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Natural orifice transesophageal mediastinoscopy and thoracoscopy

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Abstract
Background Thoracoscopy and mediastinoscopy are common procedures with painful incisions and prominent scars. A natural orifice transesophageal endoscopic surgical (NOTES) approach could reduce pain, eliminate intercostal neuralgia, provide access to the posterior mediastinal compartment, and improve cosmesis. In addition NOTES esophageal access routes also have the potential to replace conventional thoracoscopic approaches for medial or hilar lesions.
Methods Five healthy Yorkshire swine underwent non-survival natural orifice transesophageal mediastinoscopy and thoracoscopy under general anesthesia. An 8- to 9.8-mm video endoscope was introduced into the esophagus, and a 10-cm submucosal tunnel was created with blunt dissection. The endoscope then was passed through the muscular layers of the esophagus into the mediastinal space. The mediastinal compartment, pleura, lung, mediastinal lymph nodes, thoracic duct, vagus nerves, and exterior surface of the esophagus were identified. Mediastinal lymph node resection was easily accomplished. For thoracoscopy, a small incision was created through the pleura, and the endoscope was introduced into the thoracic cavity. The lung, chest wall, pleura, pericardium, and diaphragmatic surface were identified. Pleural biopsies were obtained with endoscopic forceps. The endoscope was withdrawn and the procedure terminated.
Results Mediastinal and thoracic structures could be identified without difficulty via a transesophageal approach. Lymph node resection was easily accomplished. Pleural biopsy under direct visualization was feasible. Selective mainstem bronchus intubation and collapse of the ipsilateral lung facilitated thoracoscopy. In one animal, an inadvertent 4-mm lung incision resulted in a pneumothorax. This was decompressed with a small venting intercostal incision, and the remainder of the procedure was completed without difficulty.
Conclusions Transesophageal endoscopic mediastinoscopy, lymph node resection, thoracoscopy, and pleural biopsy are feasible and provide excellent visualization of mediastinal and intrathoracic structures. Survival studies will be needed to confirm the safety of this approach.

Keywords Lymph node biopsy · Mediastinoscopy · NOTES · Pleural biopsy · Thoracoscopy · Transesophageal

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Natural orifice translumenal endoscopic surgical (NOTES) approaches for peritoneoscopy and liver biopsy [1, 2], tubal ligation [3], oophorectomy [4, 5], gastrojejunostomy [6, 7], cholecystectomy [8–10], splenectomy [11], lymphadenectomy [12], partial hysterectomy [13], and distal pancreatectomy [14] in the swine model have been reported. The evolution of NOTES procedures from animals to humans is occurring, with reports of transgastric appendectomy [15], transgastric peritoneoscopy [16], and transvaginal cholecystectomy [17]. Whereas diagnostic and therapeutic endoscopic procedures involving the thoracic cavity are common in clinical practice, transesophageal access has been confined to endoscopic ultrasound (EUS)-guided fine-needle aspiration.

To date, NOTES applications in the evaluation and treatment of diseases of the chest have attracted little attention. A transesophageal approach could permit access to the mediastinal and thoracic cavities with less pain and scarring than conventional thoracoscopic or transcervical mediastinoscopic approaches while providing greater capabilities for therapeutic intervention than EUS.

Mediastinoscopy, thoracoscopy, or both may be indicated for sampling lymph nodes, staging tumors, resecting the thymus, excising cysts, draining fluid collections, evaluating pleural disease, and performing pulmonary resection, thoracoscopic splanchnicectomy, and vagotomy [16, 18, 19]. Although video-assisted thoracoscopic surgery (VATS) is less painful than traditional thoracotomies, even small intercostal incisions are painful, and patients often require hospital stays of 3 days after the procedure [20]. In addition, anterior minithoracotomy (the Chamberlain procedure) may be required for evaluating adenopathy inaccessible by cervical mediastinoscopy. Furthermore, VATS has a low but significant rate of bleeding, air leak, empyema, pneumonia, and recurrent pneumothorax [21], and the approach requires that lesions be located in the outer third of the lung parenchyma [20]. Although percutaneous pleural biopsy is regarded as safe, the technique is blind and has a poor sensitivity for the diagnosis of pleural disease.

