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ORIGINAL ARTICLE

Co-administration of ephedrine prevents reductions in cardiac output and systemic oxygen delivery secondary to lung compression maneuvers during one-lung ventilation, without reducing arterial oxygenation

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Abstract
Purpose We previously showed that compression of the nondependent lung during one-lung ventilation (OLV) in patients undergoing esophagectomy improves arterial oxygenation but impairs cardiac output (CO) and systemic oxygen delivery (DO_2). The objective of this study was to test the hypothesis that the combination of nondependent lung compression and ephedrine improves arterial oxygenation without compromising DO_2.
Methods Twenty patients undergoing esophagectomy through a right thoracotomy were studied. Under general anesthesia, a left-sided double-lumen tube was placed, and the dependent lung was mechanically ventilated with a tidal volume of 8 ml/kg and a fraction of inspiratory oxygen of 0.8 during OLV. When nondependent lung was compressed by surgeons to improve surgical exposure, a randomly determined intravenous bolus of either ephedrine 4 mg (group E) or an identical volume of saline (group S) was administered. Arterial blood was sampled during two-lung ventilation (TLV), at 10 min of OLV (OLV1), and 5 min after nondependent lung compression (OLV2).
Results The initiation of OLV resulted in a significant drop in PaO_2 at OLV1 (group E, 136 ± 69 mmHg; group S, 138 ± 83 mmHg; $P < 0.01$) compared with TLV (group E, 404 ± 44 mmHg; group S; 367 ± 51 mmHg) and tended to improve at OLV2 (group E, 170 ± 63 mmHg; group S; 196 ± 121 mmHg). However, although CO and DO_2 significantly decreased in group S at OLV2 (4.0 ± 0.8 l/min, 621 ± 116 ml/min; $P < 0.01$) compared with OLV1 (5.1 ± 0.7 l/min, 811 ± 140 ml/min), there was no significant difference in these parameters in group E for the two time points.
Conclusion Although arterial oxygenation was not significantly improved by the nondependent lung compression, the addition of intravenous ephedrine to nondependent lung compression prevented the decrease in systemic oxygen delivery without deterioration of arterial oxygenation during OLV in patients undergoing esophagectomy.

Keywords One-lung ventilation · Esophagectomy · Ephedrine · Nondependent lung

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Introduction

Hypoxemia occurs in 1–9% of patients during one-lung ventilation (OLV) [1, 2]. A multitude of treatment approaches have been advocated, including nitric oxide [3], prostaglandin E_1 [4], prostaglandin F_2-alpha [5], almitrine [6], or different anesthetic agents [7–10]; however, hypoxemia continues to occur.

During the thoracotomy portion of an esophagectomy, the nondependent lung is routinely compressed for visualization purposes by the surgical team at our institution (Tokyo Medical and Dental University Hospital of Medicine). In a previous study [11], we showed that arterial

oxygen tension (PaO_2) increases with compression of the nondependent lung during OLV in patients undergoing esophagectomy. Based on these findings, we advocated that nondependent lung compression may be used as a measure to improve arterial oxygenation (PaO_2) in patients during OLV [11]. However, we later found that cardiac output (CO) and systemic oxygen delivery (DO_2) were impaired by this technique, presumably because of direct cardiac compression by the retractor, restriction of vena cava preload, or right ventricular impairment caused by high pulmonary vascular resistance [12].

The FloTrac sensor and Vigileo monitor (Edwards Lifesciences, Irvine, CA, USA) have recently been introduced as devices that estimate continuous CO and hemodynamic variables based on arterial pressure waveform analysis. The FloTrac/Vigileo system is considered to be less invasive than pulmonary artery catheters and is capable of measuring CO without calibration by connecting to an existing arterial catheter. Recent research has demonstrated that the cardiac index obtained by the FloTrac/Vigileo system showed good intraoperative and postoperative agreement with intermittent pulmonary artery thermodilution cardiac index measurements in patients undergoing coronary artery bypass graft surgery [13].

We speculated that intravenous ephedrine would be an effective option to mitigate the hemodynamic impairment caused by the application of the lung retractor. Although nondependent lung compression by itself improves PaO_2 but impairs DO_2, both improvement in PaO_2 and maintenance of DO_2 may be attained by adding intravenous ephedrine to nondependent lung compression during OLV. The objective of this study was to prove the hypothesis that the combination of nondependent lung compression and intravenous ephedrine would improve arterial oxygenation, without compromising systemic oxygen delivery, during OLV in patients undergoing esophagectomy.

