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REPORTS OF ORIGINAL INVESTIGATIONS

Anesthetic considerations for patients with esophageal achalasia undergoing peroral endoscopic myotomy: a retrospective case series review

Considérations anesthésiques pour la prise en charge des patients atteints d'achalasie de l'œsophage subissant une myotomie per-orale endoscopique: compte rendu rétrospectif d'une série de cas

Benjamin Löser, MD · Yuki B. Werner, MD · Mark A. Punke, MD · Bernd Saugel, MD · Sebastian Haas, MD · Daniel A. Reuter, MD · Oliver Mann, MD · Anna Duprée, MD · Guido Schachschal, MD · Thomas Rösch, MD · Martin Petzoldt, MD

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Abstract

Purpose *Peroral endoscopic myotomy (POEM) is a novel technique for treating esophageal achalasia. During POEM, carbon dioxide (CO_2) is insufflated to aid surgical dissection, but it may inadvertently track into surrounding tissues, causing systemic CO_2 uptake and tension capnoperitoneum. This in turn may affect cardiorespiratory function. This study quantified these cardiorespiratory effects and treatment by hyperventilation and percutaneous abdominal needle decompression (PND).*

Methods *One hundred and seventy-three consecutive patients who underwent POEM were included in this four-year retrospective study. Procedure-related changes in peak inspiratory pressure (p_{max}), end-tidal CO_2 levels ($etCO_2$), minute ventilation (MV), mean arterial pressure (MAP), and heart rate (HR) were analyzed. We also quantified the impact of PND on these cardiorespiratory parameters.*

Results *During the endoscopic procedure, cardiorespiratory parameters increased from baseline: p_{max} 15.1 (4.5) vs 19.8 (4.7) cm H_2O; $etCO_2$ 4.5 (0.4) vs 5.5 (0.9) kPa [34.0 (2.9) vs 41.6 (6.9) mmHg]; MAP 73.9 (9.7) vs 99.3 (15.2) mmHg; HR 67.6 (12.4) vs 85.3 (16.4) min^{-1} ($P < 0.001$ for each). Hyperventilation [MV 5.9 (1.2) vs 9.0 (1.8) $L{\cdot}min^{-1}$, $P < 0.001$] was applied to counteract iatrogenic hypercapnia. Individuals with tension capnoperitoneum treated with PND (n = 55) had higher peak p_{max} values [22.8 (5.7) vs 18.4 (3.3) cm H_2O, $P < 0.001$] than patients who did not require PND. After PND, p_{max} [22.8 (5.7) vs 19.9 (4.3) cm H_2O, $P = 0.045$] and MAP [98.2 (16.3) vs 88.6 (11.8) mmHg, $P = 0.013$] decreased. Adverse events included pneumothorax (n = 1), transient myocardial ischemia (n = 1), and subcutaneous emphysema (n = 49). The latter precluded immediate extubation in eight cases. Postanesthesia care unit (PACU) stay was longer in individuals with subcutaneous emphysema than in those without [74.9 min (34.5) vs 61.5 (26.8 min), $P = 0.007$].*

Conclusion *Carbon dioxide insufflation during POEM produces systemic CO_2 uptake and increased intra-abdominal pressure. Changes in cardiorespiratory parameters include increased p_{max}, $etCO_2$, MAP, and HR. Hyperventilation and PND help mitigate some of these changes. Subcutaneous emphysema is common and may delay extubation and prolong PACU stay.*

B. Löser, MD (✉) · M. A. Punke, MD · B. Saugel, MD · S. Haas, MD · D. A. Reuter, MD · M. Petzoldt, MD
Department of Anesthesiology, Center of Anesthesiology and Intensive Care Medicine, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20251 Hamburg, Germany
e-mail: B.Loeser@uke.de

Y. B. Werner, MD · G. Schachschal, MD · T. Rösch, MD
Department of Interdisciplinary Endoscopy, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

O. Mann, MD · A. Duprée, MD
Department of General, Visceral and Thoracic Surgery, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Résumé

Objectif *La myotomie per-orale endoscopique (POEM) est une technique innovatrice pour le traitement de l'achalasie de l'œsophage. Pendant une POEM, on insuffle du dioxyde de carbone (CO_2) afin de favoriser la dissection chirurgicale, mais le CO_2 peut accidentellement s'immiscer dans les tissus environnants, provoquant une accumulation systémique de CO_2 et un capnopéritoine de tension, lequel pourrait, à son tour, potentiellement affecter la fonction cardiorespiratoire. Cette étude a quantifié ces effets cardiorespiratoires ainsi que le traitement par hyperventilation et une décompression abdominale percutanée à l'aiguille.*

