



ORIGINAL ARTICLE

Feasibility of transumbilical anatomic Lung segmentectomy in a canine model



Ming-Ju Hsieh ^a, Yen Chu ^a, Yi-Cheng Wu ^a, Chien-Ying Liu ^b,
Chi-Ju Yeh ^c, Yun-Hen Liu ^{a,*}, Che-Chia Chang ^a

^a Department of Thoracic Surgery, Chang Gung Memorial Hospital, Chang Gung University, Linko, Taiwan

^b Department of Thoracic Medicine, Chang Gung Memorial Hospital, Chang Gung University, Linko, Taiwan

^c Department of Pathology, Chang Gung Memorial Hospital, Chang Gung University, Linko, Taiwan

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Summary *Background:* Transumbilical approach has been shown to be feasible to perform lung wedge resection and anatomic lobectomy. This study uses a canine model to assess the feasibility of transumbilical segmentectomy.

Methods: Transumbilical segmentectomy was performed in 10 beagle dogs using a 3-cm umbilical incision combined with a 2.5-cm diaphragmatic incision. We evaluated the surgical outcomes, operative complications, physiologic changes, hemodynamic changes, and inflammatory changes of the procedures.

Results: Transumbilical segmentectomy was successfully completed in eight of ten animals. There was one mortality complication related to lung injury causing hemodynamic collapse. Another animal required conventional thoracotomy to complete the surgery due to limited working space. There were no notable events in the postoperative period for all eight dogs that completed the segmentectomy via the transumbilical approach.

Conclusion: This animal study demonstrates that the pulmonary segmentectomy can be performed with current standard endoscopic instruments via a single transumbilical incision. We believe that advancing surgical innovation and good collaboration between multi-disciplinary research teams will further establish clearer roles for transumbilical segmentectomy in thoracic surgery.

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* Corresponding author. Department of Thoracic Surgery, Chang Gung Memorial Hospital, Chang Gung University, 5 Fushing Street, Gueishan Shiang, Taoyuan, 333, Taiwan, ROC. Fax: +886 3 3285818.

E-mail address: zebraairmail@gmail.com (Y.-H. Liu).

1. Introduction

Numerous studies have shown that standard multiport video-assisted thoracoscopic surgery (VATS) and single-port VATS are safe and effective endoscopic techniques for different procedures in diagnosis and therapeutic treatments. However, some patients report acute and chronic post-operative pain after thoracotomy.^{1–5} An alternative approach that avoids thoracic incision may decrease post-operative discomfort.

Natural orifice surgery (NOS) is a surgical procedure performed through a natural orifice. Such methods offer potential benefits of less postoperative discomfort and better cosmetic outcomes compared to standard laparoscopic procedures.^{6,7} In the context of thoracic surgery, NOS has been successfully used for mediastinal lymph node resection, lung biopsies, and pulmonary lobectomy in an animal model via the esophagus, vagina, urethra, or trachea, but it is associated with life-threatening complications.^{8–10} Our teams have shown the feasibility of transumbilical thoracic surgery in canine models, including surgical lung biopsy, lung wedge resection, and pulmonary lobectomy.^{11–14} The umbilicus appears to be a potential access point for the thoracic cavity because of the relatively simple techniques involved in comparison to other NOS platforms.

Surgical resection has been a standardized treatment for early lung cancer. Recent advances in endoscopic surgery have led to the development of smaller anatomical resection (segmentectomy) and resulted in better preservation of pulmonary function compared to standard anatomic lobectomy. Many researchers have further described 85 the oncologic outcomes of segmentectomy and claimed that it is an alternative to standard lobectomy in the treatment of small peripheral lung cancers (<2 cm). Furthermore, it is associated with faster post-operative recovery.^{15–17}

The present study aims to evaluate the feasibility of a transumbilical approach to performing anatomic segmentectomy in dogs. Identifying a simple and effective surgical platform that is minimally invasive will facilitate the introduction of a surgical approach with less post-operative discomfort and better patient satisfaction into clinical practice.

2. Method

This study was approved by the Ethics Committee on Animal Research of the Chang Gung Memorial Hospital. Ten dogs (weight: 7–9 kg) were used in this study. Anesthesia was induced using 5 mg/kg of ketamine and 10 mg/kg of xylazine HCL. The animals then underwent endotracheal intubation with cuffed tubes in a supine position. Next, 2% isoflurane in 100% oxygen was used to maintain anesthesia via endotracheal ventilation (tidal volume of 15 ml/kg and frequency of 10 breath/min). An antibiotic (20 mg/kg cefazoline) was administered to all animals prior to starting surgery.

