Treating children with achalasia using per-oral endoscopic myotomy (POEM): Twenty-one cases in review

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Abstract

Background: Per-oral endoscopic myotomy (POEM), a modern treatment for achalasia, has only recently emerged as an option for pediatric patients. Here we describe and characterize the success of POEM in children with achalasia.

Methods: A single-institution prospective cohort study was performed of patients <18 years old who underwent POEM from 2014 to 2019. Main outcomes were success at one year (Eckardt ≤3), procedure duration, complications, reintervention.

Results: The median age of patients (n=21) was 13 years (range 2–17). Median procedure duration was 92 min (range 52–259) with case duration plateau of 87.4 min and learning rate of 15.5 cases. Intraoperative complications included capnoperitoneum requiring needle decompression and mucosotomy requiring additional clips. One patient experienced chest pain with small capnoperitoneum seen on chest radiography, and three patients had extraluminal carbon dioxide found incidentally on routine radiography. All were managed with observation. Pre- versus 1-month postprocedure Eckardt scores were significantly improved (7 ± 2 versus 1 ± 2, p < 0.0001, and median ± SD) with 100% symptomatic relief at one year. To achieve this, 13 patients required further dilation(s), one required laparoscopic Heller myotomy, and two required repeat POEM.

Conclusions: POEM is a viable and safe treatment for pediatric patients with achalasia. We demonstrate improvement in symptoms and procedure proficiency with minimal intra- and postoperative complications.

Type of study: Prospective cohort study.

Level of evidence: Level II.

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Achalasia is a motility disorder of the esophagus characterized by lack of peristalsis of the esophageal body and inadequate relaxation of the lower esophageal sphincter, leading to symptoms of dysphagia, regurgitation, chest pain, and weight loss. It is a rare disease in children; the incidence worldwide is approximately 0.02 to 0.31 cases per 100,000 children per year [1,2]. The diagnosis in children may be particularly challenging given the heterogeneity in disease presentation and the rarity of this disease; however if achalasia is suspected, workup involving upper endoscopy, barium esophagram, and esophageal manometry facilitates diagnosis [3]. Manometry assists in categorizing types of achalasia which may predict response to operative intervention: type I (lack of distal esophageal pressurization), type II (panesophageal pressurization without peristalsis; most likely with favorable outcome), type III (two or more spastic contractions with or without pressurization; less likely to have favorable outcome) [4].

The treatment of achalasia ranges from medical management to surgical intervention. Medical management with smooth muscle relaxing agents (such as calcium channel blockers, nitrates and botulinum toxin injection) is known to be less effective long-term, but is a modality for patients who may not be candidates for surgical intervention. Traditionally, endoscopic management includes dilation and/or botox injection with higher short term success than medication but poor long term durability of symptom relief. Surgical management via laparoscopic esophagomyotomy with fundoplication has been the most effective long-term solution for achalasia [3]. A minimally invasive but effective procedure is the per-oral endoscopic myotomy (POEM), first described in an animal model by in 2007 by Pasricha et al. and introduced to clinical practice in 2010 by Inoue et al. [5,6]. In the adult population, POEM has been shown to have clinical success and durability [6,7].

We have adapted use of POEM to our pediatric patient population, further adding to the body of literature supporting this procedure as a...
viable intervention for patients with achalasia under the age of 18 years [8,9]. The purpose of this case review is to evaluate our ongoing experience performing POEM and to analyze clinical success and durability in pediatric patients.

1. Methods

This prospective cohort study recruited patients <18 years of age undergoing POEM at a single institution by a single surgeon between 2014 and 2019 on an ongoing basis; analysis was retrospective. The Stanford University Institutional Review Board approved the study.

