Review Article

Anesthesia for Per-oral endoscopic myotomy (POEM) – not so poetic!

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Abstract

Peroral endoscopic myotomy (POEM) is a promising natural orifice transluminal endoscopic procedure for the treatment of esophageal motility disorders, with similar effectiveness as of Heller myotomy. It is performed under general anesthesia in endoscopy suite. Creation of submucosal tunnel in the esophageal wall is a key component. The continuous insufflation of CO_2 inadvertently tracks into surrounding tissues and leads to capno mediastinum, capno thorax, capno peritoneum, and subcutaneous emphysema. Thus, the challenges, for an anesthesiologist are not only providing remote location anesthesia, increased risk of aspiration during induction, but also early detection of these complications and specific emergency management. Though a therapeutic innovation, POEM remains an interdisciplinary challenge with no specific anesthesia care algorithms and evidence-based recommendations. The purpose of this review is to outline the anesthesia and periprocedural practices based on existing evidence.

Keywords: Anesthesia, complications, management, POEM

In recent times, peroral endoscopic myotomy (POEM) has emerged as an effective endoscopic treatment for achalasia cardia. It is usually performed under general anesthesia in an endoscopy suite.[1] Creation of submucosal tunnel and myotomy are a key component during POEM. As a result, iatrogenic communication can occur between the submucosal space and the mediastinum, retro- and intraperitoneal cavity, which can lead to tension capnothorax, capnomediastinum, or capnoperitoneum by the endoscopically insufflated CO_2.[2] Thus, the anesthesiologists should not only be careful about the risk of aspiration during induction but also be aware of these complications and with specific emergency management. Though a therapeutic innovation, POEM remains an interdisciplinary challenge with no specific anesthesia care algorithms and evidence-based recommendations. The purpose of this review is to outline the anesthesia and periprocedural practices based on existing evidence.

'Achalasia' is derived from the Greek word 'chalasis' means relaxation. It is a motility disorder of the lower esophageal sphincter with a prevalence of 10 in 100 000 individuals.[3] It is a chronic debilitating disease that manifests as dysphagia, regurgitation, chest pain, and weight loss.[4] It usually manifests between 25 and 60 years of age.[5] The management includes pharmacotherapy with calcium-channel blockers and nitrates, endoscopic botulinum toxin injections, endoscopic pneumatic balloon dilatation, laparoscopic Heller myotomy, and POEM.[6] The basic principle of POEM is of "natural orifice transluminal endoscopic surgery (NOTES)".[7] POEM has emerged as a standard treatment of achalasia since its inception in 2010. It possesses similar effectiveness as of Heller myotomy with comparatively lower cost and morbidity.[8]

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Several studies have shown a positive intrathoracic pressure under general anesthesia with endotracheal intubation is associated with lesser incidence of iatrogenic events (perforation, bleeding, and CO_2 insufflation-related complications) than intravenous sedation.[9,10] Thus, standard equipment, monitoring, and mutual understanding along with closed-loop communication between anesthesiologists and endoscopists is the key for improving patient safety.

Peroral Endoscopic Myotomy Procedure

The patient is positioned either in supine or left lateral decubitus. At the beginning residual fluid or food is suctioned and removed from the esophageal lumen with the help of esophagogastroduodenoscope (EGD) [Figure 1]. During the POEM, carbon dioxide insufflation is used for inflation at low flow rate (~1.2 L/min). POEM is done with EGD and a mucosal cap or hood at its tip. A mucosal bleb is created 10–12 cm above the gastroesophageal junction (GEJ) with normal saline mixed with methylene blue or indigo carmine dye [Figure 2]. Colored dye is used to increase visualization and clear delineation of submucosal space. A 2.5 to 3 cm longitudinal mucosal incision is made with the electrocautery knife to expose the submucosal space and entered into the submucosal tunnel. Submucosal dissection is done to create submucosal tunnel by using the electrocautery knife and repeated dyed saline injections till 3 cm below GEJ. Two to three centimeter distal to the mucosal incision site, selective myotomy of the circular muscle fibers, sparing the underlying longitudinal fibers is performed with electrocautery knife till 2 cm below GEJ [Figures 3 and 4]. At the end, the mucosal entry point is closed with standard endoscopic hemo clips [Figure 5].[11]

Pre-anesthetic Preparation

Patients with retrosternal chest pain should have a preprocedural electrocardiogram (ECG) to rule out any pre-existing cardiac ailment. A chest x-ray is also necessary in patient with clinical suspicion of pulmonary infiltrates or history of regurgitation.[12]