Méthode *Cent soixante-dix-sept patients consécutifs ayant subi une POEM ont été inclus dans cette étude rétrospective d'une durée de quatre ans. Les changements liés à l'intervention suivants ont été analysés : la pression inspiratoire maximale (p_{max}), les taux de PCO_2 de fin d'expiration (PCO_2), la ventilation minute (VM), la tension artérielle moyenne (TAM) et la fréquence cardiaque (FC). Nous avons également quantifié l'impact de la décompression abdominale percutanée à l'aiguille sur ces paramètres cardiorespiratoires.*

Résultats *Pendant l'intervention endoscopique, les paramètres cardiorespiratoires ont augmenté par rapport aux valeurs de base : p_{max} 15,1 (4,5) vs 19,8 (4,7) cm H_2O; PCO_2 4,5 (0,4) vs 5,5 (0,9) kPa [34,0 (2,9) vs 41,6 (6,9) mmHg]; TAM 73,9 (9,7) vs 99,3 (15,2) mmHg; FC 67,6 (12,4) vs 85,3 (16,4) min^{-1} ($P < 0{,}001$ pour chaque paramètre). On a appliqué une hyperventilation [VM 5,9 (1,2) vs 9,0 (1,8) $L{\cdot}min^{-1}$, $P < 0{,}001$] pour contrecarrer l'hypercapnie iatrogénique. Les personnes ayant un capnopéritoine de tension et traitées par décompression abdominale percutanée à l'aiguille ont affiché des valeurs maximales p_{max} plus élevées [22,8 (5,7) vs 18,4 (3,3) cm H_2O, $P < 0{,}001$] que les patients qui n'ont pas eu besoin de cette intervention. Après la décompression, la p_{max} [22,8 (5,7) vs 19,9 (4,3) cm H_2O, $P = 0{,}045$] et la TAM [98,2 (16,3) vs 88,6 (11,8) mmHg, $P = 0{,}013$] ont baissé. Parmi les complications observées, citons un pneumothorax (n = 1), une ischémie myocardique transitoire (n = 1), et un emphysème sous-cutané (n = 49). Cette dernière complication a empêché l'extubation immédiate dans huit cas. La durée du séjour en salle de réveil était plus longue pour les patients ayant souffert d'un emphysème sous-cutané que pour ceux n'en ayant pas eu [74,9 min (34,5) vs 61,5 (26,8 min), $P = 0{,}007$].*

Conclusion *L'insufflation de dioxyde de carbone pendant une POEM produit une accumulation systémique de CO_2 et une augmentation de la pression intra-abdominale. Les changements au niveau des paramètres cardiorespiratoires comprenaient une augmentation de la p_{max}, du PCO_2, de la TAM et de la FC. L'hyperventilation et la décompression abdominale percutanée à l'aiguille ont aidé à mitiger certains de ces changements. L'emphysème sous-cutané est une complication fréquente et pourrait retarder l'extubation et prolonger le séjour en salle de réveil.*

Esophageal achalasia is a motility disorder characterized by dysfunction of the lower esophageal sphincter due to incomplete muscle relaxation. The standard treatment options include balloon dilatation and surgical myotomy using a laparoscopic approach (Heller myotomy).[1-3]

A purely endoscopic approach, peroral endoscopic myotomy (POEM), is a recently developed, less-invasive treatment for achalasia[4] that has been shown to be effective.[5-11] POEM is performed via endoscopic mucosal entry into, and a submucosal tunnel within, the gastrointestinal wall (Figure). The inner circular muscle bundles of the lower esophageal sphincter are dissected while preserving the outer longitudinal muscle. To facilitate the dissection, carbon dioxide (CO_2) is insufflated via the endoscope, but it may inadvertently escape into the surrounding tissues via artificially created passages, tracking into the mediastinum and abdomen. Consequences include subcutaneous emphysema, capnomediastinum, capnoperitoneum, and pneumothorax, which could compromise cardiorespiratory function.[10,12-14] Hyperventilation may be helpful for reducing the systemic CO_2 uptake. Percutaneous abdominal needle decompression (PND) may be necessary to decrease elevated abdominal pressure as a consequence of tension capnoperitnoneum.[15]

Although it is recognized that POEM poses unique anesthesia-related challenges, standard approaches have yet to be established. Moreover, complications associated with POEM are inconsistently described and variably defined.[5,10,11] The aim of this study was to quantify POEM-related changes in cardiorespiratory parameters and to determine whether PND can effectively improve compromised cardiorespiratory function in patients with tension capnoperitoneum.