Materials and methods

After institutional ethics approval and written informed consent, 20 consecutive adult patients (20 years of age or older) scheduled to undergo esophagectomy using a right thoracotomy and OLV were enrolled. Patients with pacemakers, history of cardiac arrhythmias, previous aortic replacement, severe peripheral vascular disease, cardiac support (intraaortic balloon pump), mitral or aortic valve dysfunction, and intracardiac shunt were excluded.

No premedication was administered before the patients were taken to the operating room. Before the induction of general anesthesia, an epidural catheter was inserted at the 6–7th or 7–8th thoracic interspace using a loss of resistance technique. General anesthesia was induced with intravenous propofol 2 mg/kg and fentanyl 1 μg/kg, and tracheal intubation was facilitated with intravenous rocuronium 0.6 mg/kg. A left-sided double-lumen endobronchial tube (Broncho-Cath; Mallinckrodt, Argyle, NY, USA) was placed for OLV, and correct positioning was confirmed by auscultation and fiberoptic bronchoscopy. Anesthesia was maintained with sevoflurane at an end-tidal concentration of 1.0–2.5%. Patients were ventilated mechanically at a constant tidal volume (10 ml/kg) during two-lung ventilation (TLV), and the respiratory rate was adjusted to maintain end-tidal carbon dioxide pressure at approximately 35 mmHg. The fraction of inspiratory oxygen (F_{IO_2}) was set at 0.8 and positive end-expiratory pressure was set to 0. After positioning the patient in the left lateral decubitus position, correct positioning of the double-lumen tube was reconfirmed by fiberoptic bronchoscopy. Rectal temperature was measured and kept constant using a warm-water blanket. A bolus dose of 0.3% ropivacaine 8–12 ml was injected epidurally and continuously administered at 4–8 ml/h.

A 20-gauge intravascular catheter was inserted into the left radial artery and connected to a Vigileo monitor (software version 1.14) through the FloTrac pressure transducer, for minimally invasive determination of continuous CO. The Vigileo monitor was connected to a personal computer (ThinkPad X23, IBM, USA) by a USB port, and CO was recorded every 20 s.

OLV was initiated immediately before opening of the pleura, and the tracheal lumen of the double-lumen tube was opened to allow for passive lung collapse. The dependent lung was ventilated with a tidal volume of 8 ml/kg, F_{IO_2} of 0.8, and zero end-expiratory pressure. The respiratory frequency was adjusted to maintain $PaCO_2$ at approximately 40 mmHg. If arterial oxygen saturation (SpO_2), monitored by pulse oximetry, decreased below 90% during OLV, tube malposition, circulatory problems, leaks, or disconnection were excluded as possible reasons for hypoxemia. If required, F_{IO_2} was increased to 1.0, and continuous positive airway pressure (CPAP) and/or intermittent positive pressure ventilation [14] were applied to the nondependent lung; data from these patients were excluded from analysis. Systolic blood pressure (SBP) was maintained within 20% of the preoperative value by controlling the concentration of sevoflurane, rate of continuous epidural administration, rate of intravenous fluid infusion, or by intravenous administration of inotropic agents (ephedrine or dopamine) or vasodilator (nicardipine), as needed.

To analyze the effects of nondependent lung compression on PaO_2 and systemic oxygen delivery (DO_2) during the experimental period, arterial blood samples were

collected 15 min after the patients were placed in the lateral position (TLV), 10 min (OLV1) after the start of OLV, and 5 min after nondependent lung compression (OLV2). The OLV1 time-point was chosen at 10 min of OLV because nondependent lung compression tends to occur at about 15 min of OLV at our institution. Arterial oxygen content (CaO_2) and DO_2 were calculated using the standard equations as follows:

$$\begin{aligned} CaO_2\ (\mathrm{ml/dl}) = {} & 1.34 \times \text{hemoglobin concentration}\ (\mathrm{g/dl}) \\ & \times \text{arterial oxygen saturation}\ (\%)/100 \\ & + 0.0031 \times PaO_2\ (\mathrm{mmHg}) \end{aligned}$$

$$DO_2\ (\mathrm{ml/min}) = CO\ (\mathrm{l/min}) \times CaO_2\ (\mathrm{ml/dl}) \times 10.$$

For nondependent lung compression, the lung was gently wrapped in gauze and a retractor was applied to improve exposure to the surgical field. This maneuver is routinely employed throughout the procedure at the discretion of the surgical team and has been a routine component of more than 1,000 esophagectomy surgeries at our institution during more than 35 years. To analyze the effects of the application of the lung retractor on hemodynamic parameters and arterial oxygenation, we analyzed the first 5 min of the first application of the lung retractor during the thoracic part of the esophagectomy, as changes in CO and SpO_2 are most dynamic during this period.