According to recent American Society for Gastrointestinal Endoscopy (ASGE) guidelines, POEM is the preferred treatment for management of patients with type III achalasia.[13] It has been also successfully performed in diffuse esophageal spasm, nutcracker esophagus, and hypercontractile (jackhammer) esophagus.[14] It is avoided in patients with severe cardiopulmonary or other serious disease leading to unacceptable surgical risk, pseudoachalasia, and anticipated difficulty in creation submucosal tunnel due to severe fibrosis and adhesion. Patients with severe thrombocytopenia (<30,000/mL), myelodysplastic syndrome, hypersplenism, patients with mechanical heart valves requiring high-dose anticoagulation are not eligible for POEM [Table 1][14] Periprocedural anticoagulation and/or antiplatelet therapy is maintained according to the ASGE guidelines [Table 2].[15]

Achalasia patients have an increased risk of aspiration by reflux of esophageal contents due to impaired esophageal emptying.[4] However, currently there is no guideline for pre-fasting time for POEM. Multiple case series on POEM anesthesia management have reported fasting times from 8 to 48 hours.[16] Majority of them have recommended a clear liquid diet for at least 24 hours or a low residue diet for 48 hours prior to the procedure.[17,18] At our center, we keep patients on clear liquid diet for 24 hours and keep fasting for 12 hours. Prophylactic use of esophagogastroduodenoscopy for removal of the residual food is debatable. One case series without

Figure 1: Endoscopic image shoeing dilated esophageal lumen, which is filled with food residue

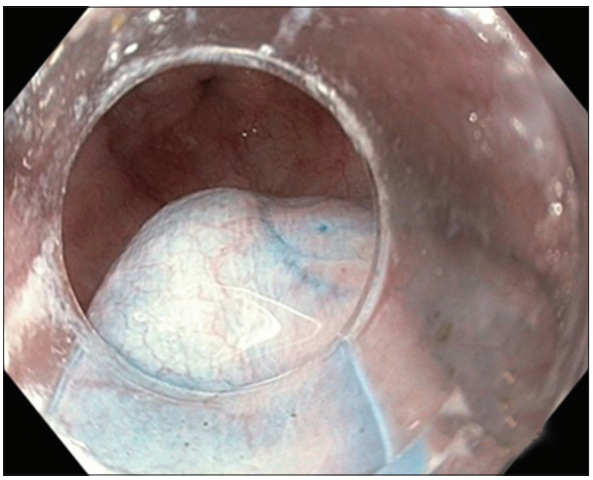

Figure 2: Mucosal bleb (blue color) after injection of normal saline mixed with methylene blue dye in the submucosal space

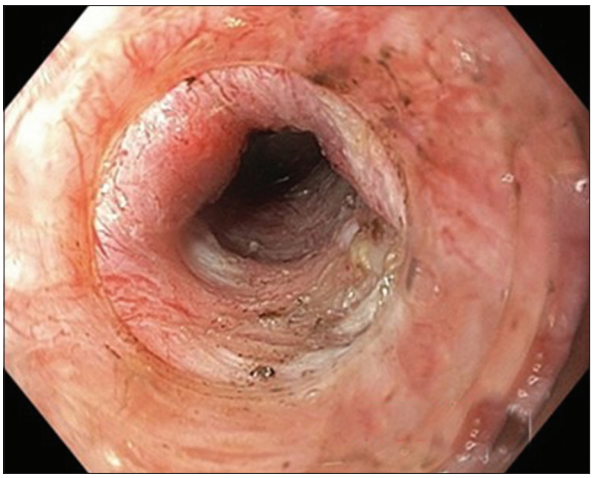

Figure 3: Submucosal tunnel after clearing of submucosal space. At 12 O'clock is the mucosa and at 6 O'clock is the muscle layer of the esophageal wall

Figure 4: Submucosal tunnel after the myotomy. At 12 O'clock is the longitudinal muscle layer visible after the selective circular muscle myotomy

