

7. Park C, Jung D, Kim D, et al. Comparative efficacy of per-oral endoscopic myotomy and Heller myotomy in patients with achalasia: a meta-analysis. Gastrointest Endosc. 2019 Oct;90(4):546-558.e3. doi: 10.1016/j.gie.2019.05.046.

8. Sanaka M, Chadalavada P, Alomari M et al. Peroral endoscopic myotomy is a safe and effective treatment modality for geriatric patients with achalasia. Esophagus. 2020 Oct;17(4):484-491. doi: 10.1007/s10388-020-00746-5

9. Chen Y, Inoue H, Ujiki M et al. An international multicenter study evaluating the clinical efficacy and safety of per-oral endoscopic myotomy in octogenarians. Gastrointest Endosc. 2018 Apr;87(4):956-961. doi: 10.1016/j.gie.2017.02.007

10. National Institutes of Health. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. US Department of Health and Human Services. November 2017

11. Leyden J, Moss A, MacMathua P. Endoscopic pneumatic dilation versus botulinum toxin injection in the management of primary achalasia. The Cochrane Collaboration. 2014. DOI: 10.1002/14651858.CD005046.pub3.

12. Hoeij F, Prins L, Smout A, et al. Efficacy and safety of pneumatic dilation in achalasia: A systematic review and meta-analysis. Neurogastroenterol Motil. 2019 Jul;31(7):e13548. doi: 10.1111/nmo.13548

13. Patel D, Kim H, Zifodya J et al. Idiopathic (primary) achalasia: a review. Orphanet Journal of Rare Disease. 10,89. 2015. DOI 10.1186/s13023-015-0302-1.

14. Cho Y, and Kim S. Current Status of Peroral Endoscopic Myotomy. Clin Endosc. 2018. doi: 10.5946/ce.2017.165

15. Inoue H, Minami H, Kobayashi Y et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy 2010 Apr;42(4):265-71. DOI: 10.1055/s-0029-1244080

16. Zhong C, Huang S, Xia, H, et al. Role of Peroral Endoscopic Myotomy in Geriatric Patients with Achalasia: A Systematic Review and Meta-Analysis. Dig Dis 2022; 40:106-114. doi.org/10.1159/000516024

17. Mari A, Sbeit W, Abboud W et al. Achalasia in the Elderly: Diagnostic Approach and a Proposed Treatment Algorithm Based on a Comprehensive Literature Review. J Clin Med. 2021 Dec; 10(23):5565. doi: 10.3390/jcm10235565

18. Lynch K, Pandolfino J, Howden C, et al. Major Complications of Pneumatic Dilation and Heller Myotomy for Achalasia: Single Center Experience and Systematic Review of the Literature. Am J Gastroenterol. 2012 Dec; 107(12): 10.1038/ajg.2012.332. doi: 10.1038/ajg.2012.332

19. Taft T, Carlson D, Triggs J, Craft J, et al. Evaluating the Reliability and Construct Validity of the Eckardt Symptom Score as a Measure of Achalasia Severity. Neurogastroenterol Motil. 2018 Jun; 30(6):e13287. doi: 10.1111/nmo.13287

20. Miao S, Wu J, Lu J, et al. Peroral Endoscopic Myotomy in Children with Achalasia: A Relatively Long-term Single-center study. J Pediatr Gastroenterol Nutr. 2018 Feb;66(2): 257-262. doi: 10.1097/MPG.0000000000001675

21. Haito-Chavez Y, Inoue H, Beard K, et al. Comprehensive Analysis of Adverse Events Associated with Per Oral Endoscopic Myotomy in 1826 Patients: An International Multicenter Study. Am J Gastroenterol. 2017 Aug;112(8):1267-1276. doi: 10.1038/ajg.2017.139