With the dogs in the supine position, transumbilical thoracoscopy was performed through one 3-cm umbilical incision and one diaphragmatic incisions, as reported in our previous study.¹⁵ Resection was then performed on the

predetermined lung (right upper [upper segment] lobe [n = 1], right upper [lower segment] lobe [n = 1], right lower [anteromedial segment] lobe [n = 1], right lower [posterolateral segment] lobe [n = 1], left upper [upper segment] lobe [n = 1], left upper [lower segment] lobe [n = 1], left lower [anteromedial segment] lobe [n = 2], and left lower [posterolateral segment] lobe [n = 2]).

The resection was performed using the following procedure. (1) First, a 3-cm-long longitudinal incision was performed through the umbilicus, and (2) a wound protector (Alexis wound retractor, Applied Medical, USA) was inserted into the umbilical wound and used to retract the wound edge to increase the working space of the transumbilical procedure. (3) A 0.5-cm incision over the diaphragm was created with an electrocautery 127 needle knife (Olympus Optical Co., Ltd. Japan), and then sequential dilatation to 25 mm was performed using a metal tube under bronchoscopic guidance via the umbilical incision. (4) Additional wound protectors were then introduced to the diaphragmatic incision to help maintain a sufficient opening of the working tunnel between the umbilical and diaphragmatic incisions to facilitate access to the thoracic cavity and anatomic segmentectomy. (5) Dissection of the pulmonary hilum was carefully performed using an endoscopic node-grasping clamp (Scanlan International, Inc., USA), endoscopic scissors (Scanlan International, Inc., USA), and 18-cm curved Adson baby forceps (Medline industries, Inc., Mundelein, IL). (6) The segmental branches of the pulmonary vein were divided using LigaSure (Valleylab, Boulder, CO) after ligation with 4/0 Prolene. (7) The segmental branches of the pulmonary artery were also divided using LigaSure (Valleylab, Boulder, CO) after ligation with 4/0 Prolene. (8) The anatomically defined lung parenchyma and segmental bronchus were simultaneously resected using endoscopic vascular staples (Echelon 45 Endopath stapler, Ethicon Endosurgery, USA), and (9) the edges of the resected bronchus and vessel were checked for hemostasis and airtight closure. (10) The lung segment was removed via the umbilical incision, and (11) the diaphragmatic wound was approximated using Cryolife (CryoLife Inc., Kennesaw, GA, USA). (12) The umbilical wound was closed with continuous 3-0 Vicryl (Ethicon, OH, USA) and an intruded 3-0 nylon suture (Ethicon, San Lorenzo, Puerto Rico). (13) The animal was allowed to recover from anesthesia and resumed a regular diet.

During the operation, the hemodynamic impacts of transumbilical segmentectomy were recorded, including the heart rate (HR), mean arterial pressure (MAP), systemic vascular resistance index (SVRI), operative time, procedural success, and complications. Following surgery, the animals were closely observed for the surgical outcomes and complications for 2 weeks. We also recorded the physiological changes (rectal temperature and respiratory rate at pre-operation and 1, 2, 3, 7, and 14 days after the surgery), the impact of lung function evaluation (arterial blood gas at pre-operation, postoperation, and 14 days after surgery), and the inflammatory reaction (complete blood count (CBC) and C-reactive protein (CRP) level at pre-operation, and 1, 2, 3, 7, and 14 days after the surgery).

Table 1 Procedure characteristics and animal outcome.