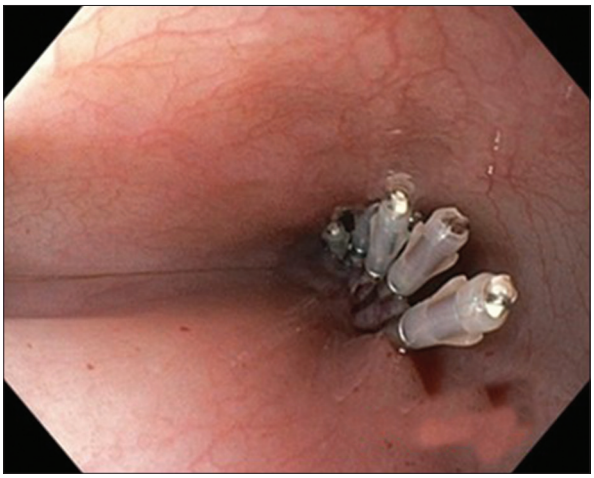

Figure 5: Closure of the mucosal incision site by the multiple hemoclips

prophylactic EGDs advocated for the necessity while the other has found increased risk of aspiration.[11,19] Nishihara *et al*.[18] has used gastric tube aspiration before induction in conscious patients for reduction of esophageal pressure. Prophylactic use of proton pump inhibitors, antibiotic prophylaxis and decontamination of oral cavity with chlorhexidine may be beneficial for preventing the postprocedural inflammatory response.[2]

Table 1: Indications and Contraindications for POEM[14]

Indications	Contra indications
Classic indication:	Absolute contraindications
Type III achalasia	Severe cardiopulmonary disease
Type I, type II achalasia	Severe thrombocytopenia
Failed prior treatments	Pseudoachalasia
Relative indications:	Cirrhosis with portal hypertension but no significant esophageal varices
Hypertensive motor disorders: diffuse esophageal spasm, jackhammer esophagus	Prior extensive esophageal mucosal resection/ablation involving the POEM field
	Relative contraindications
	Prior radiation therapy to the esophagus
	Severe esophagitis
	very large ulcer in the lower esophagus

Monitoring

During the procedure, standardized ASA monitoring of non-invasive blood pressure, electrocardiography (lead II), pulse oximetry, capnography (end tidal CO_2), urine output, and temperature are used. Invasive arterial blood pressure monitoring and serial arterial blood gas analysis may be beneficial for patients with known cardiovascular or pulmonary disease.[2] Periodic checking of abdomen, thorax, and neck is required to early detection of capnoperitoneum and subcutaneous emphysema.

Anesthesia

Prevention of aspiration during induction of anesthesia is the most important step. The incidence of aspiration during induction of general anesthesia in general population is 3 in 10,000.[20] Thus, in majority of the case series, have been advocated for rapid sequence induction (RSI).[21] There is no consensus on using of cricoid pressure and positive pressure ventilation via face mask. There is no ideal i.v. induction agent, with each having own pro and cons [Table 3].[22]

Succinylcholine- the depolarizing neuromuscular blocking agent usually preferred for RSI due to rapid onset of action. Alternatively, nondepolarizing neuromuscular blocking agent like rocuronium can also be used for the RSI. The different types and doses of anesthetic agents are individually selected based up on the patient's underlying disease and hemodynamic status. Both sevoflurane and propofol have no significant impact on the esophageal sphincter pressure in healthy individuals.[23] However, their effect on achalasia

Table 2: ASGE guidelines (2016) for antithrombotic agents in patients undergoing GI endoscopy[15]

Drugs	Low cardiovascular Risk	High Cardio vascular Risk
Anti-coagulants (AC)	1. Discontinue AC 2. Delay reinitiating until adequate hemostasis is achieved.	1. Discontinue AC 2. Bridge therapy 3. Restart warfarin on same day of procedure 4. Delay reinitiating NOACs until adequate hemostasis is achieved
Antiplatelet agents (APA)	1. Continue standard doses of aspirin/NSAIDs* 2. Discontinue thienopyridines at least 5 days before switch to aspirin 3. Dual APA, hold thienopyridines for at least 5 days, continue aspirin	1. Continue standard doses of aspirin/NSAIDs 2. Discontinue thienopyridines at least 5 days before endoscopy or switch to aspirin 3. Dual APA, hold thienopyridines for at least 5 days, continue aspirin

1. Defer elective endoscopic procedures, possibly up to 12 months, if clinically acceptable from the time of PCI to DES placement. 2. Avoid cessation of clopidogrel (even when aspirin is continued) within the first 30 days after PCI and either DES or BMS placement when possible. 3. Avoid cessation of all antiplatelet therapies after PCI with stent placement. 4. Perform endoscopic procedures, particularly those associated with bleeding risk, 5-7 days after thienopyridine drug cessation. 5. Aspirin should be continued. 6. Resumption of thienopyridine and ASA drug therapy after the procedure once hemostasis is achieved. A loading dose of the former should be considered among patients at risk for thrombosis

