Hybrid endoscopic thymectomy: combined transesophageal and transthoracic approach in a survival porcine model with cadaver assessment

João Moreira-Pinto · Aníbal Ferreira ·
Alice Miranda · Carla Rolanda · Jorge Correia-Pinto

Received: 26 August 2013 / Accepted: 22 March 2014 / Published online: 25 April 2014
© Springer Science+Business Media New York 2014

Abstract

Background Video-assisted thoracoscopic surgery thymectomy has been used in the treatment of Myasthenia Gravis and thymomas (coexisting or not). In natural orifice transluminal endoscopic surgery, new approaches to the thorax are emerging as alternatives to the classic transthoracic endoscopic surgery. The aim of this study was to assess the feasibility and reliability of hybrid endoscopic thymectomy (HET) using a combined transthoracic and transesophageal approach.

Methods Twelve consecutive in vivo experiments were undertaken in the porcine model (4 acute and 8 survival). The same procedure was assessed in a human cadaver

afterward. For HET, an 11-mm trocar was inserted in the 2nd intercostal space in the left anterior axillary line. A 0° 10-mm thoracoscope with a 5-mm working channel was introduced. Transesophageal access was created through a submucosal tunnel using a flexible gastroscope with a single working channel introduced through the mouth. Using both flexible (gastroscope) and rigid (thoracoscope) instruments, the mediastinum was opened; the thymus was dissected, and the vessels were ligated using electrocautery alone.

Results Submucosal tunnel creation and esophagotomy were performed safely without incidents in all animals. Complete thymectomy was achieved in all experiments. All animals in the survival group lived for 14 days. Thoracoscopic and postmortem examination revealed pleural adhesions on site of the surgical procedure with no signs of infection. Histological analysis of the proximal third of the esophagus revealed complete cicatrization of both mucosal defect and myotomy site. In the human cadaver, we were able to replicate all the procedure even though we were not able to identify the thymus.

Conclusions Hybrid endoscopic thymectomy is feasible and reliable. HET could be regarded as a possible alternative to classic thoracoscopic approach for patients requiring thymectomy.

Electronic supplementary material The online version of this article (doi:[10.1007/s00464-014-3525-7](https://doi.org/10.1007/s00464-014-3525-7)) contains supplementary material, which is available to authorized users.

J. Moreira-Pinto (✉) · A. Ferreira · A. Miranda · C. Rolanda ·
J. Correia-Pinto
Life and Health Sciences Research Institute (ICVS), School of
Health Sciences, University of Minho, Campus de Gualtar,
4709-057 Braga, Portugal
e-mail: moreirapinto@gmail.com

J. Correia-Pinto
e-mail: jcp@ecsau.de.uminho.pt

J. Moreira-Pinto · A. Ferreira · A. Miranda · C. Rolanda ·
J. Correia-Pinto
ICVS/3B's – PT Government Associate Laboratory,
Braga/Guimarães, Portugal

J. Moreira-Pinto · J. Correia-Pinto
Department of Pediatric Surgery, Hospital de Braga, Braga,
Portugal

A. Ferreira · C. Rolanda
Department of Gastroenterology, Hospital de Braga, Braga,
Portugal

Keywords General · Oesophageal · Surgical · Technical ·
Endoscopy · Thoracoscopy

Video-assisted thoracoscopic surgery (VATS) was first described in the early 1990's. Initial applications included chest exploration, pleural effusion or pneumothorax management, and limited resection of lung nodules [1–4]. As minimally invasive techniques improved, clinical

application of VATS became progressively widespread for more complex procedures. VATS thymectomy was first described by Landreneau et al. in 1992 [5]. VATS thymectomy offers benefits of reduced immune-mediated surgical stress response and less chest trauma, with reduced impairment of postoperative pulmonary function that translates to faster recovery and fewer complications [6, 7]. VATS thymectomy has been used for Myasthenia Gravis and for both well-encapsulated noninvasive thymomas and selected invasive thymomas [8–10].

