

## Transesophageal mediastinoscopy by submucosal endoscopy with mucosal flap safety valve technique

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**Background:** Indications for NOTES (natural orifice transluminal endoscopic surgery) studied so far are limited to intra-abdominal surgery.

**Objectives:** To determine the technical feasibility and the safety of transesophageal mediastinoscopy by using the submucosal endoscopy with mucosal flap safety valve (SEMF) technique.

**Design:** Two-week survival study with 4 porcine models.

**Interventions:** High-pressure carbon dioxide injection and balloon dissection created a large submucosal working space for insertion of a cap-fitted endoscope. The muscularis propria was resected inside the submucosal space, and the mediastinoscopy was performed by using the endoscope inserted via the myotomy site. The muscular defect was sealed with the overlying mucosal flap, and the mucosal entry site was closed with clips.

**Main Outcome Measurements:** Repeated endoscopy and necropsy were performed 2 weeks after the procedure.

**Results:** With the SEMF technique, the posterior mediastinum was successfully accessed in all animals. Three pigs survived 2 weeks without clinical complications, and the defects were completely sealed by the mucosal flap. One pig with proximal esophageal mediastinal entry managed under voluntary respiration was euthanized because of pleural injury.

**Conclusions:** The SEMF technique provided safe entry into the mediastinum, with a protective submucosal tunnel that prevented mediastinal soiling. Mid to distal esophageal access is safer than the higher level access. Mechanical ventilation might allow safer respiratory support.

Natural orifice transluminal endoscopic surgery (NOTES) is expected to offer a breakthrough for flexible endoscopy to go beyond the GI wall and access the intra-abdominal cavity without external incision.<sup>1-3</sup> Several NOTES surgeries have been described by modifying laparoscopic surgical techniques in porcine models.<sup>4-12</sup> Also, initial clinical experiences, including transgastric appendectomy have already been performed. However, transluminal efforts remain limited to the abdominal organs.

In this study, we evaluated the technical feasibility of transesophageal mediastinoscopy as an initial step to access the thoracic cavity for NOTES. We report submucosal endoscopy with a mucosal flap safety valve technique

(SEMF)<sup>13</sup> to create safe entry into the mediastinum and to avoid the risk of contamination.

### MATERIALS AND METHODS

The protocol was reviewed by the institutional animal care and use committee, with approval for the use of 4 domestic pigs.

The 4 pigs were studied while they were under standard general anesthesia. The first pig was managed under voluntary respiration, and the remaining 3 pigs were mechanically ventilated. A standard diagnostic gastroscope (GIF 130; Olympus America Inc, Center Valley, Pa), with an oblique-tip EMR cap (Olympus Optical Co, Ltd, Tokyo, Japan) was used. Initially, the mucosa of the esophagus was lavaged with a solution of sterilized water and 60-mL 10% povidone-iodine via the endoscope channel. After

submucosal saline solution injection to confirm needle-tip entry into the submucosa by bleb formation (Fig. 1A), a high-pressure carbon dioxide (CO<sub>2</sub>) millisecond burst was injected into the submucosal layer (Fig. 1B) through a prototype 23-gauge dilator injection needle (Olympus Optical) (Fig. 2) at 30 cm proximal to the esophago-gastric (E-G) junction for the first pig and 15 cm proximal to the E-G junction for the other 3 pigs to create a circumferential submucosal gas cushion (Fig. 3). The CO<sub>2</sub> injection used was a commercially available CO<sub>2</sub> cylinder (CO<sub>2</sub> Duster; American Recorder Technology Inc, Simi Valley, Calif) that is used to clean electronic equipment. The published pressure of the cylinder is 70 to 140 psi; 3-mL 5% hydroxypropyl methylcellulose (Gonak; Akorn Inc, Buffalo Grove, Ill) was then injected to prevent gas escaping from the puncture sites and maintaining the gas cushion. The needle puncture site was dilated by a blunt insertion of the dilator portion of the injection needle. A 15-mm biliary retrieval balloon (Multi-3; Olympus America) was inserted into the insufflated submucosal layer from the mucosal hole and was distended to dissect residual strands of submucosal connective tissues to create an approximately 10-cm-long submucosal tunnel. Distal to the mucosal entry point and within the submucosal tunneled space, the muscularis propria was resected by cap EMR (Fig. 1C). After cap detachment, the gastroscope was inserted into the posterior mediastinum through the myotomy site, and a detailed mediastinal inspection was performed. Retroflexion of the endoscope was performed at the level of the transesophageal entry and 10 cm beyond the transesophageal entry. Areas of scope-induced trauma on all surfaces were noted after these maneuvers. After inspection of the posterior mediastinal space, the submucosal space was closed by applying mucosal clips close to the mucosal entry site (Fig. 1D).