Patients and their families were referred to the pediatric surgeon performing the procedure by pediatric gastroenterologists; patients were candidates for POEM if manometry confirmed achalasia and EGD did not show sigmoid esophagus. Eckardt score (frequency of chest pain, regurgitation, dysphagia and degree of weight loss) was documented. Preoperative workup included, at minimum, manometry and upper endoscopy. Preoperative preparation included three days of Nystatin swish and swallow to minimize candida esophagitis and 24 h of liquid diet to limit solid food impaction in the esophagus.

1.1. Operative technique, postoperative care, and follow-up

The operation proceeded similarly to previously described, utilizing EndoFLIP® (Endoluminal Functional Lumen Imaging Probe, Crospon

Fig. 1. Per-oral endoscopic myotomy intra-operative diagrams and photographs. (A) Diagram demonstrating premyotomy esophageal anatomy. (B) Anatomy after myotomy with endoscope within methylene blue sub mucosal dissection plane, and remaining longitudinal muscle after incising the circular muscle of the LES. (C, D) Endoscopic images demonstrating sub mucosal dissection plane and circular muscle fibers. (E, F) EndoFLIP® screenshots with esophageal diameters at the LES before and after myotomy.
Medical Devices, Galway, Ireland); diagrams demonstrating dissection technique are illustrated in Fig. 1 [8]. The procedure is performed under general anesthesia. Patients are given antibiotics immediately preprocedure and for the most recent 16 patients, dexamethasone to limit mucosal swelling. An overtube is positioned in the esophagus over a standard single channel upper endoscope with a fixed oblique plastic cap. Carbon dioxide insufflation is used exclusively. The EndoFLIP® is then delivered to the gastroesophageal junction (GEJ) to distensibility (Fig. 1E). On the right lateral esophageal wall proximal to the GEJ, a submucosal lift with methylene blue is performed (with the exception of redo POEMs performed on the left lateral wall), followed by a mucosotomy using a triangle tip knife. A submucosal tunnel is then created using methylene blue injections, blunt dissection, and minimal electrocautery, traveling distally until reaching the gastric cardia (Fig. 1C). The myotomy is performed from proximal to distal 5 cm above the GEJ to 2 cm below with some adjustments made for smaller size patients (Fig. 1B). Lower esophageal sphincter (LES) distensibility index (DI) after myotomy is measured using the EndoFLIP® by calculating esophageal cross-sectional area (extrapolated from measured esophageal diameter) divided by balloon pressure. Visual inspection of the stomach and esophagus is then performed, and the mucosotomy closed using endoscopic clips.

A postoperative chest radiograph is taken in the recovery unit, and the patient is then transferred to a standard patient care unit and kept nil per os (NPO) until water-soluble contrast esophagram on postoperative day (POD) one confirms passage of contrast into the stomach with no esophageal leak. The patient is then advanced to a liquid diet, discharged without narcotics and given instructions for a liquid diet for two weeks and a proton pump inhibitor (PPI) for two months.

Upon follow up in clinic, the patient is advanced to a regular diet as tolerated if there are no increased issues with regurgitation, chest pain, or dysphagia. Eckardt scores were recorded for each clinic visit along with reflux symptoms. Given the limited experience with this procedure in children, any postprocedure Eckardt score more than 3 was used as a threshold to perform endoscopy with EndoFlip and dilation.

1.2. Statistical analysis

Demographics and intra- and postoperative details were collected and analyzed using descriptive statistics, paired t-tests, and multiple linear regression using Graphpad Prism 8 (San Diego, California, USA) and StataSE 15 (College Station, Texas, USA). Statistical significance was determined at p-values <0.05.

To determine the surgeon’s “learning plateau” and “learning rate”, a nonlinear regression inverse curve was fit using SPSS (IBM, Armonk, New York) as described by Feldman et al., and performed by this group previously [8,10]. The curve was defined by \[ Y = a - b/x \] where \( Y \) is the dependent variable procedure duration and \( x \) is the independent variable consecutive case number. A learning plateau “\( a \)” was defined as the best procedure duration achieved with an infinite amount of experience (case number \( x = n \)); the “learning rate” was defined as the number of procedures performed that could achieve 90% of the learning plateau \( (Y = 0.90a) \).