In natural orifice transluminal endoscopic surgery (NOTES), new approaches to the thorax are emerging as alternatives to classic transthoracic endoscopic surgery. In 2007, Sumiyama et al. proposed transesophageal access to the thoracic cavity [11]. Since then, transvesical-transdiaphragmatic [12], transgastric-transdiaphragmatic [13], and transtracheal thoracoscopy [14] have also been suggested. The transesophageal approach has been considered preferable as a direct entry to the thorax and posterior mediastinum for several simple thoracic procedures in porcine models [15]. However, the transesophageal approach is typically considered to be highly risky because of possible mechanical abrasion and trauma of surrounding structures. Moreover, an ineffective esophagotomy closure can be devastating, resulting in serious infectious complications. In fact, some of the recognized difficulties of NOTES procedures, such as safe port creation, infection prevention, tissue manipulation, suturing and anastomosis establishment, seem to be particularly relevant in the transesophageal approach. In view of this, Rolanda et al. proposed the combination of single transthoracic trocar assistance with transesophageal NOTES in order to increase the safety and feasibility of more complex procedures [16]. Since then, our group has proven the safety and feasibility of hybrid transesophageal pulmonary lobectomy [17] and hybrid transesophageal left atrial appendage ligation [18] in the survival porcine model.

We hypothesized that thoracic NOTES might be appropriate for thymectomy. Thus, we designed this research protocol to assess the feasibility and reliability of hybrid endoscopic thymectomy (HET) using combined transthoracic and transesophageal approach.

Methods

Study design

Twelve female pigs (*Sus scrofa domestica*) weighting 25–35 kg were used to perform HET. Consecutive in vivo experiments were undertaken (4 acute and 8 survival assessments). All surgical gastroscopic and thoracoscopic procedures were recorded. Vital signs and physiological

Fig. 1 Room ergonomics: A thoracoscope monitor; B gastroscope monitor; C ventilator; D back table for equipment

parameters were monitored during the experiment. The procedure time was recorded as well as difficulties and complications at each step of the procedure. The retrieved specimens were analyzed under a microscope to check if there was complete resection of the thymus. The animals in the survival group were monitored for 14 days. Gastroscopic and thoracoscopic examination and necropsy were performed in all animals at the end of the protocol (after the procedure in the acute animals and 14 days after when the survival animals were killed). The proximal esophagus of the pigs in the survival group was analyzed under a microscope to verify the healing process.

After the animal experiments, we performed the same procedure in a human female cadaver. Gastroscopic and thoracoscopic videos were recorded. The procedure time was recorded as well as difficulties and complications at each step of the procedure.

This study was approved by the ethical review board of Minho University (Braga, Portugal).

Pig preparation

All procedures were performed with the animals under general anesthesia with endotracheal intubation and mechanical ventilation. The pigs had no food (8 h) or water (4 h) before surgery. The pigs were premedicated with a combination of azaperone (4 mg/kg, intramuscularly [IM]), midazolam (1 mg/kg, IM), and atropine (0.05 mg/kg, IM). Anesthesia was induced with propofol (6 mg/kg, intravenously [IV]) and maintained with continuous propofol infusion (20 mg/kg/h, IV) and buprenorphine (0.05 mg/kg,

Fig. 2 Steps for hybrid endoscopic thymectomy (animal model). In **A** and **B**, main image represents thoracoscopic view, and insets represent gastroscopic view. In **C** and **D**, just gastroscopic image is represented. **A** Gastroscope going through the submucosal tunnel and thoracoscope showing the exact site for esophagotomy, between the left phrenic nerve (p), the left costocervical vein (c), and the left subclavian artery (s). **B** Dissection of the thymus (t) using a rigid

dissector introduced through the thoracoscope working channel and counter-traction using a flexible grasper introduced through the gastroscopist. One can see the counter-lateral lung (l) and the heart (h). **C** A flexible grasper through the gastroscopist introduces the specimens inside the endoscopic bag introduced through the transthoracic trocar. **D** Closing the mucosal incision of the esophagus with 5 hemoclips

IM). The pig was placed in the dorsal decubitus position. Room ergonomics is shown in Fig. 1.

Human cadaver preparation

A 72-year-old female human cadaver weighting 75 kg was defrosted 48 h prior to the operation. The cadaver was placed in the dorsal decubitus position with her left arm abducted.