The pigs were on a liquid diet for 48 hours, a softened diet on day 3, and then a normal diet as tolerated. They also received antibiotics for 5 days (enrofloxacin 10 mg/kg once a day [Baytril; Bayel Co, Shawnee Mission, Kan]) and antiacid therapy for 7 days (esomeprazole 40 mg twice a day [Nexium; AstraZeneca Pharmaceuticals LP, Wilmington, Del]). Two weeks after the procedure, endoscopy and necropsy were performed to examine the SEMF site.

## RESULTS

In all animals, the mediastinum was successfully accessed after the SEMF myotomy. A measured 10-cm-long (endoscope insertion tube) submucosal tunnel was created within 10 minutes after CO<sub>2</sub> injection. The average size of the muscularis propria myotomy specimens was 15 mm (range, 10-20 mm). Three of 4 pigs survived without any clinical complication and resumed a normal diet and activity during the follow-up period.

### Capsule Summary

#### What is already known on this topic

- NOTES has been limited to abdominal organs.

#### What this study adds to our knowledge

- By using the submucosal endoscopy with mucosal flap technique in 4 pigs, the posterior mediastinum was successfully accessed repeatedly, and the thoracic organs were visualized endoscopically without mediastinal soiling.

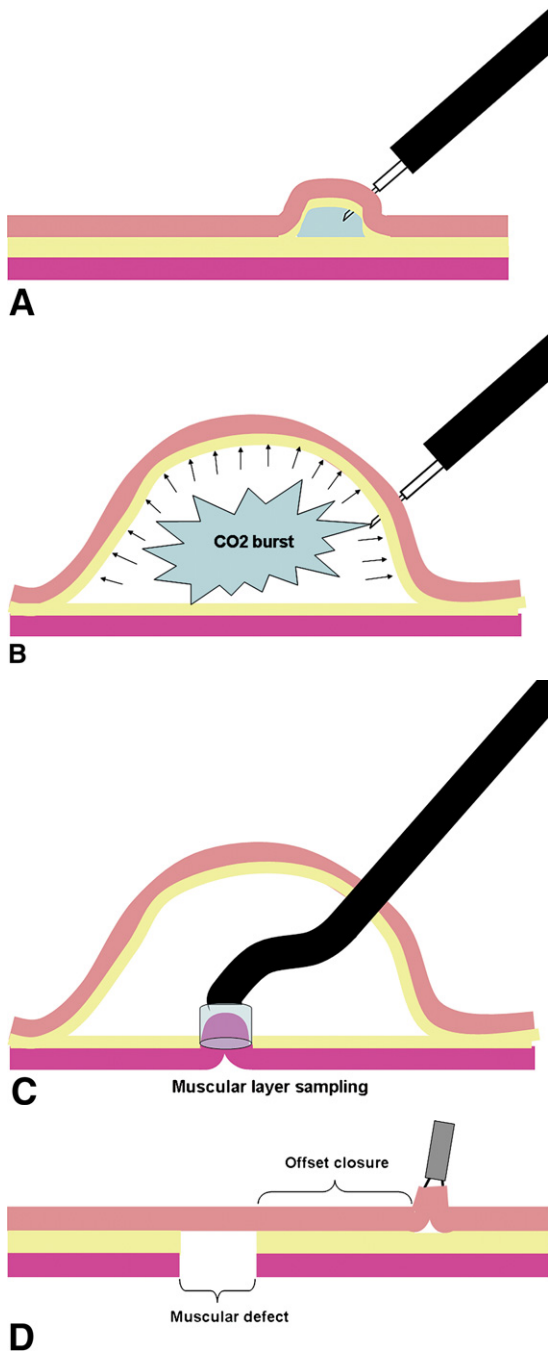
The first pig with the most proximal access to the mediastinum, and managed under voluntary respiration, had an incidental injury of the pleura, which resulted in severe respiratory distress. The animal was immediately euthanized.

In the surviving pigs, the lungs (Fig. 3A), the descending thoracic aorta (Fig. 3B), the posterior pericardial wall (Fig. 3C), the vertebra (Fig. 3D), the adventitial side of the esophagus (Fig. 3E), the azygos vein (Fig. 3F), and the vagal nerve trunks (Fig. 4) were deliberately endoscopically visualized.

The mucosal entries were successfully closed with clips. Follow-up endoscopy at 2 weeks showed healed mucosal entry sites without ulceration (Fig. 5). Necropsy revealed an open myotomy defect, with the overlying mucosal flap sealing the defect completely, accompanied by a clean posterior mediastinum (Fig. 6).

