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Efficacy of artificial pneumothorax under two-lung ventilation in video-assisted thoracoscopic surgery for esophageal cancer

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Abstract

Background One-lung ventilation (OLV) is the standard and widely applied ventilation approach used in video-assisted thoracoscopic surgery for esophageal cancer (VATS-e). To address the disadvantages of OLV with respect to difficulties in intubation and induction, as well as the risk of respiratory complications, two-lung ventilation (TLV) with artificial pneumothorax has been introduced for use in VATS-e. However, no studies have yet compared TLV and OLV with postoperative infection and inflammation in the prone position over time postoperatively. Here, we investigated the efficacy of TLV in patients undergoing VATS-e in the prone position.

Methods Between April 2010 and December 2016, 119 patients underwent VATS-e under OLV or TLV with carbon dioxide insufflation. Clinical characteristics, surgical outcomes, and postoperative outcomes, including oxygenation and systemic inflammatory responses, were compared between patients who underwent OLV and those who underwent TLV.

Results Clinical characteristics other than pT stage were comparable between groups. The TLV group had shorter thoracic operation time than the OLV group. No patients underwent conversion to open thoracotomy. The PaO_2/FiO_2 ratios of the TLV group on postoperative day (POD) 5 and on POD7 were significantly higher than those of the OLV group. C-reactive protein levels on POD7 were lower in the TLV group than in the OLV group. There were no significant differences with respect to postoperative complications between the OLV and TLV groups. In the TLV group, the white blood cell count on POD7 was significantly lower than that in the OLV group; body temperature showed a similar trend immediately after surgery and on POD1.

Conclusions In this study, we demonstrated that, compared with OLV, TLV in the prone position provides better oxygenation and reduced inflammation in the postoperative course. Accordingly, TLV might be more useful than OLV for ventilation during esophageal cancer surgery.

Keywords Esophageal carcinoma · Two-lung ventilation (TLV) · One-lung ventilation (OLV) · Thoracoscopic esophagectomy · Prone position

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Esophageal cancer is the sixth most common cause of cancer-related mortality worldwide [1]. Esophagectomy is the primary therapeutic approach for patients diagnosed with curable esophageal cancer. However, esophagectomy is a complex procedure that requires manipulation in the chest and abdomen, as well as the neck in many cases; these procedures can be associated with significant morbidity and mortality [2]. Video-assisted thoracoscopic surgery for esophageal cancer (VATS-e) was originally introduced by Cuschieri in 1993 [3]. Importantly, VATS-e reduces the incidence of postoperative systemic inflammatory response syndrome (SIRS) and related pulmonary complications [4, 5].

VATS-e is a feasible and safe surgical approach for reliable minimally invasive esophagectomy associated with reduced perioperative complications [6]. One-lung ventilation (OLV) is the standard ventilation in both conventional open thoracotomy and VATS-e; it can provide adequate surgical space in the right thoracic cavity by collapsing the right lung [7]. However, OLV exhibits several disadvantages, including difficulty in anesthetic induction/intubation and maintenance, as well as a risk of respiratory complications [8]. Such problems in patients undergoing OLV often result from inappropriate anesthetic management, which may affect postoperative respiratory function due to poor lung expansion, CO_2 retention, or lung hyperinflation [9].

Palanivelu et al. introduced two-lung ventilation (TLV) with CO_2 artificial pneumothorax for use during VATS-e in 2006 [10]. This approach yields better perioperative outcomes, including improvement of intraoperative respiratory function, easier introduction of the endotracheal tube, and management of anesthesia [11–13]. However, no studies have yet compared TLV and OLV with postoperative infection and inflammation in patients undergoing VATS-e in the prone position over time postoperatively except one that only observed the inflammatory responses [14]. Here, we retrospectively examined the efficacy of TLV with artificial pneumothorax in patients undergoing VATS-e.