Surgical technique (animal model and human cadaver)

The main steps of the procedure described here are schematically illustrated in Fig. 2. An 11-mm trocar (CTF33, Kii Access System; Applied Medical, Rancho Santa Margarita, California) was inserted in the second or third intercostal space in the left anterior axillary line. Carbon dioxide (CO₂) was inflated through the transthoracic trocar, and pressure was maintained up to 6 mm Hg. An operative thoracoscope with a 5-mm working channel (Straight Forward Telescope 0° 26034AA; Karl Storz GmbH, Tuttlingen, Germany) was introduced through the trocar. By using a rigid dissector (30310MLG; Karl Storz), the upper mediastinum was dissected allowing the identification of the esophagus with the help of gastroscopist movements (inside the esophagus) and transillumination, between the left phrenic nerve, the left costocervical vein, and the left subclavian artery (Fig. 2A).

A forward-viewing, single-channel gastroscopist (13801PKS; Karl Storz) was advanced into the esophagus, identifying the position of the thoracoscope and determining the esophagotomy site. Five milliliters of saline solution were injected into the submucosa 8 cm proximal to the esophagotomy position using an injection needle (110231-01; Karl Storz), and a 1-cm longitudinal incision was made in the mucosa using a needle-knife (KD-11Q-1; Olympus, Tokyo, Japan) through the gastroscopist working channel. Next an 6- to 8-cm long submucosal tunnel was created by blunt dissection. Esophagotomy was performed in the distal part of the submucosal tunnel (in the upper third of the esophagus).

While the submucosal tunnel was created in the esophagus, the left mediastinal pleura was opened and the left posterior limits of the thymus dissected using rigid instruments introduced through the transthoracic trocar. Once the transesophageal access was created, the dissection of the thymus was completed using both flexible (gastroscopist) and rigid (thoracoscope) instruments (Fig. 2B). The vessels were ligated using electrocautery alone, either through the flexible coagulation grasper (gastroscopist) or the rigid dissector (thoracoscope). All endoscopic procedures were performed under gastroscopic and thoracoscopic image control.

The specimens were retrieved through an endoscopic bag (Endopouch Retriever, Ethicon Endo-Surgery, Cincinnati, Ohio, USA) and introduced through the transthoracic trocar.

Table 1 Results of 4 acute and 8 survival experiments

Experiment	Esophagotomy: min, complications	Thymus dissection and retrieval: min, complications	Closure: min, complications	Acute versus survival
1	10	43	–	Acute
2	12	48 Small tear in the contralateral mediastinal pleura	–	Acute
3	15	35 3 Small tears in the pericardium	–	Acute
4	10	50	–	Acute
5	14	36 Small tear in the pericardium	15	Survival
6	15	50 Small tear in the pericardium	10	Survival
7	15	25 Small tear in the pericardium	5	Survival
8	18	19 Small tear in the contralateral mediastinal pleura	8	Survival
9	10	38 Small tear in the contralateral mediastinal pleura	12	Survival
10	15	35 Small tear in the contralateral mediastinal pleura	10	Survival
11	12	28 Small tear in the pericardium partial resection of contralateral mediastinal pleura	5	Survival
12	8	17	5	Survival

For this, the surgeon handling the gastroscope grasped the specimens and put it inside the endoscopic bag (Fig. 2C).

In the survival group, in addition to the surgical procedure described, the esophageal mucosa was closed at the proximal edge of the submucosal tunnel using 4–5 flexible hemoclips (EZ Clip HX-110LR; Olympus). At the end of the procedure, the pneumothorax was drained using a thoracic tube introduced through the transthoracic trocar. No drain was left in place after the intervention. The trocar skin incision was sutured with 2 independent knots of non-absorbable stitches.

Postoperative care (survival animal group)

At the end of the surgical intervention, all animals received a single dose of buprenorphine (0.05 mg/kg, IM) and meloxicam (0.4 mg/kg, IM). Antibiotic ceftiofur hydrochloride (5 mg/kg, IM) was repeated at 24-h intervals for 3 consecutive days. A regular diet was resumed 8 h after surgery.