Table 3: Induction agent considerations[22]

Induction agent	Advantages	Disadvantages	Suggested use
Sodium thiopental 3-7 mg kg^{-1}	Clear endpoint; rapid one arm brain circulation time	Postoperative nausea and vomiting	Traditional choice
Propofol 2-4 mg kg^{-1}	Greater suppression of laryngeal reflexes Familiarity	CVS depression	When intubating conditions are a concern
Etomidate 0.3 mg kg^{-1}	CVS stability	Adrenal suppression	CVS instability
Ketamine 1-2 mg kg^{-1}	Bronchodilation CVS stimulant; maintains cerebral perfusion pressure in hypotensive situations	Increases ICP	Asthma, Shocked states

patient has not been studied. Desflurane may be useful for earlier recovery. Cuffed flexometallic endotracheal tubes are preferred in view of less chance of kinking or obstruction.[23] Another study has used endotracheal tube with supraglottic suction port but unable to show any added advantage.[24] After intubation, the endotracheal tube is generally fixed to the right side of the mouth to facilitate entry of the EGD. The nasotracheal intubation is expected to has a relatively less chance of tube displacement in the oral cavity due to endoscopic maneuvers, with increased risk of nasal bleeding, in comparison to orotracheal intubation.[16] Accessibility to the airway may be difficult as the endoscopist usually stands by the patient's head. So, securing the proper depth and fixation of the endotracheal tube, and protection of the eyes is utmost priority before starting the procedure.[25]

Adequate neuromuscular relaxation is critical as any untoward movement of the patient during the procedure may be detrimental. Pressure control mode of ventilation is preferred as it uses decelerating flow, which tends to compensate for any potential reduction in ventilation caused by pressure limitation and allows gas to be distributed more evenly to areas of the lung with both long- and short-time constants. Adjustment of minute ventilation to maintain an end-tidal carbon dioxide tension ($ETCO_2$) of 35–45 mmHg is necessary.[11] If hyperventilation alone is insufficient to control the rising $ETCO_2$ the procedure should be temporarily interrupted for several minutes. Sudden rise in $ETCO_2$ or peak airway pressure (Ppeak) should immediately be informed to the endoscopist for decompressing the stomach by suctioning excess/CO_2. It may be an early indicator of capnothorax.

Löser *et al*.[26] has found cases with 20% increase from the baseline Ppeak required percutaneous abdominal needle decompression (PND). However, there is no consensus regarding the optimal level of Ppeak. Another study has reported successful management of cases with Ppeak >38 cmH_2O by pulling back the endoscope and suctioning the excess CO_2. PND was performed only with simultaneous rise in Pmax and $EtCO_2$.[11]

Periodic assessment of the upper abdomen is also necessary for early detection of capnoperitoneum and there by prevention of abdominal compartment syndrome.[11]

Apert from pre-existing pulmonary conditions or extensive emphysema, usually patients are extubated immediately after the procedure whenever possible. A cuff leak test should be done before extubation. Although the incidence of post POEM gastroesophageal reflux between 8.5%- 21.3%, aspiration during emergence after extubation has not been reported.[26]

Physiological Changes

During the procedure, continuous gas insufflation is essential for the creation of a submucosal tunnel and visualization.

CO_2 is the preferred gas as it is colorless, non-combustible, water-soluble, systemically absorbed and excreted by the lungs with reduced risk of embolism. Use of air insufflation in POEM is contraindicated.[21] General anesthesia and CO_2 insufflation causes significant physiological changes. Similar to laparoscopic procedure, there is rise in mean arterial pressure (MAP) and heart rate (HR) during POEM. Systemic absorption, sympathetic stimulation and increased catecholamine release may be the cause.[27] Due to persistent CO_2 insufflation, impaired systemic CO_2 balance may lead to respiratory acidosis and increases in peak airway pressure. Raised peak airway pressure implies increase in intra-abdominal pressure. It may be due to gastric distension, retro- or capnoperitoneum.[16] The minute ventilation can be controlled in intubated patients under general anesthesia. CO_2 uptake by insufflation may be alleviated to some degree by hyperventilation. However, hyperventilation is not useful for maintaining normocapnia in subcutaneous emphysema.[16]