Materials and methods

Patients and surgical procedure

A total of 119 consecutive patients who underwent VATS-e for esophageal cancer with R0 resection in our institute, during the period from April 2010 to December 2016, were included in this study. OLV was used until April 2014 (71 patients), and TLV was then introduced (48 patients). In the OLV group, patients were intubated using a double-lumen endotracheal tube (Broncho Cath, Covidien, Tokyo, Japan). In the TLV group, patients were intubated with a single-lumen endotracheal tube in the conventional manner. All inductions and intubations were performed by experienced anesthesiologists.

Intraoperative posture was well supported and fixed in a semi-prone position with the right arm abducted above the head; the table was rotated to the right, and the patient was arranged in a prone position. VATS-e was performed by two surgeons—a surgical operator and an endoscopist—both standing on the left side of the operating table; the video monitor was placed on the opposite side of the operating table. Two working ports were inserted at the fifth and seventh intercostal spaces on the posterior axillary retrograde line; the camera port was inserted at the ninth intercostal space on the posterior axillary line. CO_2 insufflation (CO_2 pressure = 6 mmHg) was used to create an artificial pneumothorax. Two- or three-field lymphadenectomy was performed as necessary. Gastric conduit reconstruction was achieved by laparoscopic procedure. The gastric conduit was pulled through the posterior mediastinum to the neck. Anastomosis was manually performed in the cervical position. Then, a jejunostomy catheter was placed in all patients for postoperative enteral nutrition.

Postoperative care, including respiratory, chest drain management, and nutritional care, was performed in the same manner during the observation period. Thoracic epidural analgesia was applied to all patients. The blood samples were collected preoperatively, immediately after surgery, postoperative day (POD) 1, 3, 5, and 7. Whenever an arterial line was inserted, blood was collected from the arterial line. PaO_2 / FiO_2 ratio were calculated by the results of arterial blood gas. The pathologic stage of disease was determined in accordance with the Tumor–Node–Metastasis (TNM) Classification of Malignant Tumors by the International Union Against Cancer (7th edition) [15]. Data regarding preoperative status, surgical procedures, and postoperative clinical and laboratory values were collected from medical records and nursing charts. In-hospital mortality was defined as death that occurred during an in-hospital stay.

Informed consent was obtained from all participants prior to entry into the study. This study was approved by the Ethics Committee of National Defense Medical College Hospital.

Statistical analysis

JMP Pro software (version 14.2.0, SAS Institute, Inc., Cary, NC, USA) was used for statistical analysis. Numerical data are presented as the mean ± standard deviation. Intergroup comparisons were performed using the Wilcoxon rank-sum test. Categorical data are presented as number or percentage (%). Intergroup comparisons were performed using the Chi-squared test. Differences with P values < 0.05 were considered to be statistically significant. A quadratic regression method with least-squares estimates was applied to model the learning curve.

Results

Attenuation of the learning curve effect for a particular operator was observed with OLV, but not with TLV (Fig. 1). All VATS-e procedures were successfully performed, and there were no incidences of conversion to open thoracotomy due to intraoperative complications (e.g., endotracheal and lung injuries or vascular injuries). A short intraoperative video segment is attached in the Supplementary Material (video). The clinical