The animals were closely monitored for any signs of postoperative complications, distress, behavior changes, anorexia, or weight loss. After the follow-up period, the animals were anesthetized for gastroscopic and thoracoscopic examination. They then were euthanized, and necropsy was performed to check for signs of cardiac or pulmonary complications. The proximal esophagus was analyzed under a microscope to verify the healing process.

Results

Animal model

The overall results of our study are summarized in Table 1. Dorsal decubitus and CO₂ inflation permitted good

visualization of the upper mediastinum. The coordination of the images from the thoracoscope and gastroscope allowed the determination of the ideal site for esophagotomy. Submucosal tunnel creation and esophagotomy were performed safely without incidents in all animals (Fig. 2A; Video 1). The mean time to perform the esophagotomy was 12.8 ± 3.0 min.

While the gastroscope operator was performing the submucosal tunnel, the surgeon with the thoracoscope opened the mediastinal pleura and began dissection of the left posterior limits of the thymus. We found that working with a single instrument without triangulation to be very limiting in terms of dissection. Nevertheless, leaving the anterior plane intact allowed the suspension of the thymus, facilitating the dissection of the posterior aspect when working together with the gastroscopic flexible instruments.

As soon as a transesophageal access was created, the instruments entering through both the gastroscope and thoracoscope created a triangulation very similar to the one experienced with the exclusively thoracoscopic approach. The flexible endoscope in retroflexion was essential for traction and counter-traction of the thymus. Lifting the thymus permitted a good dissection with the rigid dissector entering through the thoracoscope working channel. Pushing the thymus down was critical to separate it from the vessels in the upper mediastinum (Fig. 2B; Video 2). The flexible gastroscope was also useful for showing some parts of the thoracic cavity that could not be visualized with the 0-degree optic of the operative thoracoscope, i.e., the lateral thoracic wall and the entire diaphragm. Finally, retrieval of the specimens through an endoscopic bag introduced through the thoracic wall was only possible because the gastroscope gave visual control of the bag inside the chest and allowed the introduction of a grasper

that was used to put the specimens inside the bag (Fig. 2C; Video 3).

As reported in Table 1, there were only minor incidents during endoscopic thymectomy. Small tears in the pericardium and in the counter lateral pleura did not have clinical impact on the animal well-being and did not implicate suturing. As for experiment 11, where a larger amount of pleura was resected along with the thymus, hemodynamic instability was noted, but the pig recovered rapidly when we stopped CO₂ inflation. We achieved complete thymectomy in one piece in all experiments but one. In experiment number 9, two small pieces were resected. We safely retrieved the specimens using an endoscopic bag in all experiments (Fig. 3). The mean time to thymus dissection and retrieval was 35.33 ± 11.4 min. Complete thymus resection was achieved in all animals as verified by histological analysis (Fig. 4). Average specimens weight was 10.5 ± 5.4 g.

Fig. 3 Two specimens retrieved using an endoscopic bag from two consecutive experiments (animal model)

In the survival group, the esophageal mucosa was closed using hemostatic clips (Fig. 3D; Video 4). Thoracotomy was sutured after pneumothorax drainage. The mean time to esophageal mucosa closure was 8.8 ± 3.4 min. The total mean operative time in the survival group was 53.1 ± 14.4 min.

All 10 animals in the survival group lived for 14 days. After recovering from anesthesia, the pigs tolerated a regular diet started 8 h after surgery and deambulated freely, exhibiting normal behavior. No adverse events occurred during the survival period. Gastroscopic examination before sacrifice revealed complete esophageal closure in all animals. No esophageal strictures were found. In one of the animals, two esophageal hemoclips were still in place (Fig. 5).

Thoracoscopic and postmortem examination revealed pleural adhesions at the site of the surgical procedure

Fig. 5 Gastroscopic image on the 14th postoperative day of experiment 8 (animal model) showing 2 esophageal hemoclips in place

Fig. 4 Micrographs of thymic specimens of the pig (haematoxylin and eosin stain). **A** 4× Magnification: C capsule, Cx cortex, M medulla, S septum. **B** 20× Magnification: H Hassall corpuscle

(Fig. 6). There were no signs of infection in the ipsi- or contralateral pleural space and lung parenchyma. Histological analysis of the proximal third of the esophagus revealed complete cicatrization of both the mucosal defect and the myotomy site in all the animals (Fig. 7).