Methods

The Ethics Committee of the Medical Board of Hamburg, Germany approved this retrospective single-centre study (WF-072/13). Medical records of consecutive patients who underwent POEM for motility disorders of the esophagus at the University Medical Center Hamburg–Eppendorf between June 2010 and June 2014 were reviewed.

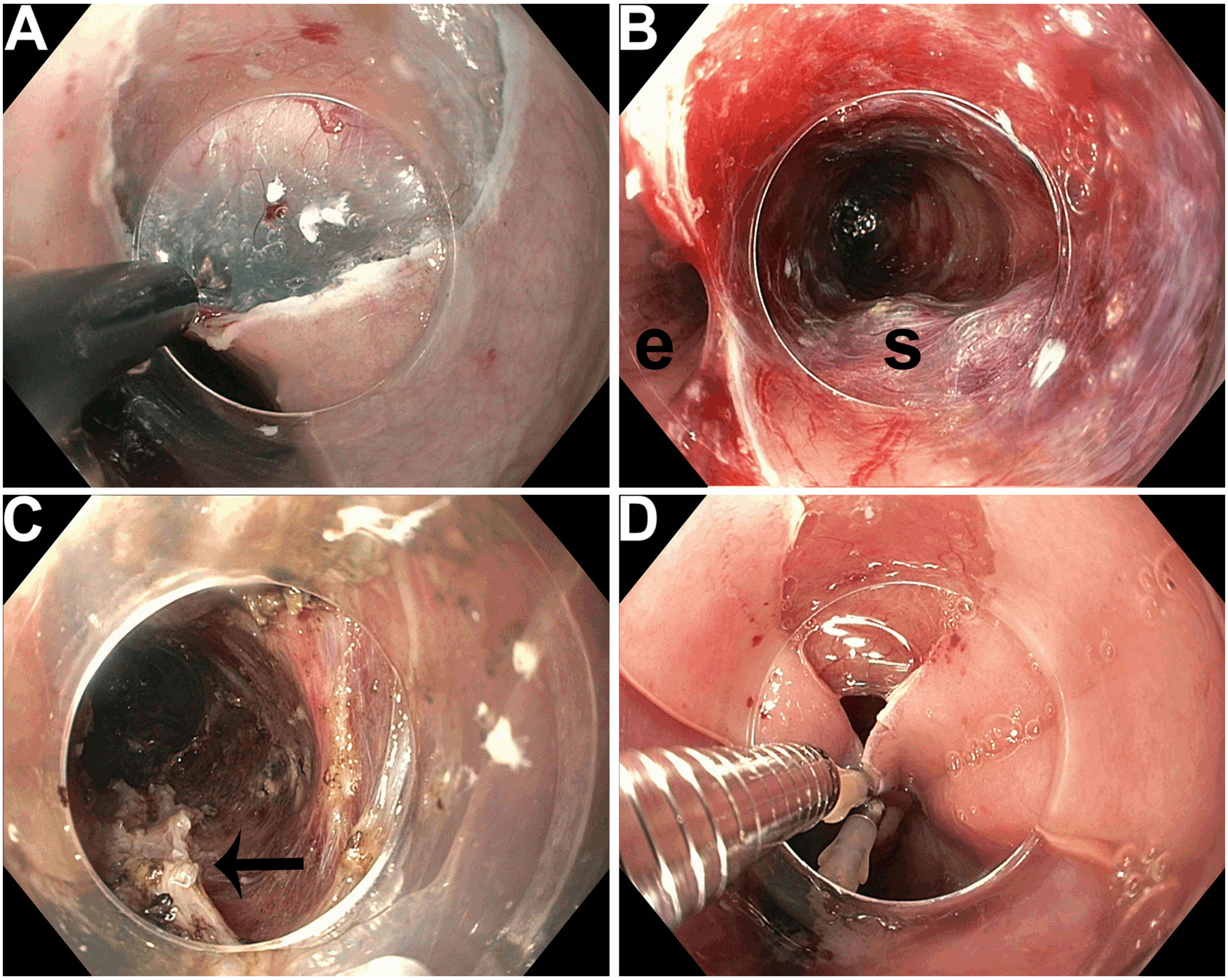

Figure Peroral endoscopic myotomy procedure: (A) Mucosal entry to the submucosal space. After injection of saline and methylene blue, a 2-cm longitudinal mucosal incision is made in a right lateral position at the level of the mid-esophagus. (B) Submucosal tunnel (s = entry in the submucosal tunnel; e = esophageal lumen). Endoscopic submucosal dissection is used for tunneling downward to the lesser curvature of the gastric cardia. (C) Submucosal tunnel after selective myotomy of the circular muscle fibres (black arrow) over a length of approximately 6-15 cm starting 3 cm distal to the initial mucosal entry and extended until 2-3 cm beyond the gastroesophageal junction. (D) Closure of the mucosal entry site with standard endoscopic clips

Electronically stored data, including anesthesia charts, were obtained from Soarian™ Health Archive (Release 3.04 SP12; Siemens Healthcare, Erlangen, Germany), Medlinq™ Anaesthesie (Medlinq Softwaresysteme GmbH, Hamburg, Germany), and the Endobase™ Documentation System (Release 12.0; Olympus, Tokyo, Japan).

Anesthesia and surgery

Patients were prepared for POEM according to institutional standards, as described previously.[7] A liquid diet was instituted for two to five days prior to surgery, and patients were kept *nil per os* overnight (for at least eight hours before induction of anesthesia). In all patients, esophagogastroduodenoscopy was performed one day before POEM to remove food remnants from the esophagus.[7] All patients were treated perioperatively with a dose of 80 mg of pantoprazole (starting from the day before POEM) and antibiotic prophylaxis.[7] All procedures were performed in our endoscopy unit in a specialized endoscopy suite.