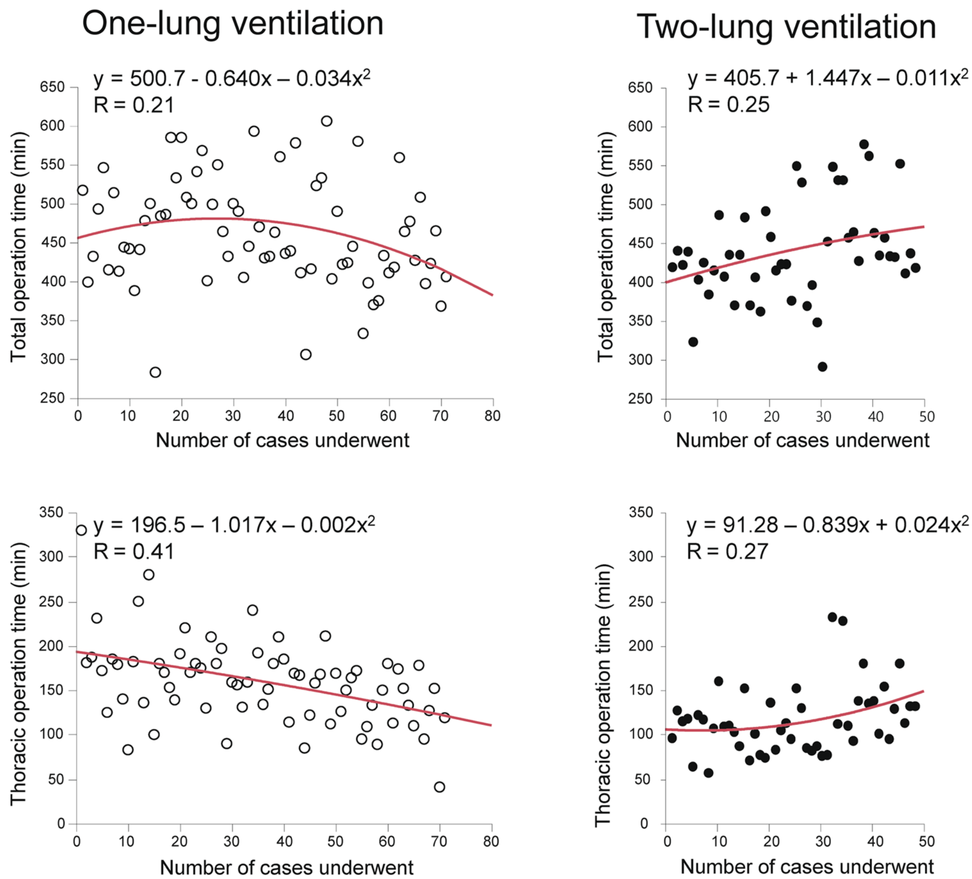

Fig. 1 Trend in total operation time and thoracic operation time for VATS-e by the ventilation

characteristics of the two groups are summarized in Table 1. The pT stage was significantly higher in the TLV group than in the OLV group ($P = 0.038$) However, there were no significant differences in clinical characteristics between the two groups, including age, sex, pulmonary function, renal function, neoadjuvant therapy, tumor location, TNM staging (except pT stage), field of lymphadenectomy, or abdominal procedure. The surgical variables are summarized in Table 2. The TLV group had significantly shorter thoracic time. However, there were no significant differences in preoperative time from the start of anesthesia until the incision, total operative time, intraoperative blood loss, intraoperative blood transfusion, or total number of dissected lymph nodes (LNs) between the two groups.

Perioperative changes in PaO_2/FiO_2 ratio and CRP

The TLV group exhibited a significant increase in the PaO_2/FiO_2 ratio on postoperative day (POD) 5 and on POD7 (Fig. 2). C-reactive protein (CRP) levels were significantly lower on POD7 in the TLV group than in the OLV group (Fig. 3).

Perioperative changes in SIRS criteria

We also assessed the postoperative time course of changes for each factor of the SIRS criteria. White blood cell count on POD7 and body temperature from immediately after the operation until POD1 in the TLV group were significantly lower than those in the OLV group ($P < 0.05$) (Fig. 4). No differences were observed in heart rate or respiratory rate between the two groups.

Comparison of postoperative outcomes between OLV and TLV procedures

Postoperative outcomes are summarized in Table 3. There were no significant differences in the incidences of postoperative complications, 30-day mortality rates, or in-hospital stays between the two groups.

