ORIGINAL ARTICLE

Outcomes of per-oral endoscopic myotomy for treatment of esophageal achalasia with a median follow-up of 49 months

Quan-Lin Li, MD,[1,*] Qiu-Ning Wu, MD,[1,*] Xiao-Cen Zhang, MD,[1,*] Mei-Dong Xu, MD, PhD,[1] Wei Zhang, PhD,[2] Shi-Yao Chen, MD, PhD,[1] Yun-Shi Zhong, MD, PhD,[1] Yi-Qun Zhang, MD, PhD,[1] Wei-Feng Chen, MD, PhD,[1] Wen-Zheng Qin, MD, PhD,[1] Jian-Wei Hu, MD,[1] Ming-Yan Cai, MD, PhD,[1] Li-Qing Yao, MD,[1] Ping-Hong Zhou, MD, PhD[1]

Shanghai, China

Background and Aims: Per-oral endoscopic myotomy (POEM) has received wide acceptance as a highly effective and safe treatment for esophageal achalasia. Short-term and small-scale studies are ample, but long-term large-scale studies are few. The aim of the study was to systematically analyze our long-term results of POEM, with particular emphasis on POEM failures and associated risk factors.

Methods: In this single-center study, consecutive patients treated with POEM between August 2010 and December 2012 were included. The Kaplan-Meier survival function was used to estimate clinical success rate at each year. The Cox proportional hazards model was used to analyze risk factors related to recurrence.

Results: A total of 564 patients were included. Major perioperative adverse events occurred in 36 patients (6.4%). After a median follow-up of 49 months (range, 3-68), the Eckardt score and lower esophageal sphincter (LES) pressure were significantly decreased (median Eckardt score, 8 to 2 [$P < .05$]; median LES pressure, 29.7 mm Hg to 11.9 mm Hg [$P < .05$]). Fifteen failures occurred within 3 months, 23 between 3 months and 3 years, and 10 after 3 years. The estimated clinical success rates at 1, 2, 3, 4, and 5 years were 94.2%, 92.2%, 91.1%, 88.6%, and 87.1%, respectively. Multivariate Cox regression revealed long disease duration (≥10 years) and history of prior interventions to be risk factors for recurrence. Clinical reflux occurred in 37.3% of patients (155/ 416).

Conclusions: POEM is a highly safe and effective treatment for esophageal achalasia with favorable long-term outcomes. (Gastrointest Endosc 2017;■:1-8.)

Per-oral endoscopic myotomy (POEM) in its current form[1] is the fruition of a long succession of trials[2-4] exploring the submucosal space as a means to access body cavities. It is also probably the most successful member in the family of natural orifice transluminal endoscopic surgery today, drawing phenomenal attention within its short history.[5-12]

Conceptually based on the surgical prototype Heller myotomy, POEM offers a less-invasive method of breaking

Abbreviations: AE, adverse event; CI, confidence interval; IQR, interquartile range; LES, lower esophageal sphincter; POEM, per-oral endoscopic myotomy.

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*Drs Li, Wu, and Zhang contributed equally to this article.

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Current affiliations: Endoscopy Center and Endoscopy Research Institute, Zhongshan Hospital (1), Department of Biostatistics, Shanghai Medical College (2), Fudan University, Shanghai, China.

Present address: Qiu-Ning Wu: Gastrointestinal Endoscopy Center, The Sixth Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China; Xiao-Cen Zhang: Mount Sinai St. Luke's-West Hospital, New York, USA.

Reprint requests: Ping-Hong Zhou, MD, PhD, Endoscopy Center and Endoscopy Research Institute, Zhongshan Hospital, Fudan University, 180 FengLin Road, Shanghai, 200032, P. R. China.

If you would like to chat with an author of this article, you may contact Dr Zhou at zhou.pinghong@zs-hospital.sh.cn.

the pressurized zone of the esophageal gastric junction. Because both POEM and Heller myotomy render basically the same result anatomically (myotomy across the esophageal gastric junction, leaving esophageal mucosa intact), it is reasonable to infer they would lead to a similar clinical response. Indeed, the effect of POEM has been proven to be comparable with Heller myotomy by small-scale short-term studies.[13-16] Nevertheless, concerns exist regarding POEM's durability, whereas Heller myotomy has stood the test of time.[17] Inoue et al,[18] who developed and named POEM, reported their favorable 3-year results in 2015. As 1 of the earliest centers to perform POEM and the highest in volume, we herein present our 5-year results regarding the long-term outcomes of POEM.