A transesophageal approach to the mediastinum and pleural spaces would eliminate skin incisions, would spare deep dissection of the pretracheal fascia, and could prevent cutaneous surgical site infections. This approach could be applicable for small patients (infants and children) and patients with limited extension at the neck (due to cervical arthritis), and could be performed in patients with a cutaneous tracheostomy for whom conventional mediastinoscopy may be contraindicated.

An endoscopic approach could be combined with EUS for precise location and tattoo marking of pathologic lymph nodes or tumors, and could permit examination and biopsy of lesions not accessible without a minithoracotomy. The central or medial location of thoracic cavity entry with a transesophageal approach could complement VATS procedures, which more easily access peripheral lesions. In transesophageal procedures that use a submucosal tunnel, the initial mucosal incision is offset from the final site of exit through the muscular layers. With good closure of the mucosal layer, postprocedure leaks may be prevented. This article aims to evaluate the feasibility of transesophageal mediastinoscopy, mediastinal lymph node resection, thoracoscopy, and pleural biopsy in a swine model.

Materials and methods

This study was approved by the Subcommittee for Research Animal Care of the Massachusetts General Hospital, Boston, Massachusetts. The study aimed to determine the technical feasibility of peroral transesophageal mediastinoscopy, lymph node resection, thoracoscopy, and pleural biopsy using an 8- to 9.8-mm single-channel gastroscope (Pentax Medical Inc., Montvale, NJ, USA) and commercially available flexible endoscopic devices.

Five Yorkshire breed swine were fed liquids for 1 day before endoscopy, then fasted overnight. The animals underwent general anesthesia with induction by Telazol/xylazine 4.4 mg/kg administered intramuscularly (IM) plus 2.2 mg/kg IM and endotracheal intubation. Anesthesia was maintained with isoflurane (1.5–3.0%) and oxygen (3 l/min).

After adequate anesthesia was achieved, the gastroscope was introduced perorally into the esophagus and stomach. Access to the esophageal lumen was secured with an overtube. Just distal to the end of the overtube, the site of interest in the esophagus was located. Using either a Huibregtse single-lumen needleknife (Cook Medical Inc., Winston-Salem, NC, USA), a prototype flexible carbon dioxide (CO_2) laser fiber (OmniGuide Inc., Cambridge, MA, USA), or the Duette multiband mucosectomy device (Cook Medical Inc.), a superficial incision was created through the mucosal layer of the esophagus. Using blunt dissection through the mucosal incision with the tip of a catheter or closed forceps, a submucosal tunnel of 10 cm was created, and the small-caliber endoscope was introduced into the submucosal space. The channel was extended down to the gastroesophageal junction with blunt dissection.

Using the needleknife, a small full-thickness incision was created distal to the mucosal incision through the submucosal, circular, and longitudinal muscular layers. The endoscope then was passed into the mediastinal space. The mediastinal compartment, mediastinal lymph nodes, pleura, lung, thoracic duct, and the exterior surface of the esophagus were identified.

Lymph node resection was performed using biopsy forceps and snare with electrocautery. A small incision was then created through the pleura. The endoscope was introduced into the thoracic cavity. The lung, chest wall, pleura, pericardium, and diaphragmatic surface were identified. A pleural biopsy was obtained with endoscopic forceps. The endoscope was withdrawn from the mediastinum through the esophageal wall and into the lumen. The proximal mucosal incision was closed with endoscopic clips. The animals were sacrificed at the end of the procedure.

Results

The esophageal mucosal incision was created successfully in all five animals (Fig. 1). Several techniques were examined. In three animals, we used the Huibregtse single-lumen needleknife (Cook Medical Inc.). The needleknife required the most meticulous attention to the depth of the dissection. We experimented with both saline-lift and air-lift before the needleknife incision. Both techniques were successful. The saline diffused more quickly (under endoscopic observation), and the saline ran into the visual field after the initial incision, which made the subsequent submucosal dissection more difficult.