Animal	Duration (min)	Body weight (Kg)	Target lung region (lobe)	Target lung region (segment)	Success of procedures	Lung specimen (cm)	Complication	Necropsy (lung)	Necropsy (Diaphragm)	Necropsy (Diaphragm)	Necropsy (umbilicus)	Pathology (diaphragm)
Dog 1	120	8.45	LUL	Upper	Yes	7.5	No	Adhesion with Mediastinum	Complete healing	Adhesion with lung/liver	–	Fibrosis, inflammation, granulation, calcification
Dog 2	154	10.95	LUL	Lower	Yes	6	No	Adhesion with Mediastinum	Complete healing	Adhesion with liver	–	Fibrosis, inflammation, granulation
Dog 3	139	11	LLL	Anteromedial	No	5	Air leakage/ Mortality	–	–	–	–	–
Dog 4	137	10.45	LLL	posterolateral	No	8	Thoracotomy	Adhesion with Mediastinum	Complete healing	Adhesion with lung	–	Fibrosis, inflammation, granulation
Dog 5	85	9.1	RUL	Upper	Yes	5	No	Adhesion with Mediastinum	Complete healing	Adhesion with liver	Adhesion with mesenterium	Fibrosis, inflammation, granulation
Dog 6	112	10.1	RUL	Lower	Yes	4	No	Adhesion with Mediastinum	Complete healing	Adhesion with lung/liver	–	Fibrosis, inflammation, granulation, calcification
Dog 7	135	11.75	LLL	Anteromedial	Yes	6	No	Adhesion with Mediastinum	Complete healing	–	–	Fibrosis, inflammation, granulation
Dog 8	125	11.75	LLL	posterolateral	Yes	7	No	Adhesion with Mediastinum	Complete healing	Adhesion with lung/liver	–	Fibrosis, inflammation, granulation
Dog 9	113	8.35	RLL	Anteromedial	Yes	3.8	No	Adhesion with Mediastinum	Complete healing	Adhesion with liver	–	Fibrosis, inflammation, granulation, calcification
Dog 10	198	9.1	RLL	Posterolateral	Yes	7	No	Adhesion with Mediastinum	Complete healing	Adhesion with liver	Adhesion with mesenterium	Fibrosis, inflammation, granulation

Necropsies were performed on day 14 post-operation to evaluate the success of the anatomic segmentectomy, the integrity of the diaphragmatic wound, and the presence of operative complications.

3. Result

Transumbilical endoscopic anatomic segmentectomy was successfully completed in 8 of the 10 animals. Intra-operative lung injury developed in one animal during lung resection, and the animal was sacrificed due to hemodynamic instability. For the other animal, thoracotomy was required to complete the operation (Table 1).

3.1. Respiratory rates

After surgery, there was a significant increase in respiratory rates, but they returned to pre-operative levels 14 days after surgery (Fig. 1A).

3.2. Body temperature

There were no significant changes in body temperature between before surgery, immediately post-surgery, and on days 1, 3, 7, and 14 after surgery (Fig. 1B).

3.3. Pulmonary parameters

There was a significant increase in paCO_2 values post-operation compared to pre-operative levels. The paCO_2 value returned to the pre-operative levels before day 14 post-operation (Fig. 1C).

3.4. Physiologic study

During surgery, there was a significant reduction in HR and MAP from the baseline level. The MAP returned to pre-operative levels after the surgical procedure (Fig. 2).

3.5. White blood cells

After the operation, there was a significant elevation in white cell count, but they returned to pre-operative levels on day 14 (Fig. 3A).

3.6. Neutrophils

The number of neutrophils increased significantly following surgery, and they returned to the baseline levels by 3 days post-surgery (Fig. 3B).