2. Results

2.1. Demographics

Twenty-one subjects between 2 and 17 years of age (median 13 years) underwent the POEM procedure between 2014 and 2019. Table 1 provides additional demographics.

2.2. Clinical and perioperative characteristics

The clinical, preoperative and operative details can be found in Table 1. Two patients received treatment for their achalasia prior to the POEM procedure: one underwent upper endoscopy, dilation, and Botox injection of the LES; the other underwent upper endoscopy and dilation alone. The median preoperative Eckardt score was 7 (range 2–11, standard deviation SD = 2.4); the lowest score patients underwent POEM given symptomatology and chronicity. Patient body mass index (BMI) median was 17.3 (range 13.0–36.7, SD = 5.6); the highest BMI patient was obese prior to onset of symptoms, six months before intervention.

EndoFLIP® data were available for 19 of 21 patients; preoperative DI was median 1.0 mm²/mmHg (range 0.4–3.5 mm²/mmHg; SD = 0.9) after myotomy (paired t-test, \( p < 0.0001 \); Fig. 2A). The median myotomy length was 7 cm (SD = 1.1). The procedure lasted a median of 92 min (range 52–259 min, SD = 52). Patients at most stayed 2 days postoperatively, with 67% of patients discharged on POD1.
2.3. Postoperative outcomes

No procedures needed to be converted to laparoscopic or open surgical approaches. Two patients experienced adverse events requiring intraoperative intervention; four additional adverse events required observation alone. Intraoperatively, one patient developed symptomatic capnoperitoneum requiring decompression using a Veress needle (Grade III Clavien–Dindo classification); postoperative esophagram demonstrated a small esophageal tunnel leak that was not full thickness to the mediastinum. This was managed with NPO and feeding through a preexisting gastrostomy tube for two weeks. Intraoperatively, the second patient had a distal mucosotomy during submucosal tunneling which was repaired primarily with endoscopic clips (Grade III); an esophagram postoperatively demonstrated no leak and the patient proceeded on the standard postoperative protocol. The four events that did not require intervention included a patient who experienced subternal chest pain postoperatively, with a chest leak and the patient proceeded on the standard postoperative protocol. Two underwent a second POEM procedure, and one patient underwent laparoscopic Heller myotomy; these clinical details have been included in Table 2. The patient requiring a laparoscopic Heller myotomy was noted to have severe aperistalsis prior to and after her POEM and Heller myotomy; repeat endoscopy and dilation after Heller showed a widely patent GEJ. An additional patient required placement of a gastrostomy tube 1.5 months after POEM owing to ongoing dysphagia and weight loss. Repeat EndoFLIP® at that time showed a 10 mm LES that would normally predict symptom relief. The patient regained weight with the gastrostomy tube and experienced improvement in symptoms after further dilation.

No patients at the one-year follow-up mark experienced reflux symptoms; four patients requiring prolongation of standard two month PPI use were able to be weaned at subsequent follow-up visits. Please cite this article as: L.S.Y. Wood, J.M. Chandler, K.E. Portelli, et al., Treating children with achalasia using per-oral endoscopic myotomy (POEM): Twenty-one cases in review, Journal of Pediatric Surgery, https://doi.org/10.1016/j.jpedsurg.2020.02.028
Table 2
Clinical details of patients requiring additional surgical intervention after initial POEM.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age at first POEM / gender</th>
<th>Number reinterventions before reoperation</th>
<th>Reoperation</th>
<th>Months after POEM</th>
<th>Achalasia type</th>
<th>Most recent Eckardt score / months after reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13 / M</td>
<td>3</td>
<td>POEM</td>
<td>37.5</td>
<td>1</td>
<td>0 / 2</td>
</tr>
<tr>
<td>2</td>
<td>15 / F</td>
<td>2</td>
<td>POEM</td>
<td>4.3</td>
<td>2</td>
<td>1 / 9</td>
</tr>
<tr>
<td>3</td>
<td>14 / F</td>
<td>2</td>
<td>Lap Heller, Dor fundoplication</td>
<td>3.6</td>
<td>2</td>
<td>2 (preceded by dilation) / 2.5</td>
</tr>
</tbody>
</table>

Table 3
Multiple linear regression: relationship of postoperative distensibility index and outcome.