The air-lift resulted in a well-defined cushion into which the dissection could be initiated. In the first case, a 2- to 3-mm full-thickness incision was created during the initial planned mucosal incision. The small full-thickness incision was used for the subsequent mediastinoscopy and thoracoscopy, but was noted as a complication. A deep submucosal tunnel could be created easily in all animals using blunt dissection (Fig. 2).

In one animal, we used a prototype, experimental, endoscopic flexible CO_2 laser fiber (OmniGuide Inc.).The CO_2 laser uses a flow of helium for cooling. In this case, the mucosal incision was performed with a brief pulse of the CO_2 laser with subsequent pneumodissection into the submucosal space. The submucosal plane was easily opened. Deep submucosal dissection then was performed bluntly.

In the thoracoscopy phase, the CO_2 laser was used to incise the pleura, facilitating the pleural biopsy. With the prototype 180-cm flexible fiber, torque and angulation of the fiber reduced the maximal power that could be delivered. Nevertheless, incision through fibrous tissue could be performed with application of laser energy. There were no complications during the use of the CO_2 laser.

Fig. 1 Endoscopic view of the esophageal lumen and the submucosal tunnel. The flap of the dissected mucosa appears in the middle of the image. The submucosal space can be seen on the left after blunt dissection

Fig. 2 Endoscopic view of the submucosal tunnel. The submucosal space is characterized by scant vascularity and a filmy weblike appearance

Finally, in the last animal, we used the Duette multiband mucosectomy device (Cook Medical Inc.) to make the superficial incision through the mucosal layer of the esophagus. The submucosal plane was easily opened, and the tunnel was again created using blunt dissection.

Endoscopic transesophageal mediastinoscopy was successful for all the animals, with no immediate complications. The site of exit opposite the cardiac impression was selected. However, using only the endoscopic view, it was difficult to determine which side of the chest had been entered. Visualization of the mediastinal structures was excellent (Fig. 3). The mediastinal compartment, mediastinal lymph nodes, pleura, medial surface of the lung, and lateral margin of the external esophagus were consistently identified. The thoracic duct was identified. Lymph node resection was performed using the forceps and a hot snare without complication. Lymph nodes were easily withdrawn for pathologic examination.

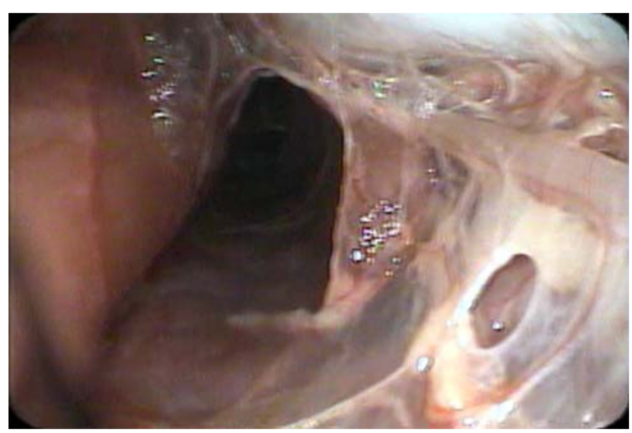

Fig. 3 Transesophageal flexible endoscopic view of the mediastinum. The pleura can be seen on the right side of the image. The lateral wall of the esophagus can be seen on the left side of the image

Fig. 4 Transesophageal flexible endoscopic view of the thoracic cavity. The collapsed lung can be seen in the inferior portion of the image

Fig. 5 Flexible endoscopic view of the thoracic cavity during pleural biopsy with conventional endoscopic forceps

After the mediastinoscopy, a thoracoscopy was performed in each animal. Transesophageal thoracoscopy was accomplished by making a small incision in the pleura. The thoracoscopy was easily accomplished in all the animals. Selective intubation of the contralateral lung and collapse of the ipsilateral lung facilitated thoracoscopy. In the first case, pleural dissection was complicated by a 4- to 5-mm needle knife lung incision that led to a pneumothorax. This animal had a transient drop in the blood pressure and heart rate that required creation of a small venting intercostal incision. The venting incision promptly restored the vital signs to baseline but was noted as a complication. In later cases, dissection through the pleura was performed with endoscopic forceps. It was easy to create a small pleural tear with forceps to enable thoracic cavity entry, and the needleknife was abandoned for this step (Fig. 4).