No standardized anesthesia protocol was implemented during the study period, with its management left to the discretion of the anesthesiologist. However, the following generalizations can be made. Procedures were performed under general anesthesia that typically included rapid sequence induction followed by orotracheal intubation. All individuals received a single dose of a neuromuscular blocking agent to facilitate endotracheal intubation. Muscle paralysis was not maintained throughout the procedure. General anesthesia was maintained by standard inhalational and/or intravenous anesthetic drugs. Cuffed reinforced endotracheal tubes (Woodbridge type; Mallinckrodt Lo-Contour™, Covidien, Dublin, Ireland) − internal diameter 7.5−8.5 mm for men and 7.0−7.5 mm for women − were used to avoid kinking or obstruction of the endotracheal tube during endoscopy. To prevent interference with the gastroscope, the endotracheal tube was positioned in the right lateral angle of the mouth and taped independently from the endoscopy mouthpiece. Of note, we did not use endotracheal tubes with subglottic evacuation ports and a suction lumen, as has been used in other studies.[16] Patients were positioned supine on the endoscopy table with the head elevated 30° and arms tucked. The abdomen was left exposed to assist in identifying and treating capnoperitoneum (below). Patients were subjected to volume-controlled mechanical ventilation with an oxygen/air mixture. N_2O was never used. Initial ventilation parameters (tidal volume 6−8 $mL \cdot kg^{-1}$, respiratory rate 10−16 $breaths \cdot min^{-1}$, positive end-expiratory pressure 3−8 cm H_2O) were adjusted to achieve normocapnia prior to commencement of endoscopy [end-tidal CO_2 ($etCO_2$) values of 4.0−6.0 kPa (30−45 mmHg)]. Standardized monitoring consisted of three-lead electrocardiography, oscillometric noninvasive blood pressure (NIBP) monitoring, side-stream capnography, and pulse oximetry. Invasive cardiovascular monitoring was not routinely employed, and the decision was left to the discretion of the anesthesiologist as per the patient's underlying medical state.

Peroral endoscopic myotomy was performed as described previously[4,6,7] using GIF HQ 180/190™ gastroscopes (Olympus, Tokyo, Japan). This consisted of A) an initial mucosal incision, B) submucosal endoscopic tunneling, C) selective myotomy of the circular muscle fibres, and D) closure of the mucosal entry (Figure).[4,7] For POEM, CO_2 insufflation via the endoscope is required for esophageal and tissue distension. Carbon dioxide-insufflation was provided via an UCR™ CO_2 insufflator (Olympus, Tokyo, Japan) with a preset CO_2 flow of 1.2 $L \cdot min^{-1}$, which could be intermittently released, on demand, via fingertip control.