<table>
<thead>
<tr>
<th>Multiple Linear Regression: Relationship of Postop Distensibility Index to Outcome</th>
<th>Absolute Change in Eckardt (n = 18)</th>
<th>Reintervention (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted Odds Ratio</td>
<td>0.497 (0.461)</td>
<td>-0.113 (0.399)</td>
</tr>
<tr>
<td>Adjusted for Achalasia Type Distensibility Index</td>
<td>0.438 (0.534)</td>
<td>-0.145 (0.277)</td>
</tr>
<tr>
<td>Achalasia Type</td>
<td>0.576 (0.651)</td>
<td>0.322 (0.173)</td>
</tr>
<tr>
<td>Adjusted for Achalasia Type &amp; Demographics Distensibility Index</td>
<td>0.549 (0.371)</td>
<td>-0.146 (0.127)</td>
</tr>
<tr>
<td>Achalasia Type</td>
<td>-0.340 (0.779)</td>
<td>0.459 (0.093)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.383 (0.012)</td>
<td>0.0496 (0.096)</td>
</tr>
<tr>
<td>Female</td>
<td>0.254 (0.840)</td>
<td>-0.128 (0.647)</td>
</tr>
</tbody>
</table>

Note: p value in parentheses.

2.4. POEM learning curve

The modeled inverse curve for case duration by surgeon case number yielded a case duration plateau of 87.4 min and learning rate of 15.5 cases (Y = 87.4 + 135/X; R² = 0.322; Fig. 3A). Grouping cases based on our prior estimate to reach 90% of the learning plateau shows continued improvement in mean case duration (±SD, cases 1–10 = 137.2 min ± 64.7 min, versus cases 11–21 = 86.9 min ± 19.4 min, p = 0.02; Fig. 3B). Mean postmyotomy esophageal diameter was significantly larger in the second half of cases as compared to the first (±SD, cases 1–10 = 10.5 mm ± 1.7 mm, versus cases 11–21 = 12.7 mm ± 1.4 mm, p = 0.006; Fig. 3C): no significant was found in other operative metrics of percent increase of diameter, myotomy length, DI, or percent increase in DI (p > 0.05; Figs. 3D–G).

3. Discussion

The per-oral endoscopic myotomy (POEM) procedure is a successful and safe method of treatment of achalasia in a pediatric population. Advantages to POEM include limited hospital stay, “no scar” surgery, and esophagomyotomy without the need for a hiatal dissection. We were able to show early safety and feasibility in our initial cohort of 10 patients [8]; here, these patients have progressed to demonstrate 100% symptomatic relief (Eckardt score ≤ 3 at one year post-POEM regardless of need for re-intervention), with 30% of our patients requiring no re-intervention by one year follow-up. This is a rate similar to that seen in the literature for adult and pediatric patients [7,9].