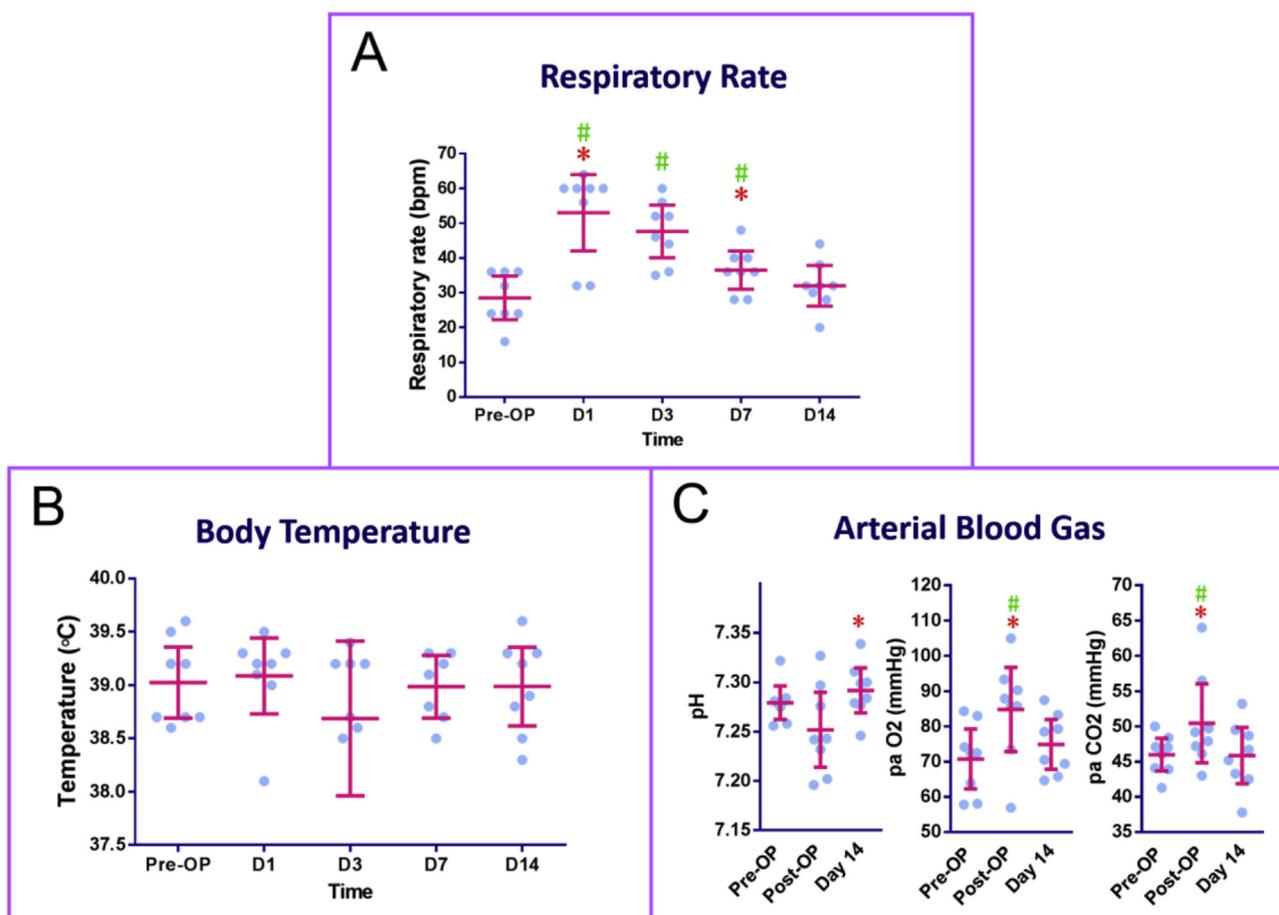


Figure 1 Physiological changes ($n = 8$) including (A) respiratory rate, (B) body temperature, and (C) arterial blood gases based on the Wilcoxon sign ranked test. * $P < 0.05$ compared with previous time interval; # $P < 0.05$ compared with the preoperative level.