Endpoints

Patient records were assessed for the following items:

Patient characteristics including age, sex, American Society of Anesthesiologists classification, body mass index, significant co-morbidities, and the Eckardt symptom score.[17] Information was also sought concerning duration of the anesthesia and the endoscopic procedure. Achalasia subtypes were classified using the Chicago Classification Criteria, which are based on high-resolution esophageal manometry findings.[18]

Procedure-related respiratory parameters [peak inspiratory pressure (p_{max}), $etCO_2$ levels, minute ventilation (MV)] and cardiovascular parameters [mean arterial pressure (MAP) and heart rate (HR)] were measured at several points during the procedure. Baseline values were recorded prior to POEM (after induction of general anesthesia, they were the last values recorded prior to endoscopy). Peak values were recorded during POEM (from mucosal incision until re-closure) and prior to and after PND (below). Baseline and peak values represent single measurements. During the procedure, respiratory parameters (P_{max}, $etCO_2$, MV) and HR were displayed continuously. The MAP was measured every two to five minutes (NIBP) or continuously (invasive blood pressure monitoring). The results of the measurements were recorded every five minutes.

Percutaneous abdominal needle decompression: Elevated abdominal pressure requiring intervention was determined from clinical signs, such as visible abdominal distension, tympanic percussion sounds, subcutaneous emphysema, and elevated inspiratory peak pressure (p_{max}). The upper p_{max} alarm setting was adjusted to trigger at approximately +20% from baseline. The indication for PND was a consensus decision by the endoscopist and anesthesiologist based on those signs. For PND, a 14G or 16G cannula was inserted under sterile conditions through the abdominal wall in the right upper quadrant at least 5 cm below the rib cage after ensuring that the lower edge of the liver could not be palpated in this area. A catheter was left in situ for continuous venting.

Post-procedural course: Charts were assessed for length of stay in the postanesthesia care unit (PACU), postoperative requirement for invasive respirator support, unplanned admission to an intermediate or intensive care unit, and length of hospital stay. Particular attention was given to adverse events associated with POEM, including transient cervical/upper thoracic subcutaneous emphysema, aspiration, and pneumothorax.

Statistical analysis

Statistical analysis was performed using SPSS 22.0.0 (SPSS Inc., Chicago, IL, USA). Data were checked for normal distribution. Differences between measurement points were determined using one-way analysis of variance with repeated measures. The Tukey test was used for post hoc analysis. Differences between subgroups (PND-treated patients *vs* non-PND-treated patients or patients with emphysema *vs* patients without emphysema) were analyzed with independent-samples *t* tests. Unless otherwise stated, data are presented as means (standard deviation; SD). Ordinal data are presented as medians [interquartile range]. Categorical data are presented as percentage values calculated as (frequencies/number of valid data). A value of $P < 0.05$ was considered to indicate statistical significance.

Table 1 Patient baseline characteristics (n = 173)

Characteristics	
Demographics	
Sex (male/ female)	106/ 67
Age (yr)	47.0 (16.2)
ASA physical status classification (grade)	
I	17.0% (29/171)
II	64.3% (110/171)
III	18.7% (32/171)
Body mass index ($kg \cdot m^{-2}$)	25.5 (4.8)
Relevant co-morbidities, total	31.2% (54/173)
Coronary heart disease	8.7% (15/172)
Heart failure	2.9% (5/171)
Hypertension	24.3% (42/173)
Diabetes mellitus	5.2% (9/173)
Chronic obstructive pulmonary disease	1.7% (3/173)
Asthma	5.8% (10/173)
Chicago classification of esophageal motility disorders[18]	
Achalasia	
Type I (classic achalasia, failed peristalsis)	20.2% (35/173)
Type II (compressive achalasia)	53.8% (93/173)
Type III (peristaltic fragments or spastic achalasia)	15.6% (27/173)
Motility disorders	
Nutcracker esophagus (hypertensive peristalsis)	1.2% (2/173)
Jackhammer esophagus (hypercontractile esophagus)	1.7% (3/173)
Esophagogastric junction outflow obstruction	1.2% (2/173)
Not classifiable*	1.7% (3/173)
Re-myotomy	4.6% (8/173)
Eckardt symptom score[17] [0–12] (median [IQR])	7 [5–8]
Dysphagia [0–3]	3 [2–3]
Regurgitation [0–3]	1 [1–2]
Chest pain [0–3]	1 [0–2]
Weight loss [0–3]	1 [0–2]