Human cadaver

We found thoracoscopic visualization in the human cadaver very similar to the one we saw in the porcine model (Fig. 8). Submucosal tunnel creation and esophagotomy was performed safely without incidents, besides some difficulties related to dead tissues manipulation. The time to perform the esophagotomy was 23 min.

We could not identify the thymus, because of the cadaver's older age. Even though, we dissected all the fat

from major structures in the anterior mediastinum. Again, starting dissection posteriorly permitted suspension of the mediastinal fat, facilitating the dissection. Instruments entering both through the gastroscope and thoracoscope allowed good triangulation. Flexible gastroscope was useful in showing the lateral thoracic wall and the right-side of the anterior mediastinum. The overall time to mediastinal fat dissection and retrieval was 65 min.

Discussion

Thymectomy plays an important role in the treatment of Myasthenia Gravis and thymomas (that may coexist). Sternal approach for thymectomy has been widely used for

Fig. 6 Thoracoscopic image on the 14th postoperative day of experiment 12 (animal model) showing the thoracotomy site (T) after dissecting local adhesions and some pleural adhesions in the apex and next to the left subclavian artery (s)

Fig. 8 Thoracoscopic view (left side) of the human cadaver. Exact site for esophagotomy

Fig. 7 Micrographs of esophageal specimens of the pig on the 14th postoperative day (Masson's trichrome stain). **A** Site of mucosal incision: *m* mucosa, *sm* submucosa. **B** Site of myotomy: *M* outer muscle layer

decades. VATS thymectomy has great advantage over sternotomy because of avoidance of muscle division and bone fractures, allowing for diminished duration and intensity of pain and shorter time to return to full activity [19]. Previous studies comparing different operative techniques showed that VATS thymectomy produced a long-term clinical outcome equivalent to that of the extended sternal approach, with lower complication rates [20, 21]. Although some of the reports have suggested the need to perform a bilateral VATS, most perform from the right chest [22]. Approach from the left chest can also be used, but the arch of aorta and the brachycephalic vein might difficult thoracoscopic access [23].

In the NOTES era, transesophageal endoscopic surgery is emerging as an alternative to the classic thoracoscopic surgery. The theoretical advantages of NOTES over open surgery and conventional thoracoscopy include decreased postoperative pain, reduction/elimination of general anesthesia, performance of procedures in an outpatient or even office setting, and possible cost reduction. Additionally, eliminating a skin incision avoids associated complications such as wound infections and hernias, and facilitates a shorter hospital stay, faster return to regular activity, improved cosmetic outcomes, and increased overall patient satisfaction. Rolanda et al. introduced the concept of hybrid thoracic NOTES [16]. By introducing a transthoracic trocar, the authors overcame some potential risks of the transesophageal approach, i.e., blind esophagotomy creation, thoracic drainage at the end of the procedure, and triangulation of instruments.

We have already described several advantages of using the single transthoracic assistance, in previous reports [17, 18]. First of all, the trocar site is used for CO₂ inflation and pressure control. At the end of the experiments, it permits tube insertion and acute pleural drainage. This port might be important in the human setting, as thoracoscopic procedures always need some time of thoracic drainage. Transthoracic visualization allows control of esophagotomy creation, performed from the inside to the outside of the esophagus, pointing out the exact place where it should be created, side and level, and avoiding lesions of arteries, veins, and nerves. The visual control provided by the thoracoscope permits guiding of instruments introduced transesophageally and manipulated through the mouth.