Discussion

In this study, we demonstrated several advantages of TLV over OLV with respect to thoracic operation time, postoperative oxygenation, and systemic inflammation. In addition,

Table 1 Demographic data in one-lung ventilation and two-lung ventilation

	OLV ($n=71$)		TLV ($n=48$)		*P* value
Age (means ± SD, year)	71.1 ± 5.8		69.9 ± 10.1		0.86
Male/ Female	59/12		41/7		0.80
%VC (means ± SD)	103.8 ± 17.3		106.2 ± 17.7		0.51
FEV 1% (means ± SD)	76.7 ± 12.3		75.8 ± 13.8		0.54
DLCO% predicted (means ± SD)	95.4 ± 28.9		90.5 ± 22.6		0.49
Renal dysfunction	7	9.9%	8	16.7%	0.40
Tumor location					
Upper	9	12.7%	6	12.5%	1.00
Middle and lower	62	87.3%	42	87.5%	
Neoadjuvant chemotherapy					0.26
No	36	50.7%	30	62.5%	
Yes	35	49.3%	18	37.5%	
pT					0.038
1	26	36.6%	25	52.0%	
2	6	8.5%	9	18.8%	
3	35	49.3%	12	25.0%	
4a	4	5.6%	2	4.2%	
pN					0.85
0	29	40.8%	20	41.7%	
1	21	29.6%	17	35.4%	
2	14	19.7%	7	14.6%	
3	7	9.9%	4	8.3%	
pStage					0.32
I	22	31.0%	21	39.6%	
II	7	9.9%	1	2.0%	
IIIA, IIIB	32	45.0%	26	47.9%	
IVa	10	14.1%	6	10.4%	
Fields of lymphadenectomy					0.25
Two-field	46	64.8%	36	75.0%	
Three-field	25	35.2%	12	25.0%	

OLV One-lung ventilation, *TLV* Two-lung ventilation, *SD* standard deviation, *VC* vital capacity, *FEV* forced expiratory volume, *DLCO* diffusing capacity of the lung for carbon monoxide

Table 2 Surgical outcomes in one-lung ventilation and two-lung ventilation

	OLV ($n=71$)		TLV ($n=48$)		*P* value
Preoperative time (means ± SD, min.)	45.0 ± 10.5		41.9 ± 9.1		0.085
Total operation time (means ± SD, min.)	463.0 ± 69.4		439.1 ± 62.8		0.055
Thoracic operation time (means ± SD, min.)	158.9 ± 47.2		116.5 ± 37.2		< 0.001
Intraoperative blood loss (means ± SD, g)	315.8 ± 455.0		250.6 ± 367.7		0.45
Intraoperative blood transfusion					0.24
No	60	85.7%	43	93.5%	
Yes	10	14.3%	3	6.5%	
Lymph node (means ± SD, *n*)	40.9 ± 17.5		42.1 ± 17.0		0.77
Conversion to open thoracotomy	0	0.0%	0	0.0%	1.00

OLV One-lung ventilation, *TLV* Two-lung ventilation, *SD* standard deviation

there was no significant difference in intraoperative blood loss, intraoperative blood transfusion, harvested lymph nodes, and postoperative outcomes between the two groups.

Saikawa et al. previously reported that TLV was more effective than OLV for the maintenance of stable hemodynamics and oxygenation during the perioperative period,

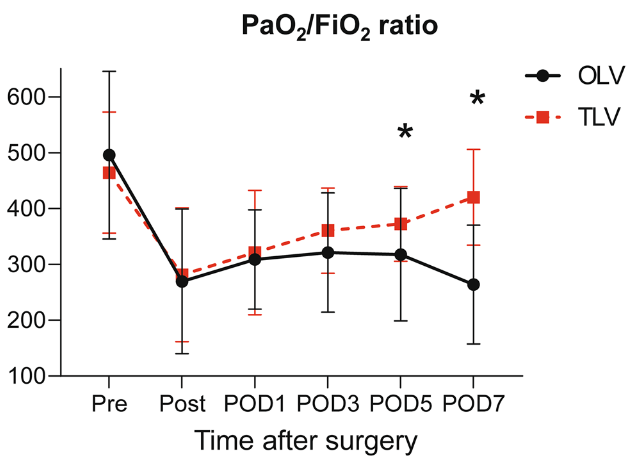

Fig. 2 Perioperative changes in PaO_2/FiO_2 ratio. *$P<0.05$ versus patients with postoperative pneumonia; ●: one-lung ventilation; ■: two-lung ventilation. *Pre* preoperatively, post immediately after surgery