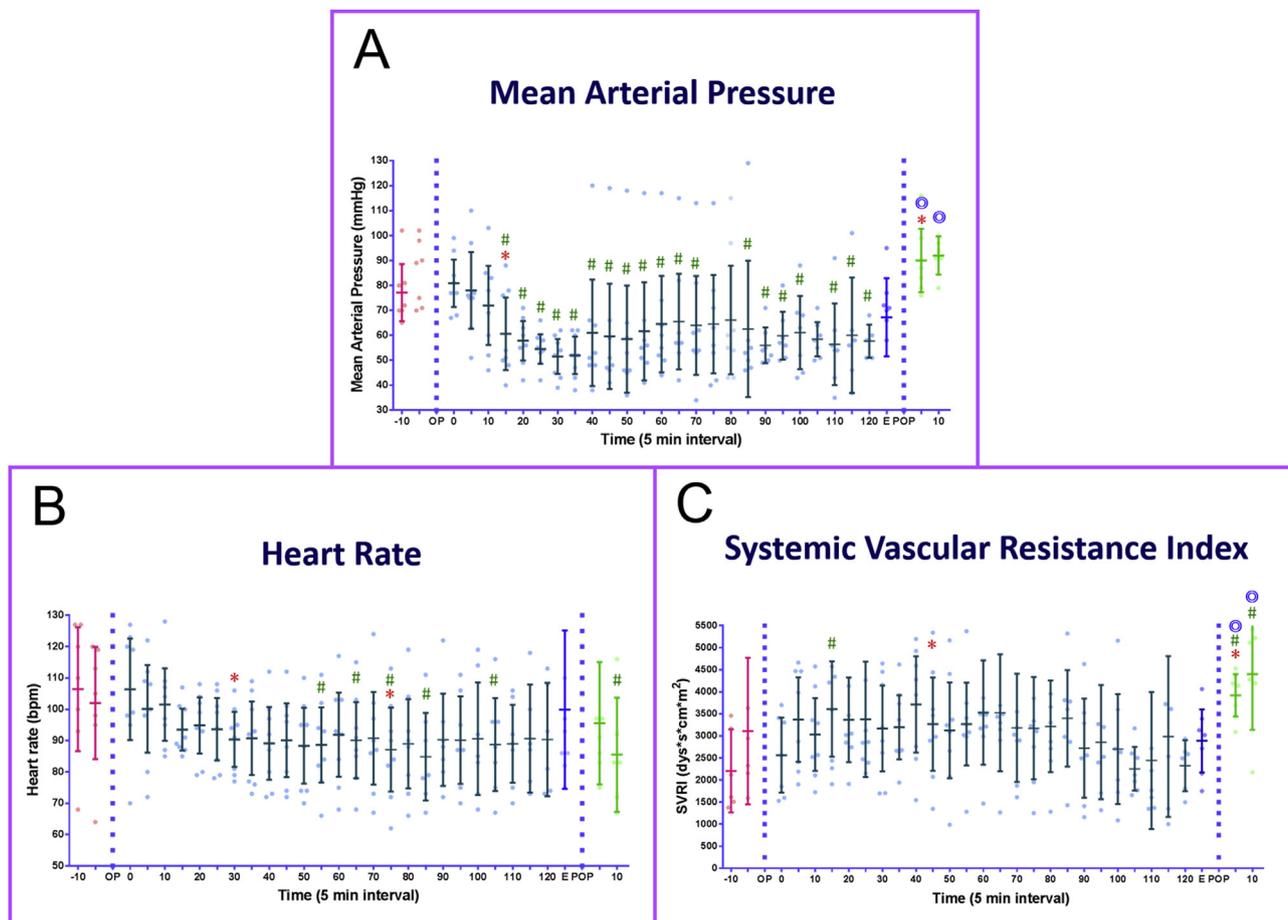


Figure 2 Hemodynamic changes (n = 8) including (A) mean arterial pressure, (B) heart rate, and (C) systemic vascular resistance index based on the Wilcoxon sign ranked test. *P < 0.05 compared with previous time interval; #P < 0.05 compared with T0 of operation; ⊙p < 0.05, compared with End of operation.

3.7. Monocytes

The monocyte count increased on day 1 post-operation, but they returned to the baseline by 14 days post-surgery (Fig. 3C).

3.8. Lymphocytes

The number of lymphocytes decreased significantly following surgery, but they returned to the baseline levels at 3 days post-surgery (Fig. 3D).

3.9. C-reactive protein level

The CRP values increased from baseline on POD 1, POD 3, and POD 7, but they returned to preoperative levels on day 14 (Fig. 3E).

3.10. Necropsy

Postmortem examinations demonstrated success in anatomic segmentectomy in the 8 animals receiving transumbilical segmentectomy. There were no signs of infection

or injury to the vital organs. The diaphragmatic wounds were completely healed in all animals. All animals had adhesion between the mediastinum and the lung, and 7 of 9 animals had liver adhesion over the diaphragmatic access region, while 4 animals had liver adhesion.

4. Discussion

This animal study shows that transumbilical segmentectomy is a feasible technique in a canine model. These findings are clinically relevant because segmentectomy is commonly used to manage benign lesions or early-stage lung cancer nodules in daily practice. We expect that this evidence will facilitate the discovery and development of novel surgical platforms related to thoracic surgery.

Since minimally invasive surgery was developed, various approaches have been developed in thoracic surgery to minimize the postoperative discomfort of patients. These include standard multiport VATS, single-port transthoracic VATS, single-port subxiphoids VATS, and single-port transumbilical VATS. According to the literature, standard multiport VATS is a safe and effective approach for the diagnosis and surgical management of thoracic disease.