The concurrent use of two opposite sites for the entrance of scopes and respective instruments allowed for the establishment of regular triangulation and counter-traction thus simulating the two hand movements of the surgeon and promoting secure manipulation of tissues, careful dissection, and effective electrocoagulation for hemorrhagic control. As mentioned before, the flexible endoscope inside the thorax makes possible to examine the whole cavity including sites that rigid transthoracic

endoscopes cannot reach—namely the chest wall and counter-lateral mediastinum. Furthermore, the gastroscopic visual control permits guiding of blind-rigid instruments introduced through the transthoracic trocar, as happened with the endoscopic bag. Using the intrathoracic visual control provided by the gastroscope, the surgeon working through the thoracic wall positioned and opened the endoscopic bag. Then, the surgeon handling the gastroscope put the specimens inside the bag. We opted to extract the thymus using this method, because of the risk of disseminating thymus cells along the esophageal submucosal tunnel.

As stated before, most surgeons perform thoracoscopic thymectomy from the right chest or perform bilateral VATS. In our study, thymectomy was done from the left side, because transthoracic visual control for safe esophagotomy was only possible from the left chest. Again, the fact of having a flexible gastroscope entering from the apex permitted clear visualization of both sides of the anterior mediastinum and thoracic cavities. So, approaching the thymus from the left was not a limitation in our experiments.

The submucosal tunnel before esophagotomy creates a valve system that collapses as soon as the procedure is completed. Some authors have suggested leaving the mucosal defect open [24]. Mediastinal and lung infection could be of some concern. So we opted to close the mucosa with hemoclips, and this technique was found to be effective in all of our survival experiments. And as shown, combining the esophageal submucosal tunnel with antibiotic prophylaxis was enough to avoid any type of infection. Esophageal submucosal tunnel with antibiotic prophylaxis has been used for per oral endoscopic myotomy (POEM) for the treatment of achalasia. POEM uses submucosal dissection to reach and divide the inner muscle layer of the cardia. Although there is not a true esophagotomy in POEM, outcomes are excellent, and clinical data support theoretical advantages of transesophageal endoscopic surgery over conventional laparoscopy and thoracoscopy [25]. Despite this, true advantages of transesophageal access for thoracoscopic procedures over the risk of mediastinal infection are still a matter of concern.

We always thought the animal model could be a limitation of our study. Although the esophageal and cardiopulmonary porcine anatomy is very similar to that of humans, the sternum of the pig protrudes, resembling pectus carinatum. Surprisingly, we did not find that much difference when performing the hybrid endoscopic approach in the human cadaver. Even though, working space is described as a major hurdle in VATS thymectomy, specially in larger tumors. For that, some authors suggest retracting the sternum using a 10 mm cotton string caught on the stainless steel rod at the head of the table and tied to

the hook of a Kent retractor at the thigh level [10]. Because of the age of the Human cadaver, we could not identify any thymus tissue. The average size of the resected thymus in patients with thymoma is bigger than the one of our study in porcine model. On one hand, identification of the limits of a large thymus is easier than a small one mixed with the surrounding fat. On the other hand, manipulating and dissecting “healthy” thymus might be easier than pathologic, infiltrating ones.

Survival experiments were essential to prove that transesophageal HET was feasible and reliable. The cadaveric experiment proved that technically HET might be translated to humans. We believe that in the future HET could be regarded as an alternative to classic thoracoscopic approach for patients requiring thymectomy.

Acknowledgments This project was funded by the FCT Grants project PTDC/SAU-OSM/105578/2008.

Disclosures J Correia-Pinto is a consultant for Karl Storz GmbH. Aníbal Ferreira, Alice Miranda, Carla Rolanda have no conflict of interest.