Using random numbers generated by the mathematical software (Mathematica 5.2; Wolfram Research), patients were randomly allocated into the ephedrine group (group E) or the saline group (group S) immediately before application of the lung compression maneuver. Predrawn syringes of ephedrine at 4 mg/ml or normal saline were supplied. Concomitant with nondependent lung compression, 1 ml of the treatment syringe was administered intravenously, consisting of 4 mg ephedrine (group E) or saline (group S). SBP, heart rate (HR), CO, and SpO_2 were recorded every minute for a total of 5 min after the initiation of lung compression. Systemic oxygen delivery was estimated as the product of CO and SpO_2, as changes in hemoglobin concentration and dissolved oxygen content during this interval were believed to be negligible. We did not sample arterial blood and calculate DO_2 during this period, as it would have resulted in interruption of the continuous CO monitoring via the FloTrac/Vigileo system, resulting in inaccurate CO data.

Application of the retractor is usually accompanied by a decrease in blood pressure [12]. Hemodynamic parameters were managed differently during the first 5 min after application of the lung retractor than the rest of the study period, where SBP was maintained within 20% of the baseline value. During the first 5 min of lung compression, an SBP of 70 mmHg or higher was allowed. Concentration of sevoflurane, infusion rate of dopamine and/or nicardipine, infusion rate of epidural ropivacaine, and infusion rate of intravenous fluid were not changed during this interval. No additional ephedrine was intravenously administered, except for the rescue of severe hypotension (SBP <70 mmHg). If SBP dropped below 70 mmHg and the rescue was required, the study protocol was terminated and the patients were excluded from the analyses.

After the surgery, the patients were transported to the intensive care unit (ICU), sedated, and mechanically ventilated until the next morning as a part of our routine practice. They were extubated on the next morning if their respiratory condition was satisfactory and stable. Duration of surgery, anesthesia, and ICU stay were analyzed retrospectively using the electronic medical charts. Arterial blood gas sampled on arrival to ICU was also retrospectively checked because reexpansion of the nonventilated lung after OLV could lead to release of free oxygen radicals relating to reperfusion injury [15]. Whether the patients were reintubated for respiratory failure was also checked in the course of the postoperative period.

Demographic data, duration of surgery, anesthesia, ICU stay, and PaO_2/F_{IO_2} ratio (P/F ratio) and $PaCO_2$ on arrival to ICU were compared between the groups using one-way analysis of variance (ANOVA). Sequential changes in arterial blood gas data, hemoglobin concentration, SBP, HR, CO, DO_2, SpO_2, and the product of CO and SpO_2 were analyzed using two-way repeated measures ANOVA. Post hoc analyses were adjusted for multiple comparisons using the Bonferroni correction when appropriate. Statistical significance was established at the $P < 0.05$ level.

Results

All patients included in the study had American Society of Anesthesiologists (ASA) physical status II or III. Demographic data of the patients are shown in Table 1. There were no statistically significant differences in gender, age, height, weight, or spirometry data between the groups. Lung compression always occurred after the OLV1 time-point. Because all patients maintained an SpO_2 of 90% or higher, no interventions to improve arterial oxygenation (increase in F_{IO_2}, CPAP, and intermittent positive pressure ventilation) were required. Similarly, no cases of severe hypotension (SBP <70 mmHg) occurred during nondependent lung compression, and therefore no patients needed to be excluded from the analyses. No patient required intravenous nicardipine throughout the study. The rate of continuous dopamine administration was unchanged (group E, 2.1 ± 1.4 μg/kg/min; group S, 1.9 ± 1.5 μg/kg/min) during the 5-min observation period.