## DISCUSSION

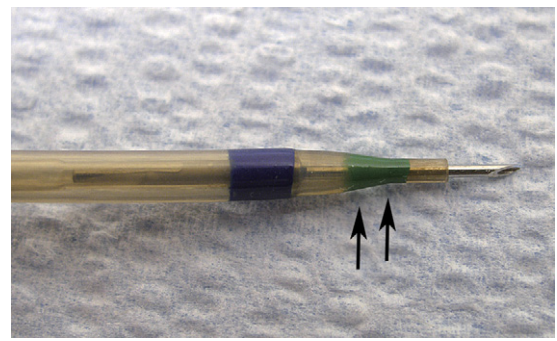
The posterior mediastinum contains important organs, such as the descending thoracic aorta, the esophagus, the azygos vein, and the autonomic ganglia and nerves, which were endoscopically visualized in this study. Seventy-five percent to 95% of neurogenic tumors, which comprise 12% to 21% of all mediastinal masses, present in the posterior mediastinum.<sup>14-17</sup> Also, prevalent GI surgeries, such as transhiatal esophagectomy and vagotomy, are performed in the posterior mediastinum. However, the posterior mediastinum is remote from the body surface and bounded with critical and delicate organs: the pericardium; the posterior surface of the diaphragm; the vertebral column, from the lower border of the fourth to the twelfth thoracic vertebra; and the mediastinal pleura. Recently, percutaneous mediastinoscopy was used as a minimally invasive access to the mediastinal cavity, but it still requires thoracotomy and pleural incision to access the posterior mediastinum. In contrast, transesophageal mediastinoscopy eliminated the trauma to important surrounding organs by using the esophagus, one of the intramediastinal organs, as the entry site into the posterior mediastinum. When considering the anatomic



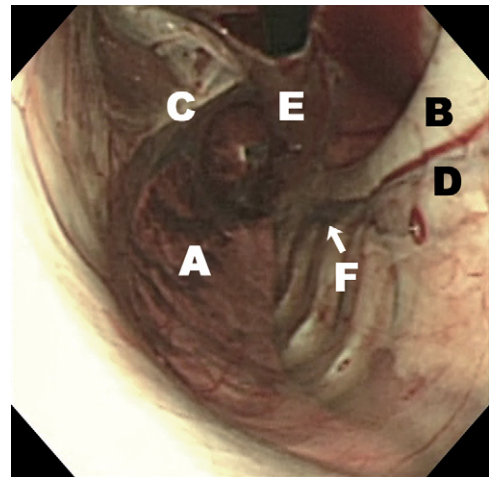
**Figure 1.** Transesophageal mediastinoscopy technique. **A**, Saline-solution-injection test to confirm needle-tip entry into the submucosa. **B**, Gas submucosal dissection with high-pressure CO<sub>2</sub>. **C**, Muscular-layer resection with cap-EMR technique inside of the submucosal space. **D**, Offset closure of the muscular defect with overlying mucosal flap.

environment accessed, transesophageal submucosal endoscopy into the mediastinum may have more immediate clinical appeal than transgastric access to the peritoneal cavity.

For the SEMF technique used in this study, a 10-cm-long mucosal strip was physically isolated from the muscularis propria. The myotomy was performed within the EMR cap, drawing the ensnared muscularis propria into

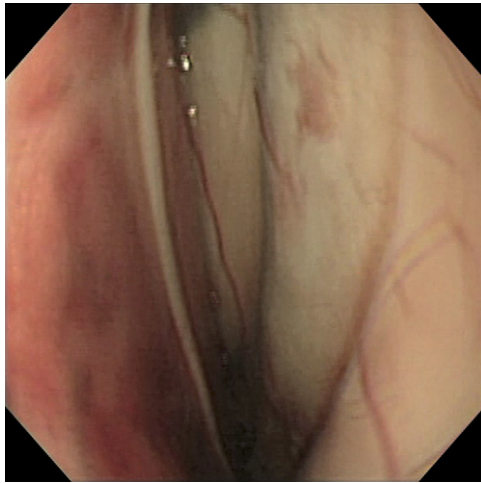


**Figure 2.** A prototype 23-gauge dilator injection needle. Tip of the outer sheath is tapered as a dilator portion (arrows).

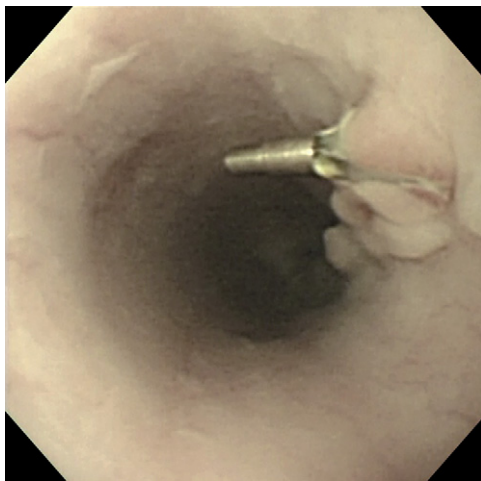


**Figure 3.** Retroflexed endoscopic view of the posterior mediastinum. **A**, The lung. **B**, The descending thoracic aorta. **C**, The posterior pericardial wall. **D**, The vertebra. **E**, The adventitial side of the esophagus. **F**, the azygos vein.