ASA = American Society of Anesthesiologists

Data are presented as mean (SD). Categorical data are presented as percentage values [calculated as: (frequencies/number of valid data)]. Ordinal data are presented as the median [interquartile range]

Dysphagia/regurgitation/chest pain were scored as follows: 0, none; 1, occasional; 2, daily; 3, each meal. Weight loss was scored as follows: 0, none; 1, < 5 kg; 2, 5–10 kg; 3, > 0 kg

*Not classifiable because esophageal manometry was not available or was refused

Results

Of the 175 consecutive patients who underwent POEM during the study period, two were excluded because their charts were unavailable, leaving 173 patients for further consideration. Patients' baseline characteristics, co-morbidities, classification of esophageal motility disorders (Chicago Classification Criteria),[18] and clinical grading of severity (Eckardt Symptom Score)[17] are shown in Table 1.

The duration of general anesthesia was 120 (35) min, and the duration of the procedure was 96 (33) min. During the endoscopic procedure, p_{max}, $etCO_2$, MAP, and HR increased from baseline values (Table 2, columns A and B). Therapeutic hyperventilation was applied to reduce the iatrogenic hypercapnia, although end-tidal CO_2 levels remained elevated compared with baseline values (Table 2, columns A and B).

Of the 173 patients, 55 (31.8%) were treated with PND. Their baseline respiratory and cardiovascular parameters were similar to those who did not require PND (Table 2, columns C and E). PND-treated patients were differentiated from the non-treated patients only by their procedure-related higher p_{max} (Table 2, columns D and F). Reductions in p_{max} and MAP were observed following PND (Table 2, columns F and G). No PND-related complications were observed.

Cervical/upper thoracic subcutaneous emphysema occurred in 49 of the 173 patients (Table 3). By the end of endoscopy, however, it had resolved sufficiently to permit immediate extubation after surgery in all but eight patients. These eight patients with persistent emphysema were brought to the PACU still intubated. The neck circumference was sequentially measured to track resolution of the cervical emphysema, and pneumothorax (if suspected) was excluded by plain chest radiography. These eight patients were extubated after ensuring a negative cuff leak test (5–25 min after PACU admission) and were discharged uneventfully to a general ward. The PACU stay, but not the hospital stay, was prolonged in patients with subcutaneous emphysema compared with

Table 2 Procedure- and PND-related cardiorespiratory changes during POEM

Respiratory and cardiovascular parameters	Entire POEM cohort (n=173)			Non-PND-treated patients (n=118)		PND-treated patients (n=55)				
	(A) Baseline prior to POEM	(B) Peak during POEM	P (A *vs* B)†	(C) Baseline prior to POEM	(D) Peak during POEM	(E) Baseline prior to POEM§	(F) Peak prior to PND	P (D *vs* F)*	(G) After PND	P (F *vs* G)†
p_{max} (cm H_2O)	15.1 (4.5)	19.8 (4.7)	<0.001	15.1 (5.2)	18.4 (3.3)	15.1 (2.2)	22.8 (5.7)	<0.001	19.9 (4.3)	0.045
$etCO_2$ kPa	4.5 (0.4)	5.5 (0.9)	<0.001	4.6 (0.4)	5.6 (1.0)	4.5 (0.3)	5.4 (0.6)	0.23	5.1 (0.4)	0.10
$etCO_2$ mmHg	34.0 (2.9)	41.6 (6.9)		34.3 (3.0)	42.1 (7.6)	33.4 (2.5)	40.7 (4.8)		37.9 (3.3)	
MV ($L \cdot min^{-1}$)	5.9 (1.2)	9.0 (1.8)	<0.001	6.0 (1.2)	9.1 (1.8)	5.7 (1.1)	8.8 (1.8)	0.34	8.6 (1.8)	0.91
MAP (mmHg)	73.9 (9.7)	99.3 (15.2)	<0.001	74.5 (10.1)	99.9 (14.8)	72.7 (8.7)	98.2 (16.3)	0.51	88.6 (11.8)	0.013
HR (min^{-1})	67.6 (12.4)	85.3 (16.4)	<0.001	68.0 (13.0)	85.2 (14.9)	66.8 (11.1)	85.7 (19.4)	0.85	79.9 (12.6)	0.37