After OLV was commenced, PaO_2 significantly decreased at OLV1 compared with TLV. PaO_2 tended to be

Table 1 Demographic data

	Group E ($n = 10$)	Group S ($n = 10$)
Gender (M/F)	9/1	8/2
Age (years)	67.4 ± 7.7	66.2 ± 7.7
Height (cm)	162.1 ± 5.4	164.0 ± 7.6
Weight (kg)	56.5 ± 7.1	54.9 ± 5.7
%VC (%)	102.2 ± 10.0	103.8 ± 14.9
FEV 1/FVC (%)	71.5 ± 11.2	73.2 ± 8.1

Data are presented as mean ± SD

%VC vital capacity (VC)/predicted VC ratio, *FEV 1* forced expiratory volume in 1 s, *FVC* forced vital capacity

higher at OLV2 compared with OLV1; however, the difference of PaO_2 between OLV1 and OLV2 did not reach statistical significance (Table 2). SBP, CO, and DO_2 in group S significantly decreased at OLV2 compared with OLV1, whereas there was no significant difference in these parameters in group E at different time-points. SBP in group E was significantly higher than in group S at OLV2.

In group E, mean SBP increased by approximately 25 mmHg at 2–5 min after nondependent lung compression, compared with 0 min in group E. In group S, however, SBP gradually decreased during the 5 min of the observation period (Table 3). There were significant differences in SBP at 2–5 min of nondependent lung compression between the groups. CO was significantly higher in group E than group S at 3–4 min of nondependent lung compression. In six patients in group E, SpO_2 had already been as high as 99–100% when ephedrine was administered. Their SpO_2 values were kept at 99–100% during the 5-min observational period. In three patients in group E with SpO_2 of 95% or less, improvement in SpO_2 by 3–5% was recorded at 2–3 min after nondependent lung compression. The product of CO and SpO_2 was significantly higher in group E than in group S at 3 min of nondependent lung compression and was maintained over time.

In all patients, anesthesia and surgery proceeded without major complications. There was no significant difference in duration of surgery (group E, 370 ± 43 min; group S, 392 ± 39 min), duration of anesthesia (group E, 449 ± 46 min; group S, 473 ± 30 min), and period of ICU stay (group E, 3.1 ± 2.1 days; group S, 2.9 ± 1.5 days) between the groups. The number of administrations of intravenous ephedrine during the surgery except on the first nondependent lung compression was 3.4 ± 1.0 in group E and 3.0 ± 1.3 in group S (no statistical difference). No significant difference was found in P/F ratio (group E, 375 ± 114; group S, 352 ± 48) or $PaCO_2$ (group E, 41.0 ± 3.5 mmHg; group S, 41.9 ± 3.6 mmHg) on arrival to ICU between the groups. One of the group E patients with pneumonia was extubated on postoperative day 8, whereas all the other patients were extubated on the next day after surgery as was planned. No patients were reintubated for respiratory failure during the postoperative period.

Table 2 Sequential changes in arterial blood gas values and hemodynamic data in group E and group S

	TLV	OLV1	OLV2
pH			
Group E	7.41 (0.04)	7.40 (0.04)	7.41 (0.03)
Group S	7.40 (0.02)	7.39 (0.03)	7.40 (0.03)
PaO_2 (mmHg)			
Group E	404 (44)	136 (69)$^{\#\#}$	170 (63)$^{\#\#}$
Group S	367 (51)	138 (83)$^{\#\#}$	196 (121)$^{\#\#}$
$PaCO_2$ (mmHg)			
Group E	40.2 (5.4)	40.9 (5.5)	39.4 (2.9)
Group S	41.9 (3.0)	42.2 (2.6)	39.4 (2.8)
Hb (g/dl)			
Group E	12.1 (1.3)	12.1 (1.3)	12.1 (1.3)
Group S	11.8 (1.4)	11.8 (0.8)	11.5 (0.8)
SBP (mmHg)			
Group E	112 (12)	132 (15)	126 (25)$^{++}$
Group S	114 (20)	137 (12)	97 (17)**
HR (bpm)			
Group E	64 (8)	76 (15)	80 (11)$^{\#}$
Group S	65 (14)	81 (17)	75 (17)
CO (l/min)			
Group E	4.0 (0.6)	5.2 (1.0)	4.9 (1.5)
Group S	4.3 (0.7)	5.1 (0.7)	4.0 (0.8)**
DO_2 (ml/min)			
Group E	692 (130)	857 (231)	825 (311)
Group S	714 (83)	811 (140)	621 (116)**