METHODS

Patients

Patients were diagnosed with established methods: clinical symptoms, barium swallow, EGD, manometry, and/or chest CT scan. Exclusion criteria included coagulopathy and systemic disorders that precluded safe general anesthesia. The procedures and study were conducted in accordance with the Declaration of Helsinki and had approval from the Ethical Board of Zhongshan Hospital. Written informed consent was obtained from all patients before the procedure.

Outcome measurements

The primary outcome of the study was the clinical success rate of POEM (Eckardt score $\leq$3) during follow-up. The secondary outcomes included procedure-related adverse events (AEs), lower esophageal sphincter (LES) pressure on manometry pre- and post-POEM, reflux symptoms (grade 0, absent; grade 1, <2 days a week; grade 2, 2-4 days a week; grade 3, >4 days a week),[19] reflux esophagitis on EGD, and procedure parameters such as operation time, length of hospital stay, and myotomy length. Baseline and postmyotomy LES pressures were recorded using a high-resolution manometry system (Sierra Scientific Instruments Inc, Los Angeles, Calif) as previously described.[20]

POEM procedures

The POEM procedure we used was largely the same as the original protocol raised by Inoue et al[1] and has been reported by our previous publication.[21] Four major steps were involved: submucosal injection, submucosal tunneling, myotomy, and closure of the mucosotomy. Several important technical modifications[22] were put forward by our group and have become our standard practice over time: myotomy at the posterior (5-6 o'clock) rather than anterior esophageal wall, (2) full thickness rather than selective circular muscle myotomy, and (3) push and pull myotomy: in the esophagus anchor the knife tip at the muscle fibers from the extraluminal side and PUSH the scope, and at the cardia lay the knife on top of the muscle fibers intraluminally and PULL the scope.[23] We were also among the first to apply a water jet–assisted knife in POEM.[24] One technical drawback was that the CO_2 insufflator did not become readily available in our center until late 2011, and this had an effect on our gas-related AEs.

Adverse events

Major perioperative AEs were defined as conditions that resulted in vital-sign instability, intensive care unit stay, hospital readmission, conversion to open surgery, invasive postoperative procedures, blood transfusion, or hospitalization >5 days because of functional impairment of the patient.[25] Minor perioperative AEs were defined as AEs that called for clinical interventions but did not qualify for major AE, including bouts of intraoperative subcutaneous emphysema/pneumoperitoneum that required needle decompression only and prolonged intraoperative bleeding (>200 mL) that did not require transfusion. Accidental mucosal injury was recorded given its call for special management (eg, clipping, prolonged fasting, and/or nasogastric tube placement) but not graded major or minor AEs per se. Long-term AEs were associated with acid reflux, including gastroesophageal reflux symptoms, strictures, and Barrett's esophagus.

Mucosal edema and mucosal injury, 2 risk factors for perioperative AEs, were graded and categorized.[25] Mucosal edema was characterized by mucosa surface texture abnormality (cobblestone sign, milky color of the injection wheal, jelly-like adhesions, etc) and/or increased cutting-edge thickness (inward folding, high tension during clipping, etc.), and graded in severity accordingly.[25] Mucosal injuries were categorized as 1 of 2 types based on difficulty of repair. Type I injuries were easily repairable injuries (small, whitish, linear/dotted, or mucosal color change), whereas type II injuries were difficult-to-repair injuries (big, scorched, round/unevenly bordered, and often related to submucosal adhesion).[25]

Follow-up

Patients were scheduled to follow-up at the center 1 month, 3 months, 6 months, and 1 year postoperation and yearly afterward, during which symptom assessment, physical examination, and objective tests including EGD and barium esophagram were performed. High-resolution manometry was recommended to be done at least once postoperatively.

Clinical response was evaluated using the Eckardt score.[26] Post-POEM Eckardt score $\leq$3 was considered the benchmark for treatment success. Those with Eckardt scores >3 were grouped according to time of failure: within 3 months, nonresponders; between 3 months and 3 years, early recurrence; and after 3 years, late recurrence.

Barium swallow was performed to document treatment results objectively. EGD was recommended because it provided both treatment outcome assessment and esophageal cancer surveillance.[26] Manometry, although strongly advised, tended to be poorly welcomed by the patients