Data are presented as mean (SD); $etCO_2$ = end-tidal CO_2 level; HR = heart rate; MAP = mean arterial pressure; MV = minute ventilation; p_{max} = peak inspiratory pressure; PND = percutaneous needle decompression; POEM = peroral endoscopic myotomy. †: Differences between: (A) baseline prior to POEM, (B) peak values during POEM, (F) peak values prior to PND and (G) after PND were assessed using a one-way analysis of variance with repeated measures. The Tukey test was used for post hoc analysis. Differences between subgroups (PND vs no PND) regarding baseline values (**§**: C *vs* E) or peak values (*: D *vs* F) were determined using an independent-samples *t* test. Baseline values did not differ significantly between subgroups (§). Baseline values were assessed prior to POEM (after induction of general anesthesia, they were the last values recorded prior to endoscopy). Peak values were assessed during POEM (from mucosal incision until re-closure) and prior to and after PND. A value $P < 0.05$ was considered to indicate statistical significance

Table 3 Adverse events and outcome (n = 173)

Events and outcomes	% (no.)
Peri-interventional adverse events	
Subcutaneous emphysema	28.3% (49/173)
PND for treatment of tension capnoperitoneum	31.8% (55/173)
Aspiration	0.0% (0/173)
Radiological evidence of pulmonary infiltrates*	0.0% (0/119)
Difficult airway	5.3% (8/150)
Myocardial ischemia	0.6% (1/173)
Pneumothorax	0.6% (1/173)
Post-procedural recovery	
Length of hospital stay (days)	4.7 (2.0)
In-hospital and 30-day mortality	(0/173)
Length of PACU stay (min)	65.3 (29.7)
Patients with emphysema	74.9 (34.5)
Patients without emphysema	61.5 (26.8)
Prolonged postinterventional respirator support	4.6% (8/173)
Planned admission to an intermediate care unit	1.2% (2/173)

Data are presented as mean (SD); Categorical data are presented as percentage values calculated as (frequencies/ number of valid data)

PND = percutaneous needle decompression; POEM = peroral endoscopic myotomy

Peri-procedural adverse events were recorded during the intervention or the early postoperative period until discharge from the postanesthesia recovery unit (PACU)

Difficult airway was defined as Cormack and Lehane ≥ 3

*Chest plain radiography was performed in 119 of the first 121 POEM cases between the first and third postoperative day

those without it [74.9 (34.5) min *vs* 61.5 (26.8) min, P = 0.007 and 5.0 (3.0) *vs* 4.6 (1.4) days, P = 0.247, respectively]. Among the 173 patients, two had a planned admission to an intermediate care unit because of preexisting medical conditions (Table 3).

Other complications (Table 3) included one case of transient myocardial ischemia (inferior ST segment changes), which accompanied a brief episode of supraventricular tachycardia, and one case of pneumothorax, which was confirmed by intraoperative chest radiography and was drained during the endoscopic intervention. In the latter case, the procedure was eventually abandoned because of technical problems associated with establishing the submucosal tunnel. The patient underwent uneventful laparoscopic Heller myotomy six weeks later. None of the patients in this series experienced aspiration.

Discussion

Endoscopic therapeutic interventions have become increasingly sophisticated in recent years. The introduction of POEM marks a cornerstone of increased invasiveness in therapeutic gastrointestinal endoscopy. For the first time, an endoscopic procedure is being performed during which the integrity of the gastrointestinal tract is deliberately interrupted. During POEM, endoscopically insufflated CO_2 may inadvertently track into surrounding tissues. Unlike laparoscopic surgery, however, CO_2 feedback pressure regulation is not available during POEM. This situation likely contributes to the high incidence of mediastinal and cervical emphysema and capnoperitoneum, which may be considered inevitable consequences of the endoscopic intervention.

Although it is recognized that POEM poses unique anesthesia-related challenges, standardized management has yet to be established. Until now, only two small case series have been published that described anesthetic considerations for patients undergoing POEM. Neither of these reports quantified the effects of CO_2 insufflation on cardiorespiratory function or the impact of therapeutic interventions such as hyperventilation or PND.[19,20]

In our study, MAP and HR increased during POEM. These findings should be revisited in the context of the existing evidence regarding intended pressure-regulated capnoperitoneum during laparoscopic surgery. Many studies have shown that HR, MAP, and systemic vascular resistance increase during the pressure-regulated capnoperitoneum that occurs during laparoscopic surgery.[21-23] Although this hemodynamic response to capnoperitoneum is almost uniform, the underlying mechanisms appear to be multifactorial.[21] It has been suggested that the MAP increase might be a direct effect of absorbed CO_2,[24] mechanical vascular compression,[21] sympathetic stimulation,[23] and/or release of norepinephrine,[23,25] vasopressin,[22] renin, and aldosterone.[21,23] Perhaps the etiology of the cardiovascular responses associated with the inadvertent capnoperitoneum during POEM is similar to that associated with the intended capnoperitoneum during laparoscopic surgery.