Data are presented as mean ± SD

TLV two-lung ventilation, *OLV1* 10 min of one-lung ventilation, *OLV2* 5 min of nondependent lung compression, *Hb* hemoglobin, *SBP* systolic blood pressure, *HR* heart rate, *CO* cardiac output, DO_2 systemic oxygen delivery

$^{\#}$ $P < 0.05$, $^{\#\#}$ $P < 0.01$, versus TLV; ** $P < 0.01$, versus OLV1; $^{++}$ $P < 0.01$, between the groups

Discussion

We assessed the effects of intravenous ephedrine on hemodynamic indices and arterial oxygenation during OLV after nondependent lung compression in patients undergoing esophagectomy. Nondependent lung compression significantly decreased SBP, CO, and DO_2 compared with the values before compression in the placebo group, although ephedrine administration mitigated any changes in hemodynamic variables (see Table 2).

Table 3 Sequential changes in hemodynamic values and oxygenation indices during the first 5 min of nondependent lung compression in group E and group S

	0 min	1 min	2 min	3 min	4 min	5 min
SBP (mmHg)						
Group E	103 (20)	114 (23)	128 (27)$^{+}$	127 (27)$^{+}$	126 (27)$^{++}$	126 (25)$^{++}$
Group S	114 (17)	105 (18)	102 (17)	98 (19)	95 (18)	97 (17)
HR (bpm)						
Group E	76 (12)	78 (8)	78 (10)	78 (11)	79 (10)	80 (11)
Group S	79 (14)	78 (16)	76 (17)	77 (16)	75 (17)	75 (17)
CO (l/min)						
Group E	4.0 (1.0)	3.8 (0.9)	4.6 (1.4)	5.0 (1.5)$^{+}$	5.0 (1.5)$^{+}$	4.9 (1.5)
Group S	4.6 (1.4)	4.0 (0.7)	3.8 (0.9)	3.7 (1.1)	3.8 (0.7)	4.0 (0.8)
SpO_2 (%)						
Group E	97.5 (3.0)	98.8 (1.1)	98.8 (1.2)	98.6 (1.6)	98.5 (1.6)	98.5 (1.6)
Group S	98.7 (1.7)	99.2 (0.8)	98.9 (1.0)	98.7 (1.1)	98.5 (1.2)	98.5 (1.2)
CO × SpO_2 (l/min × %)						
Group E	392 (87)	370 (90)	453 (140)	496 (154)$^{+}$	487 (147)	486 (147)
Group S	453 (136)	396 (71)	375 (89)	366 (106)	379 (76)	390 (80)

Data are presented as mean ± SD

SBP systolic blood pressure, *HR* heart rate, *CO* cardiac output, *SpO_2* arterial oxygen saturation monitored by pulse oximetry

$^{+}$ $P < 0.05$, $^{++}$ $P < 0.01$, between the groups

Based on a previous study, we had advocated that compression of the nondependent lung during OLV may be a potentially useful measure to treat hypoxemia [11]. The most likely explanation for changes in arterial oxygenation after compression of the nondependent lung is the diversion of blood flow to the dependent lung by physical compression and kinking of the lung vessels. However, our recent follow-up study using a minimally invasive CO monitor suggested that nondependent lung compression reduced DO_2 despite improvement in arterial oxygen saturation [12]. Because the decrease in DO_2 was mainly caused by the reduction of CO associated with the compression of the nondependent lung [12], we aimed to maintain CO without compromising arterial oxygenation in the present study. Ephedrine was selected as an inotropic agent because it anecdotally had been found to be effective in case of hypotension during lung retractor application in our institution, but also because of its favorable pharmacodynamic and safety profile. The other justification for the use of ephedrine in our study was the fact that a bolus dose of 0.15 mg/kg intravenous ephedrine has been shown to increase PaO_2 during OLV without impacting the intrapulmonary shunt fraction [16].

We chose to administer ephedrine boluses for CO and blood pressure support, rather than titrate an intravenous infusion of, for example, dopamine. Even though the effects of repetitive nondependent lung compression on arterial oxygen partial pressure may be long lasting [17], the effects of a single nondependent lung compression on hemodynamic parameters and arterial oxygen saturation may be observed for only a couple of minutes [12]. We therefore chose to use a more vigorous inotropic effect that could be obtained by a single bolus administration of ephedrine rather than that gradually exerted by an increasing continuous intravenous infusion of dopamine for the purpose of proving our hypothesis.