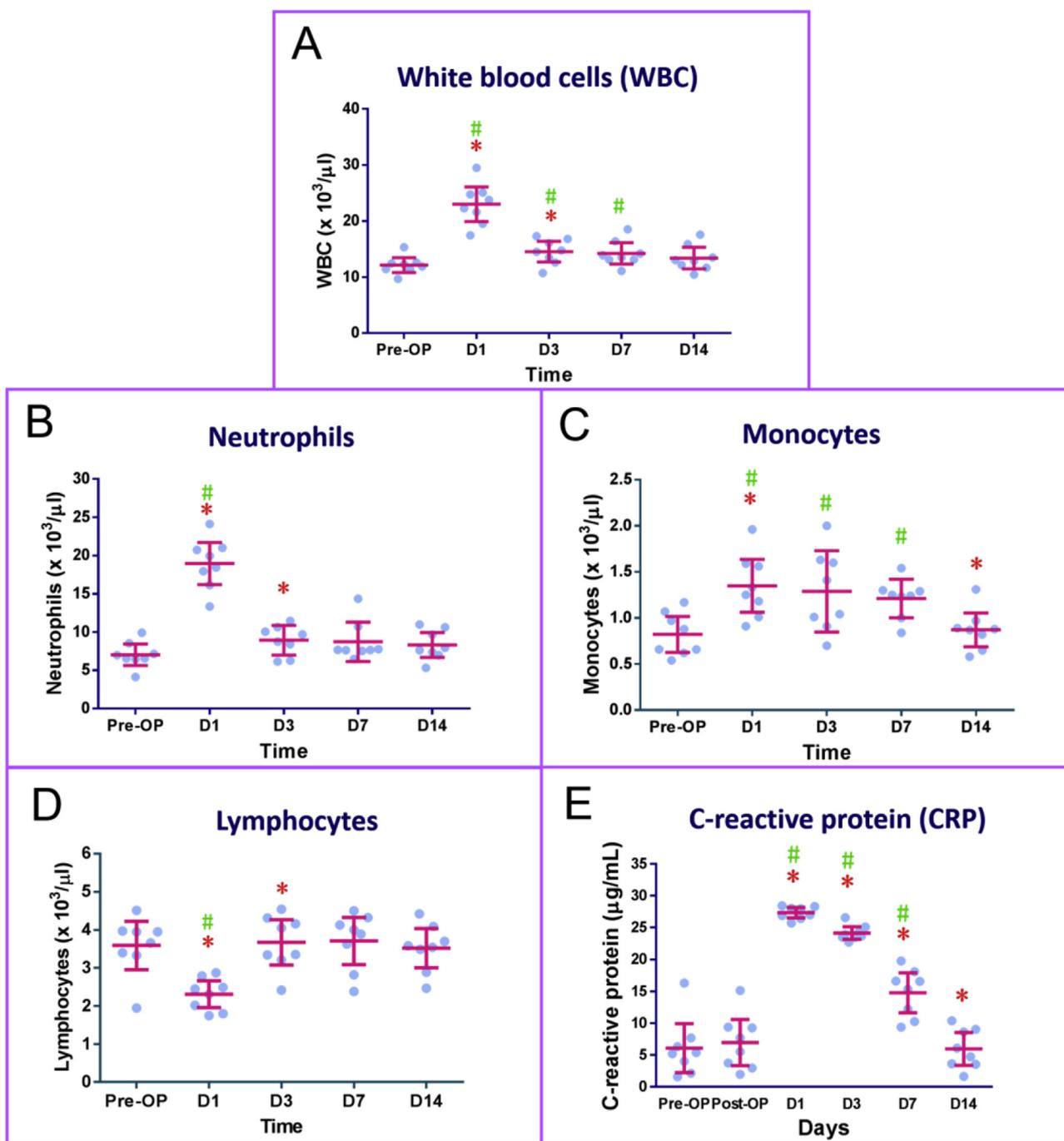


Figure 3 Inflammatory changes ($n = 8$) including (A) white blood cell (WBC) count, (B) neutrophil cell count, (C) monocyte cell count, (D) lymphocyte cell count, and (E) the serum levels of C-reactive protein based on the Wilcoxon sign ranked test. * $P < 0.05$ compared with t previous time interval; # $P < 0.05$ compared with the preoperative level.