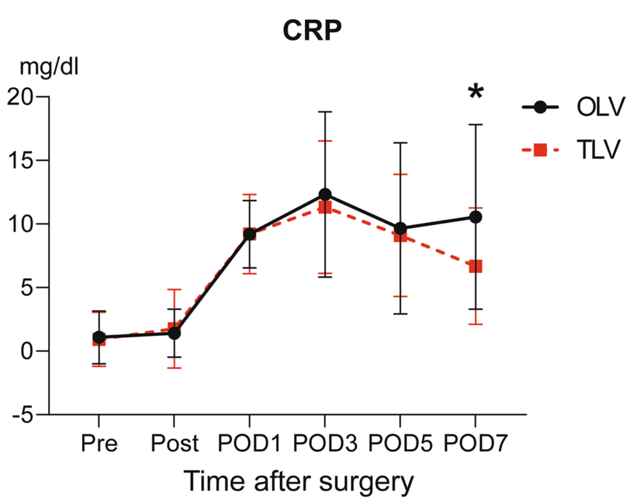

Fig. 3 Perioperative changes in CRP. *$P<0.05$ versus patients with postoperative pneumonia; ●: one-lung ventilation; ■: two-lung ventilation. *Pre* preoperatively, *post* immediately after surgery

in a study of 14 patients who underwent VATS-e [16]. In that study, although the left mediastinal pleurae were damaged by the thoracoscopic procedure and bilateral pneumothorax that occurred, there were no increases in airway pressure or instances of apparent circulatory depression. In contrast, some reports have shown that, although the use of TLV resulted in shorter thoracic operation time relative to the use of OLV, no differences were observed in pulmonary complications between the two groups [12, 13]. To the best of our knowledge, there have been no reports regarding the time courses of postoperative oxygenation or inflammation. Although our results also indicated that there were no differences in pulmonary complications, we found that the PaO_2/FiO_2 ratio was significantly higher in the TLV group on POD5 and POD7 and that the CRP level was significantly lower on POD7 in the TLV group. The white blood cell count on POD7 and body temperature from immediately after the operation until POD1 were both significantly lower in the TLV group.

Prior studies reported that surgical variables of TLV, such as operative time and hospital stay, were superior to those of OLV in patients who underwent VATS-e by experienced surgeons [12, 13]. Our results also showed that the TLV group had significantly shorter thoracic operation time than the OLV group. These results suggest that, to secure space in the right thoracic cavity, CO_2 artificial pneumothorax in TLV can provide a superior surgical view, compared with collapse of the right lung in OLV. A hard, large-caliber, double-lumen endotracheal tube placed in the main bronchus limits endotracheal mobility during surgery, making it difficult to remove LNs along the recurrent laryngeal nerve in OLV. In addition, TLV did not require the positioning of double-lumen tube and inflation or deflation of the balloon by anesthesiologist. These may contribute to the superiority of TLV over OLV with respect to the operation time during the thoracic procedure.

There were two limitations in this study. First, this was a single-center, retrospective study; the study design thus might have led to selection bias. Second, the patients in the OLV group had more advanced pT stages than patients in the TLV group; this may have influenced the results with respect to mobilization of the esophagus.

In conclusion, the current study demonstrated that TLV with artificial pneumothorax can be beneficial for postoperative oxygenation and systemic inflammation in patients undergoing VATS-e. Thus, TLV might be more useful than OLV for ventilation during VATS-e in the prone position.