While two-thirds of our patients required re-intervention (most commonly dilation) for recurrent symptoms, only 3 required a repeat myotomy; these rates are similar to rates seen in an adult population undergoing POEM [11]. Of note, literature reviewing the use of thorascoscopic esophagomyotomy in children suggests a 15%–26% need for re-intervention/dilation; however, this study had higher reflux rates and was limited by lack of objective symptom scoring to determine the need for reintervention [12]. In a study with careful five-year follow-up for pediatric patients after Heller myotomy, 65% required reintervention (Botox or dilation) after initial surgery, and 29% required repeat myotomy for symptomatic relief, similar to our 14% rate of initial POEM failure [9,13]. As postmyotomy dilations via balloon or bougie are common practice in adult POEM patients and there is relative uncertainty of POEM in children, we have a very low threshold to perform these re-interventions. Three out of our four patients lost to follow-up had Eckardt scores ≤ 2 at the time of most recent follow-up, and the fourth after esophageal dilation occurring four months post-POEM. While these patients did not return for scheduled follow-up for unknown reasons, it may reflect an improvement in symptoms that the patients and families felt did not necessitate further medical treatment, change in insurance or geographic status. With regards to adverse events, we find similar rates to largely adult cohorts demonstrating extravuminal air in up to one-third of cases, and other pediatric case reviews reporting pneumoperitoneum requiring decompression, or leak requiring NPO [9,14].

Owing to the need for reintervention in the first 10 patients, we intentionally extended the myotomy in both directions in the second half of patients to increase distensibility. Our results suggest that increased DI does indeed have a positive correlation with the absolute change in Eckardt, and a negative correlation with the need for reintervention, although these results are not statistically significant in our limited sample and these patients have shorter follow-up.

This study also provides a framework for the learning curve associated with this procedure, with continued decrease in case duration with an increased number of cases. In our initial case series of 10 patients we reported a plateau of 107 min, with ability to reach 90% of this speed by 9.6 cases [8]; here we show an ability for the same surgeon to have continued improvement to reach a plateau of 87 min, and 90% of this speed in 15 cases, which is consistent with a reported learning curve of approximately 20 cases in adult patients [15].

There are a number of challenges associated with operating in children. First, as is the case with many procedures in pediatric surgery, certain pieces of equipment commonly used in the adult setting do not scale to smaller children. In the case of our two youngest patients, we were able to use a standard size upper endoscope with a dissecting cap, but were not able to use the overture for esophageal access. Second, the absolute length of myotomy was scaled down in the cases of small children owing to the relatively smaller length of their esophagus. In these cases, the EndoFLIP® was particularly helpful in confirming an adequate myotomy (Figs. 1E, F).

Limitations of this study include short length of follow-up for half of the patient cohort, performance by a single surgeon at a single institution, and small sample size. Additional correlates such as a follow-up upper endoscopy to measure LES pressure would be beneficial in a longitudinal study of POEM in children, but upper endoscopy, pH study and manometry are not standard follow up procedures in asymptomatic patients in our practice. An additional challenge is the Eckardt score is scaled for use in adults, which may not adequately capture symptomatology in children with achalasia as there is no scoring system in use for a pediatric population.
This study is one of the larger analyses for longer-term follow up of POEM in children. Randomized control trials are needed to further support the durability and clinical success of the POEM procedure in children; however, this study adds to the literature encouraging the use of the POEM procedure in a pediatric population.

4. Conclusions

Per-oral endoscopic myotomy is a feasible and safe procedure to use in a pediatric achalasia population, with significant improvement in symptoms. The procedure offers potential benefits of minimizing surgical trauma with no abdominal access incisions, no dissection of the esophageal hiatus, and decreased pain. Complications and need for reintervention occur at rates comparable to laparoscopic Heller myotomy in children and POEM in adults. Furthermore, the procedure is able to be learned and performed by a pediatric surgeon, with a learning curve similar to that of adult patients.

Appendix A. Discussions

DR. ISLAM: Any questions from the audience? It looks like we have someone coming up.
MALE VOICE: Thank you so much for this great presentation. Mohamed Agil [phonetic] from Children’s, Colorado. Have you thought about doing the high resolution manometry for those kids preoperatively, I mean in adult literature they talk about the subtypes of achalasia and how the POEM can actually affect those and stratify those patients for effectiveness of the procedure? Thank you.

DR. WOOD: Great. So with regards to the high resolution manometry, so these patients routinely undergo the endoscopy and manometry with our PI colleagues, so that’s something that occurs routinely. And so these patients will have that as part of their workup before they are referred to us for intervention. And sometimes we’ll also perform the EndoFLIP measurements as well at the same time when they are undergoing the initial endoscopy for a diagnosis of achalasia, but in general many of these patients actually do undergo the high resolution manometry before they come to us.