Thoracoscopy allowed identification of the lung, the pleura, the pericardium, and the superior diaphragmatic surface. Pleural biopsy was easy to accomplish and could be performed under direct visualization (Fig. 5). Areas of interest could be selected and biopsies directed to that site. The pleura was fibrous and required a forceful application of the endoscopic forceps for biopsy. At the end of the procedure, the proximal esophageal mucosal incision could be closed with the application of endoscopic clips (Olympus America Inc., Center Valley, PA, USA). No difficulties were encountered in closing the esophageal mucosal incision. At the end of the procedure, the animals were sacrificed as required by our approved protocol.

Discussion

This is the first report of transesophageal mediastinal lymph node resection and transesophageal thoracoscopy with pleural biopsy. The transesophageal approach provides ready access to the mediastinum and thoracic cavities. It was easy to perform lymph node resection and pleural biopsies using commercial endoscopic devices. In contrast to EUS-guided fine-needle biopsy and percutaneous pleural biopsy approaches, this technique allowed direct visualization for tissue sampling. The swine in this series did not have enlarged mediastinal lymph nodes or lesions involving the chest wall. However, this technique could have been used to target pathologic pleural deposits or mediastinal mass lesions and secure biopsies from them.

The optimal method for performing the esophagotomy was evaluated in this series using a needleknife, a prototype flexible endoscopic CO_2 laser fiber, and a commercial band-assisted endoscopic mucosal resection (EMR) device. One inadvertent full-thickness esophageal incision occurred using the needleknife. In this animal, we enlarged the small full-thickness esophagotomy for the subsequent mediastinoscopy and thoracoscopy. However, the occurrence highlights the ease of full-thickness incision when the needleknife is used to dissect in the esophagus. Using forceps to make a small tear allowed safe entry into the thoracic cavity, and we recommend this approach for pleural dissection in the mediastinum. The CO_2 laser, although effective in our study, is still in its prototype phase and is limited by loss of power with torque and angulation.

Cap- and band-assisted EMR provided the superior technique for creating the initial mucosal incision in this series. The device easily created the initial mucosal incision and allowed blunt dissection into the submucosal space. Findings have shown EMR to have a very low rate of complications in clinical practice [23]. On the basis of these results, we recommend the use of cap and band EMR for the initial mucosal incision in future studies involving the endoscopic esophageal submucosal tunnel technique.

This study confirms the applicability of the transesophageal submucosal tunnel technique and reproduced a thorough examination of the mediastinal compartment [22]. In addition, mediastinal lymphadenectomy was easily accomplished using standard endoscopic forceps and a hot snare, as was retrieval of the specimen for pathologic examination. There were no immediate complications. In this series, the endoscope easily reached the distal margin of the mediastinal compartment. In current practice, minithoracotomy is required in some instances when adenopathy is beyond the reach of cervical mediastinoscopy [20]. We did not find any limitation in the evaluation of the mediastinal compartment. If perfected in a human population, this technique also could find application for patients with cervical arthritis (limited neck extension), small habitus (infants and small children), or cutaneous tracheostomy for whom conventional mediastinoscopy is contraindicated [20].

In this series, the transesophageal approach also permitted examination of the thoracic cavity. Identified structures included the chest wall, lung, external surface of the pericardium, and superior diaphragmatic surface. The transesophageal approach could be used to perform a visually directed biopsy of the pleura. With the high false-negative rate of thoracentesis and blind percutaneous pleural biopsy, a visually directed transesophageal technique would probably have a superior rate of diagnosis, likely similar to that found with conventional thoracoscopy.