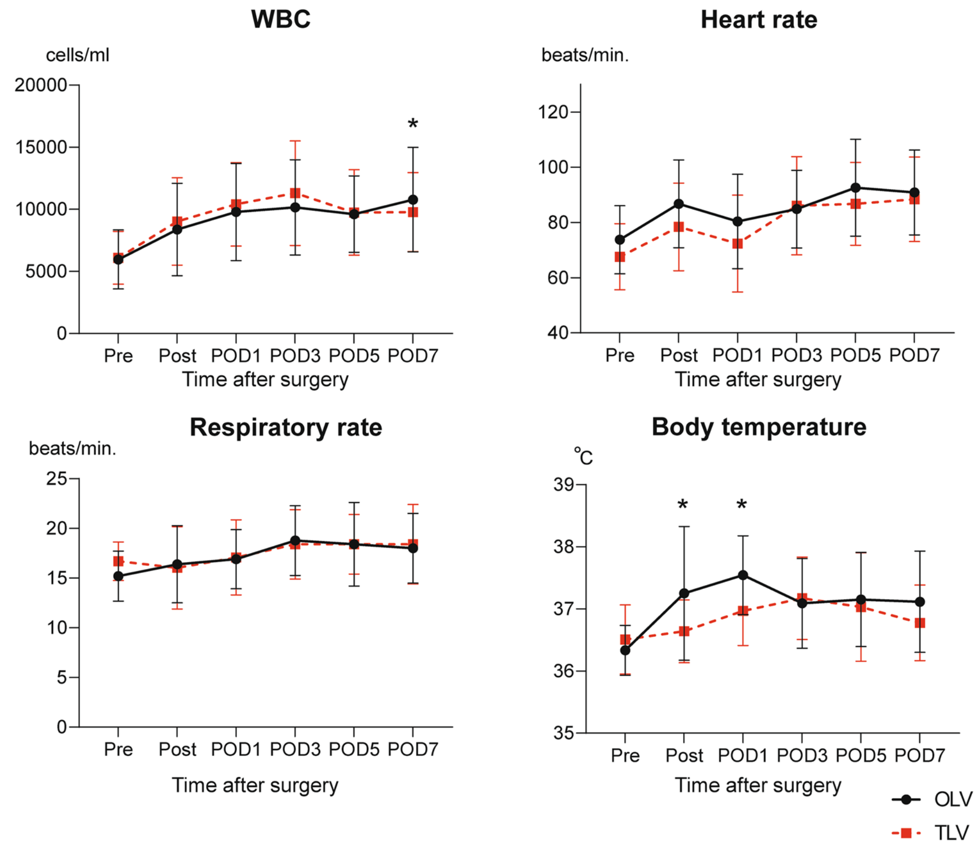

Fig. 4 Perioperative changes in SIRS criteria. *$P<0.05$; ●: one-lung ventilation; ■: two-lung ventilation. *Pre* preoperatively, *post* immediately after surgery

Table 3 Postoperative outcomes in one-lung ventilation and two-lung ventilation

	OLV ($n=71$)		TLV ($n=48$)		*P* value
Respiratory complications	17	23.9%	8	16.7%	0.37
Re-intubation	13	18.3%	4	8.3%	0.18
Anastomotic leakage	19	26.8%	12	25.0%	1.00
Length of stay in hospital (means ± SD, days)	38.0 ± 35.7		31.9 ± 23.5		0.19
30-day mortality	0	0%	0	0%	1.00
In-hospital mortality	0	0%	0	0%	1.00

OLV one-lung ventilation, *TLV* two-lung ventilation, *SD* standard deviation

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Author contributions SN and HT conceived the idea of this research, designed the protocol, and supervised the analysis of the results. YI, SF, KK, MH, NI, YY, SH, DS, TI, KH, and YK developed and supervised all work and analyzed the results. HU supervised the study.

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Compliance with ethical standards

Disclosures All authors (Shinsuke Nomura, Hironori Tsujimoto, Yusuke Ishibashi, Seiichiro Fujishima, Keita Kouzu, Manabu Harada, Nozomi Ito, Yoshihisa Yaguchi, Daizoh Saitoh, Takehiko Ikeda, Kazuo Hase, Yoji Kishi, Hideki Ueno) report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

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