References

- Allen MS, Deschamps C, Lee RE et al (1993) Video-assisted thoracoscopic stapled wedge excision for indeterminate pulmonary nodules. *J Thorac Cardiovasc Surg* 106:1048–1052
- Hazellrigg SR, Nunchuck SK, LoCicero J et al (1993) Video-assisted thoracic surgery study group data. *Ann Thorac Surg* 36:1039–1043
- Lewia RJ, Caccavale RJ, Sisler GE et al (1992) One hundred consecutive patients undergoing video-assisted thoracic operations. *Ann Thorac Surg* 54:421–426
- Coltharp WH, Arnold JH, Alford WC et al (1992) Videothoracoscopy: improved technique and expanded indications. *Ann Thorac Surg* 53:776–778
- Landreneau RJ, Dowling RD, Castillo WM et al (1992) Thoracoscopic resection of an anterior mediastinal tumor. *Ann Thorac Surg* 54:142–144
- Yim AP, Wan S, Lee TW et al (2000) VATS lobectomy reduces cytokine responses compared with conventional surgery. *Ann Thorac Surg* 70:243–247
- Ruckert JC, Walter M, Muller JM (2000) Pulmonary function after thoracoscopic thymectomy versus median sternotomy for myasthenia gravis. *Ann Thorac Surg* 70:1656–1661
- Mack MJ, Landreneau RJ, Yim AP et al (1996) Results of video-assisted thymectomy in patients with myasthenia gravis. *J Thorac Cardiovasc Surg* 112:1352–1360
- Agasthian T (2011) Can invasive thymomas be resected by video-assisted thoracoscopic surgery? *Asian Cardiovasc Thorac Ann* 19:225–227
- Takeo S, Tsukamoto S, Kawano D et al (2011) Outcome of an original video-assisted thoracoscopic extended thymectomy for thymoma. *Ann Thorac Surg* 92:2000–2005
- Sumiyama K, Goustout CJ, Rajan E et al (2007) Transesophageal mediastinoscopy by submucosal endoscopy with mucosal flap safety valve technique. *Gastrointest Endosc* 65:679–683
- Lima E, Henriques-Coelho T, Rolanda C et al (2007) Transvesical thoracoscopy: a natural orifice transluminal endoscopic approach for thoracic surgery. *Surg Endosc* 21:854–858
- De Palma GD, Siciliano S, Addeo P et al (2010) A NOTES approach for thoracic surgery: transgastric thoracoscopy via a diaphragmatic incision in a survival porcine model. *Minerva Chir* 65:11–15
- Yang C, Liu HP, Chu Y et al (2010) Natural orifice transtracheal evaluation of the thoracic cavity and mediastinum. *Surg Endosc* 24:2905–2907
- Moreira-Pinto J, Ferreira A, Rolanda C, Correia-Pinto J (2012) Natural orifice transesophageal endoscopic surgery: state of the art. *Minim Invasive Surg* 2012:896952
- Rolanda C, Silva D, Branco C et al (2011) Peroral esophageal segmentectomy and anastomosis with single transthoracic trocar assistance: a step forward in thoracic NOTES. *Endoscopy* 43:14–20
- Moreira-Pinto J, Ferreira A, Miranda A et al (2012) Transesophageal pulmonary lobectomy with single transthoracic port assistance: study with survival assessment in a porcine model. *Endoscopy* 44:354–361
- Moreira-Pinto J, Ferreira A, Miranda A, Rolanda C, Correia-Pinto J (2012) Left atrial appendage ligation with single transthoracic port assistance: a study of survival assessment in a porcine model (with videos). *Gastrointest Endosc* 75:1055–1061
- Yu L, Zhang XJ, Ma SM et al (2012) Thoracoscopic thymectomy for myasthenia gravis with and without thymoma: a single-center experience. *Ann Thorac Surg* 93:240–244
- Meyer DM, Herbert MA, Sobhani MC et al (2009) Comparative clinical outcomes of thymectomy for myasthenia gravis performed by extended transsternal and minimally invasive approaches. *Ann Thorac Surg* 87:385–391
- Mack MJ, Scruggs G (1998) Video-assisted thoracic surgery thymectomy for myasthenia gravis. *Chest Surg Clin North Am* 8:809–825
- Parikh K, Vaidya A, Jain R (2011) Preliminary results of VATS thymectomy for pediatric myasthenia gravis. *Pediatr Surg Int* 27:595–598
- Loscertales J, Ayarra Jarne J, Congregado M et al (2004) Video-assisted thoracoscopic thymectomy for the treatment of myasthenia gravis. *Arch Bronconeumol* 40:409–413
- Gee DW, Willingham FF, Lauwers GY et al (2008) Natural orifice transesophageal mediastinoscopy and thoracoscopy: a survival series in swine. *Surg Endosc* 22:2117–2122
- Inoue H, Tianle KM, Ikeda H et al (2011) Peroral endoscopic myotomy for esophageal achalasia: technique, indication, and outcomes. *Thorac Surg Clin* 21:519–525