In contrast to intercostal percutaneous thoracoscopy, transesophageal thoracoscopy begins near the hilar surface of the lung and central region of the thoracic cavity. As such, the transesophageal route may provide a superior access point for central lesions.

As described earlier, a needleknife incision into the pleura caused a small 4- to 5-mm lung laceration in our first case. In the only previously published study of transesophageal mediastinoscopy, one instance of pleural injury also was reported that resulted in tension pneumomediastinum and death of that swine [22]. In that case, the procedure was performed during unassisted voluntary ventilation. The quick recovery with the venting intercostal incision in our experiment was aided in the setting of intubation and mechanical ventilation.

Together, these two incidents highlight the serious complications that may develop with NOTES procedures in the chest. We consider intubation and mechanical ventilation to be a requirement for NOTES experiments involving mediastinoscopy and thoracoscopy. In addition, we found that blunt forceps dissection was sufficient for transgression of the muscle layers of the esophagus and entrance to the thoracic cavity, with no resulting complications. None of the animals in the series required intraoperative chest tube placement.

Finally, as in clinical situations, intubation of the contralateral mainstem bronchus allowed collapse of the lung in the cavity of interest. Just as with VATS, lung collapse greatly improves exposure in the pleural cavity of interest.

Given that this was not a survival animal series, we did not test esophageal closure techniques. The submucosal tunnel creates a flap valve that offsets the proximal mucosal incision from the distal muscular incision. At withdrawal of the endoscope, the tunnel collapses, and we believe that this may serve as sufficient closure. Mucosal clips at the proximal entry site may further minimize the risk of esophageal leak. These techniques, however, need to be examined in survival studies.

This study had a number of limitations. In all published NOTES studies, the large animal model severely constrains the sample size and reduces data to case series reports. We view this limitation as one of the major hurdles for NOTES research in general. Although the series demonstrates several new techniques (mediastinal lymphadenectomy, transesophageal thoracoscopy, and transesophageal pleural biopsy) and replicates the transesophageal mediastinoscopy and submucosal tunnel technique recently reported [22], survival studies are needed to examine the occurrence of complications, especially with regard to infection, mediastinitis, and security of the esophageal closure. Because the esophagus lacks a serosal layer and is a relatively thin organ, leaks may lead to contamination of the mediastinal and/or thoracic cavities. Although esophageal leaks are a life-threatening complication, a NOTES approach involves healthy uninflamed tissues that may heal more rapidly and be less prone to leak than diseased tissue. The submucosal tunnel technique also may prevent leak and infection [22].

Another significant and initially unforeseen limitation involves difficulty in determining which side of the thoracic cavity is being entered with the esophageal approach. In the chest, palpation for siting (as would be done for a transgastric access route to the peritoneal cavity) cannot be performed because of the rigid chest wall. Possible solutions to this problem include the use of position changes and gravity-based techniques (pooling of fluid in the lumen) to determine location, the use of EUS to confirm the location of the azygos vein and aorta, or fluoroscopy.

Finally, the magnitude of immediate complications with transesophageal NOTES procedures may be greater than found with intraperitoneal procedures. Therefore, a cautious, stepwise approach to NOTES procedures above the diaphragm is advised.

This *in vivo* study is the first report of mediastinal lymphadenectomy, transesophageal thoracoscopy, and transesophageal pleural biopsy and demonstrates successful application of the submucosal tunnel technique. Although the transesophageal approach challenges the dogma about transgressing the wall of this fragile organ, our series suggests that the transesophageal approach is feasible and potentially safe. Were it to be perfected in a human population, the approach could address some limitations of conventional mediastinoscopy and thoracoscopy. Because thoracoscopy is much more painful than laparoscopy, there is potentially greater patient benefit from NOTES approaches in the thorax than in the abdomen.

Going forward, we believe that this technique could be combined with EUS and fine-needle tattoo to allow identification and marking of structures of interest (lymph nodes or tumors), enabling very precise sampling or excision. Whereas studies investigating NOTES in the abdomen have dominated the literature to this point, there may be a significant role for NOTES procedures above the diaphragm.

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