Endoscopic CO_2 insufflation during POEM has an important impact on systemic CO_2 balance. We observed high systemic CO_2 uptake during POEM that was difficult to counterbalance by therapeutic hyperventilation. We propose that not only peritoneal absorption of CO_2, as occurs during laparoscopy,[21] but also submucosal, subcutaneous, and mediastinal CO_2 absorption contribute to this high CO_2 uptake during POEM.

We observed a POEM-related increase in p_{max}, which served as a marker of elevated intra-abdominal pressure and as a clinical indicator of the need for PND. As p_{max} and MAP decreased after abdominal pressure decompression, monitoring them could be helpful for evaluating the effectiveness of PND. Percutaneous abdominal needle decompression is an established technique for treating tension capnoperitoneum secondary to iatrogenic bowel perforation during endoscopy, with established clinical indications for its implementation.[15] Data supporting such clinical indications for POEM, and the effectiveness of PND during it, were heretofore not available.

Our findings show that, although insufflation-related cardiorespiratory responses are likely inevitable during POEM, they appear to be of little consequence so long as they are treated promptly and correctly. To this end, hyperventilation for treating iatrogenic hypercapnia and PND to release abdominal pressure may be considered complementary therapeutic strategies.

We found a low incidence of severe adverse events and a 30-day mortality rate of zero in our study cohort. Subcutaneous emphysema occurred in 28% of our patients, but it appeared to be transient and without relevant clinical sequelae other than slightly prolonging extubation and the PACU stay. Severe operation-related infections such as mediastinitis or peritonitis were rarely reported (approximately 0.1%) in previous studies[5,11] and were not observed in our cohort. Previous studies, however, have reported varying rates of other adverse events in patients undergoing POEM. Whereas Familiari *et al.*[26] did not report any severe perioperative complications among 100 patients, Ren *et al.*[13] reported incidences of subcutaneous emphysema (56%), pneumothorax (25%), mediastinal emphysema (29%), hemorrhage (1%), pleural effusion (49%), and minor inflammation or segmental lung atelectasis (50%) in 119 patients.

Of note, we did not observe any evidence of aspiration in our study cohort. Most patients with achalasia undergoing POEM have severe regurgitation and dysphagia. Evacuation of solid esophageal contents via esophagogastroduodenoscopy prior to POEM has been recommended.[7,19] Although there is no clear evidence that this measure prevents peri-procedural aspiration, it is part of our routine preparation prior to POEM. We also strongly recommend a pre-surgery liquid diet, antacid therapy, and the use of rapid sequence induction to avoid aspiration in these unique patients.

The study did have limitations. Our data represent a single-centre experience, so caution should be taken when they are extrapolated to other institutions with variable surgical and anesthesia management strategies for these cases. Confounding variables – procedure time, mucosal incision, tunnel width, myotomy depth, sigmoid-type esophagus – represent important risk factors for gas-related complications.[27] The retrospective nature of this study is a well-recognized limitation. Importantly, patients were not randomized to blinded PND/non-PND treatment, so the differences between these two groups should be treated with appropriate caution. The study was not sufficiently powered to assess the incidence of rare, severe adverse events. The absence of these events, as reported, should also be regarded cautiously. End-tidal CO_2 is only a surrogate marker for arterial CO_2 partial pressure, and we likely underestimated the hypercapnia resulted from systemic uptake of CO_2. Finally, the periodic recording of cardiorespiratory data is an acknowledged source of error, and the peak changes in these parameters may have been missed in some cases.

In conclusion, endoscopically insufflated CO_2 during POEM may inadvertently track into surrounding tissues, causing transient cervical/upper thoracic subcutaneous emphysema, free abdominal CO_2 with increased intra-abdominal pressure, and high systemic CO_2 uptake. These situations, in turn, can affect cardiorespiratory parameters such as increased p_{max}, $etCO_2$, MAP, and HR. Hyperventilation and PND can help mitigate some of these changes. Subcutaneous emphysema, which is common, may delay extubation and prolong the PACU stay.

Conflict of interest All authors state that they have no conflict of interest and no financial ties relevant to this study.

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