POEM-related Adverse Events

Early adverse events are mucosal injury, bleeding, subcutaneous emphysema, capnothorax, capnomediastinum, capnoperitoneum, and pleural effusion. Symptomatic gastroesophageal reflux disease and esophagitis are the late complications.[28] The most common adverse events associated with POEM are related to CO_2 insufflation. In contrast to laparoscopic surgery, CO_2 flow is regulated during POEM.[26] Continuous insufflation by CO_2 inadvertently track into surrounding tissues and cause capnomediastinum, capnothorax, capnoperitoneum, and subcutaneous emphysema. The incidences of insufflation-related adverse events, ranges from 7.5% to 55.5%.[29,30] About 5.1% of the patients develop capnothorax and mucosal tear during POEM has been reported between 0–7%.[31] These are now considered as an integral part of the procedure rather than complications.[32] Mucosal injury, subcutaneous emphysema, and capnoperitoneum can be managed conservatively. Tense capnoperitoneum and capnothorax require needle decompression and chest tube placement.[33]

Subcutaneous emphysema is the common insufflation related adverse event. Earlier detection is important. It has been found that 60% of the instances of raised $ETCO_2$ >50 mm Hg is associated with subcutaneous emphysema.[34] For extensive cases hyperventilation is not useful, subcutaneous needle drain is required. A careful assessment of airway is necessary due to potential risk of airway obstruction.

The capnoperitoneum (Pnp) may also lead to inferior vena cava compression, preload reduction, and subsequent compromised cardiopulmonary functions. If Pnp occurs percutaneous abdominal needle decompression is required. A study has proposed for a needle decompression in the event of $ETCO_2$ > 50 mm Hg, or peak airway pressure (Pmax) >35 cm H_2O along with abdominal distension.[26] Intra-abdominal pressure cannot be measured directly during POEM but the Pmax act as an indirect marker for it. Another study has suggested that Pmax <38 cm H_2O reduces the risk of capnoperitoneum.[11]

The crucial factor for minimizing these events is the total amount of gas insufflated. It has been found in a recent study that a low-flow CO_2 tubing caused no events of Pnp in comparison to medium- or high-flow CO_2 tubing resulting into 36.7% tense capnoperitoneum.[35] It is has been found that a sparing use of CO_2 in a flow around 1.2 L/min is associated with negligible complication.

The control of Peak airway pressure during POEM is a challenging task. It increases due to gastric distension or capnocapnoperitoneum. A low tidal volume with increased respiratory rate may be helpful for maintaining minute ventilation. However, Inoue *et al*.[10] concluded that positive pressure ventilation with higher pressures than those generated by endoscopic CO_2 insufflation is necessary for reducing the risk of mediastinal emphysema and embolization.

Although the POEM-related adverse events are usually well managed without clinical morbidity, patient's pain and increased use of resources should be reduced. Thus, early detection of the preceding signs with close communication and cooperation are valuable with endoscopists. Finally, a quick procedure may also be helpful for averting these incidents.

Postoperative Care

POEM results in a considerable amount of postoperative pain. It is not only one of the most undesirable experience but also bears undesirable cardiovascular effects, respiratory depression, urinary and neuroendocrine dysfunction.[16] Patient-controlled analgesia (PCA) with an opioid may be beneficial. However, they may lead to nausea, vomiting, pruritus, and respiratory depression. Use of multi-modal analgesia by using non-steroidal anti-inflammatory drugs, ketamine, and anti-emetics, has been used to minimize opioid-related side effects.[36]

Exposure to general anesthesia and use of opioids for postoperative pain management can cause postoperative nausea and vomiting (PONV). PONV immediately after the procedure can precipitate bleeding and mucosal tear or esophageal perforation. Women, non-smoker, history of motion

sickness, and the use of postoperative opioids are known as risk factors of PONV. Serotonin (5-hydroxytryptamine, subtype 3 [5-HT3]) receptor antagonists, metoclopramide and dexamethasone have been used for prevention. Alternatively, use of total intravenous anesthesia with propofol reduces the risk of PONV.[37]

Postprocedural management including investigations and resumption of diet differs between centers. Usually all patients are kept NPO over night after the procedure and continued on intravenous antibiotics. After ensuring no evidence of leakage by water-soluble contrast esophagogram on a postoperative day one, a soft pureed diet is started. Postoperative supervised incentive spirometry is beneficial for preventing atelectasis.[11]

In conclusion, POEM is endoscopic minimally invasive treatment modality for achalasia. The communication between anesthesiologists and endoscopists is the key for reduction in iatrogenic complications. Further studies regarding preprocedure fasting, ventilation strategies, optimum CO_2 insufflation rate is need of the hour.

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Conflicts of interest

There are no conflicts of interest.

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