MALE VOICE: Thank you.

DR. ISLAM: Dr. Heiss.
DR. HEISS: Kurt Heiss from Atlanta. Thanks for a nice presentation. I may have missed this bit, what is the POEM approach, how is reflux managed afterwards, and is there a level of symptomatology that’s different than if we did a traditional Heller?

DR. WOOD: Right. So with regards to reflux that was certainly something we were worried about when this was first brought about at our institution. So they are prescribed an oral PPI when they are discharged and it’s a medication that they will take up to I believe it’s two or three months postoperatively. And so we continue to follow them with regards to their symptoms and then we’ve noticed that in the short term obviously they’re on their PPI so they don’t experience reflux symptoms, but it is something that can be kind of challenging particularly in our younger children to diagnose. But with regards to then the one year follow-up again in those 10 patients who we’ve seen they have not demonstrated to us that even being off of a PPI for at least six months when they come to see us at one year follow-up, that they have no symptoms of reflux.

**Fig. 3.** Learning curve and operative characteristics by surgeon case number. (A) Nonlinear regression inverse curve fit to duration of procedure and surgeon case number. (B) ”Second half” or cases 11–21 were significantly faster than ”first half” or cases 1–10 (*p < 0.05). (C–G) Differences between first half and second half of surgeon cases by operative characteristics demonstrated significance of postmyotomy diameter (***p < 0.01).
DR. ISLAM: A second question real briefly, when you talk about 100% symptom improvement, oftentimes as I read the literature about adults with longer term follow-up, a large percentage, maybe 75, are really, really good, and then there's a smaller group that's a little bit better but may be not perfect. Is the 100% success rate a little bit of a euphemism and there's a breakdown in there of good, better, or best?

DR. HEISS: A second question real brief –

DR. WOOD: Certainly. So I think another challenge that I didn't mention as far as the limitation is the Eckardt score was developed for achalasia symptoms in adults, and so I think that that's one of the challenges that maybe in the future is something we can adapt to children. And so, it's I think for being able to tell how these kids do in the longer term I think being able to grade them in good, better or best would be a great idea. We've looked at percentage improvement over time as well to see if that's something that we can tell if we have greater percentage improvements over time. That's something that we're continuing to track in our longer term outcomes as well.

DR. ISLAM: So just a couple of quick comments. It's very well presented. You quote 100% success rate, however, you had 10 patients who required dilations and three patients required redo, including one who needed a redo lap Heller. So I think if you include those secondary intervention rates in that, I think your success rate maybe would be, have to be modified. And then second, did you think about comparing this to your pre-POEM lap, straightforward lap Heller myotomy and seeing if the results were equivalent in that? Because this seems to be a relatively high rate of secondary interventions required.

DR. WOOD: Sure. So with regards to the 100% success rate, right, I think it's something that we wanted to have a relatively simple outcome and then develop a way to then describe the patients who--what they required to get to that point. So the success rate as far as trying to define the Eckardt score less than or equal to 3 is something that in the adult literature for POEMS is pretty routinely used. So as far as trying to define a very sort of basic way of how these patients did at one year is comparable to what has been done in the adult literature. And then with regards to some of the reoperations and things like that, so in Heller myotomy it's something that some patients even after Heller myotomy do require esophageal dilation as well, so I think we've seen literature up to about 65% of patients, which is pretty similar to our two-thirds of patients requiring dilation after a POEM. And one of the benefits we believe of the POEM procedure is it doesn't necessarily preclude patients from moving on to further interventions whether endoscopic or surgical, so we feel it's a good primary way of intervention as compared to maybe potentially just going straight for surgical intervention.

DR. ISLAM: Thank you very much.

DR. WOOD: Thank you.

References