With advancements in surgical instruments and familiarity with endoscopic techniques, some authors have reported that the single-port VATS diminished postoperative pain and improved patient satisfaction compared to multiport VATS in the management of primary spontaneous pneumothorax patients.⁴ In 105 patients, Song et al confirmed the safety and lower pain from postoperative incision in single-port subxiphoids VATS compared to multi-port VATS in treatments of early-stage lung cancer and benign disease.¹⁸ More recently, Zhu et al reported the safety and

efficiency of transumbilical thoracic sympathectomy without chest wall paraesthesia and chronic chest discomfort in 148 patients.¹⁹

In 2013, we reported the feasibility of the transumbilical approach for surgical lung biopsy in 12 dogs and demonstrated that the approach was comparable to conventional thoracoscopy in terms of efficacy and postoperative complications for lung wedge resection.^{12,13} In 2014, we also reported the feasibility of transumbilical anatomic lobectomy in 15 dogs but with higher rates of mortality for

bleeding complications.¹⁴ In 2016, we also found that the electrosurgical apparatus was not efficacious for sealing the pulmonary vessel during anatomical lobectomy.²⁰ More recently, our research group introduced a conventional suture ligation technique to secure the pulmonary vessel before division with electrosurgical devices, which significantly reduces bleeding complications after subxiphoid anatomic pulmonary lobectomy in the canine model.²¹ Based on these findings, we extended the transumbilical approach from standard lobectomy to more complicated techniques for lung resection (segmentectomy).

In this study, we were able to complete the segmentectomy with the transumbilical technique in 8 of the 10 animals. However, we did encounter certain technical difficulties during surgery. First, the resection of the segment of the left lower lobe was difficult due to the limited working space caused by obstruction of the heart chamber. Second, we were unable to complete the dissection and isolation of the segmental bronchus after division of the segmental vessel because of the small size of the dog bronchi. Third, it is impossible to complete standard segmentectomies of individual segments of various lung lobes in daily practice. We modified the procedure by separating the lung lobe into two segments. We believe that further clinical studies will elucidate the safety and efficacy of transumbilical segmentectomy.

The complication rate was high in this study (1 death and 1 conversion to thoracotomy). Intraoperative lung injury is the probable reason for hemodynamic collapse during the perioperative period. However, we believe that such complications can be reduced with increasing experience. Due to short distance between the chest wall and the lung in this current animal model, the working space is limited during the procedure, and thoracotomy is required to complete the procedure. Nevertheless, we also feel that these difficulties could be greatly reduced by implementing pulmonary segmentectomy in larger animal models or in humans.

This study has several limitations. First, dogs and humans have distinct anatomy, and the transumbilical approach to the upper lung region with currently available instruments could be restricted due to the long distance between the umbilical incision and the pulmonary hilum in humans. Second, chronic complications following a diaphragmatic incision could not be evaluated, and the long-term sequelae of the transumbilical approach should be investigated in future clinical studies.

Third, only segmentectomy was performed. Mediastinal lymph node dissection might be more challenging due to the limited working space. Fourth, we were unable to isolate the segmental bronchus before division. Therefore, simultaneous parenchyma and bronchus resections of the anatomically defined lung segment were required to complete the surgery. Despite these limitations, we believe that the role of transumbilical approach in thoracic surgery can be clarified further by increasing investment in advanced technology in surgical innovation, collaboration in multi-disciplinary teams (scientists, researchers, and clinicians), and better reimbursement policy to facilitate the development of novel therapeutic platform in surgical disease.

In summary, this study demonstrates that the transumbilical and transdiaphragmatic approach for anatomic

segmentectomy is practicable in a canine model. More preclinical evidence of transumbilical thoracic surgery would further clarify the role of the transumbilical technique in the management of thoracic disease.

Author contributions

(I) Conception and design: Ming-Ju Hsieh, Yun-Hen Liu, Yi-Cheng Wu.

(II) Administrative support: Yun-Hen Liu.

(III) Provision of study materials or patients: Yun-Hen Liu.

(IV) Collection and assembly of data: Yun-Hen Liu.

(V) Data analysis and interpretation: Ming-Ju Hsieh, Chi-Ju Yeh.

(VI) Manuscript writing: All authors.

(VII) Final approval of manuscript: All authors.

Conflict of interest

Ming-Ju Hsieh, Yen Chu, Yi-Cheng Wu, Chien-Ying Liu, Chi-Ju Yeh, Yun-Hen Liu, have no conflicts of interest or financial ties to disclose.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.asjsur.2018.07.002>.

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