the cap before applying the electrosurgical current. We anticipated that blind electrosurgical needle puncture followed by balloon dilation would provide access to the mediastinum, because this method was used to access the peritoneal cavity in previously reported studies of NOTES techniques. Both needle-knife and subsequent balloon puncture carry a risk of inadvertent injury of important organs surrounding the esophagus. These risks were theoretically eliminated with the aspiration myotomy method used to access the mediastinum in this study. Also, because the mucosal entry point was a (vertical) tear, should urgent closure to the mediastinum become necessary, this can readily be accomplished by simple clip mucosal apposition. The 3 survival pigs did not have any clinical symptoms of infection, and the necropsy revealed a clean mediastinum. This demonstrated that submucosal offset entry into the mediastinum created by SEMF and clip mucosal apposition can effectively prevent mediastinal soiling. In clinical practice, the Heller myotomy for achalasia essentially creates a similar situation



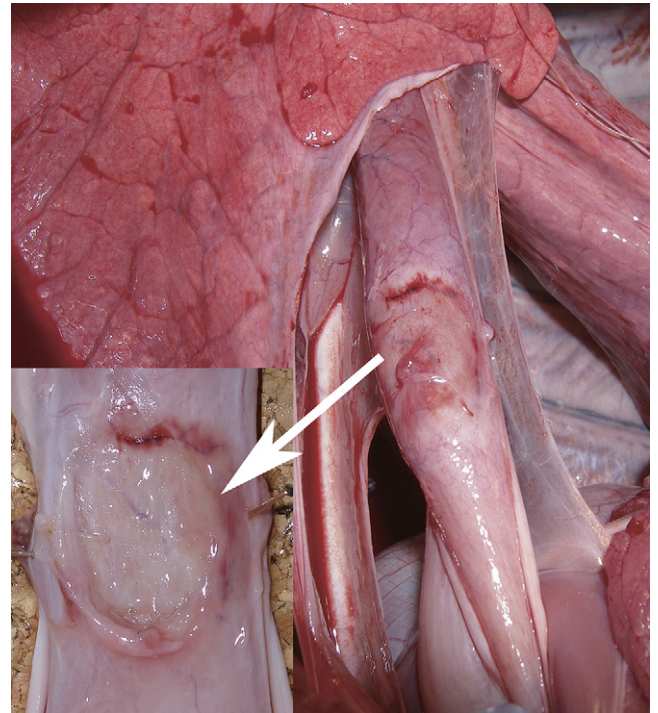
**Figure 4.** The vagus nerve.



**Figure 5.** A repaired mucosal entry site at repeated endoscopy after a 2-week survival period.

with a mucosal flap overlying the myotomy. Historically, and in current practice, this mucosal overlay is robust enough to maintain the integrity of the esophageal wall and offers some indirect reassurance to this new method.

The first pig studied for upper esophageal access had inadvertent injury of the pleura that resulted in fatal respiratory distress with a tension pneumomediastinum. There are important observations to be made from this adverse event. The upper posterior mediastinum has insufficient space to accommodate the regular gastroscope, placing the pleural tissue at risk for mechanical abrasion and disruption. The mediastinoscopy was performed with unmeasured air insufflation during unassisted voluntary ventilation. For safer transesophageal mediastinoscopy, the myotomy should be located in the distal esophagus and mechanical positive-pressure ventilation provided to prevent acute lung decompression by any positive intramediastinal pressure. Monitoring air insufflation similar



**Figure 6.** A myotomy site 2 cm in size, sealed with an overlying mucosal flap during necropsy. Overlying mucosal flap completely sealing the muscular defect.

to a pneumoperitoneum, as well as using CO<sub>2</sub> for insufflation, may add greater safety to the procedure. Although we did not attempt to repair the pleural injury in this evaluation of the technical feasibility of transesophageal mediastinoscopy, standard treatment for the pleural injury, such as pleural sac decompression and chest-tube placement, should be used for this complication in additional studies before clinical trials.

Our endoscopic developmental unit is developing therapeutic interventions in the thoracic cavity by using the SEMF technique. We anticipate that SEMF in the esophagus will allow myotomy for treatment of achalasia and also will allow widespread mucosal resection, with a minor modification of the methodology to primarily undermine the mucosa for controlled en bloc excision. SEMF might also provide the platform to allow access to the cardiovascular system and the peripheral respiratory system.

In this preliminary in vivo survival study, use of the SEMF technique allowed repeated safe access to the posterior mediastinum and endoscopic visualization of important thoracic organs without mediastinal soiling. The results of this study may encourage future development of NOTES in the thoracic cavity.

## DISCLOSURE

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