Several factors are known to contribute to the magnitude of intrapulmonary shunt during OLV, including hypoxic pulmonary vasoconstriction (HPV) [18], CO, and positioning of patients [19]. CO, when augmented to double or triple baseline, can increase shunt by increasing pulmonary artery pressure that results in opposing the weak forces affecting HPV [20, 21] and by increasing mixed venous oxygen tension, which is shown to inhibit HPV [22]. Furthermore, some inotropic agents are shown to directly inhibit HPV in animal experiments [23, 24]. Thus, there was concern that intravenous ephedrine may increase venous admixture by increasing shunt flow through the nondependent lung, thereby impairing arterial oxygenation. Although to our knowledge, there has been only one study that investigated the effects of ephedrine on arterial oxygenation during OLV [16], the relationships between CO and arterial oxygenation have been studied extensively. Slinger and Scott [7] showed that PaO_2 significantly correlated with CO in the range of approximately 2.5–7.5 l/min CO during OLV. Nomoto and Kawamura [25] described the relationship between CO and arterial oxygenation in patients during OLV using three different drugs. In their study, an increase

in CO by approximately 25% using dobutamine 5 μg/kg/min led to significant improvements in arterial oxygenation during OLV, whereas 1 μg/kg/min of nitroglycerin, which decreased CO by approximately 15%, decreased PaO_2 significantly, and furthermore, dopamine 5 μg/kg/min, which had no effect on CO, did not change PaO_2 significantly. Mathru et al. [26] also administered dobutamine 5 μg/kg/min to increase CO by 25% and found that PaO_2 significantly increased during OLV in patients undergoing pneumonectomy.

In contrast, it has been shown that increasing CO to very high values can cause deterioration in arterial oxygenation during OLV. Russell and James increased CO to two- or even threefold baseline value with dopamine, dobutamine [27], adrenaline, or isoprenaline [28] and found that elevated oxygenation in mixed venous blood is offset by increased shunt fraction, resulting in impaired arterial oxygenation. The increase in the shunt fraction at higher CO level may be partially explained by the fact that even small increases in pulmonary artery pressure oppose the weak forces affecting HPV [20, 21]. Animal studies have shown that a high dose (20–25 μg/kg/min) of dopamine and dobutamine inhibits the response of HPV in dogs with left lower lobe hypoxia [24] and with unilateral hypoxia [29].

In the present study, 4 mg intravenous ephedrine increased CO by 25% in group E at 3–5 min, when SpO_2 increased by approximately 1% compared with that at 0 min of nondependent lung compression. Although arterial oxygenation was not significantly improved by nondependent lung compression, as opposed to our hypothesis and our previous studies [11, 12], the present study showed that the addition of intravenous ephedrine to nondependent lung compression prevented the decrease in systemic oxygen delivery without deterioration of arterial oxygenation during OLV. The mild increase in CO may not result in a clinically relevant increase in the shunt flow via the nondependent lung, as the lung is compressed by the retractor and the nondependent lung vessels are most likely kinked. However, as increasing CO to very high values can cause deterioration in arterial oxygenation [27, 28], CO monitoring is recommended when inotropic agents are administered for the purpose of improving arterial oxygenation during OLV. It should be noted that arterial blood pressure monitoring may not serve as a surrogate for CO monitoring in this context because it is not possible to calculate CO reliably without information on peripheral resistance and aortic compliance even though the arterial blood pressure waveform is available [30].

The decrease in CO associated with the application of the lung retractor may have seemed relatively mild in group S (Table 2). However, it should be noted that CO at OLV2 was not the lowest value during the time-course of nondependent lung compression in group S. In fact, the lowest CO was recorded at 3 min after the lung retractor application (Table 3).

There are several limitations in the present study. First, the usage of dopamine may have been a confounding factor, because both dopamine and ephedrine stimulate β-receptors on the heart. Because this is a follow-up study, dopamine was used to maintain systemic blood pressure within the target range as in our previous studies [11, 12]. Second, the compression of the nondependent lung was not controlled and was at the discretion of the surgical team. Third, the effects of ephedrine on hemodynamic parameters and arterial oxygenation were not compared with other inotropic or vasoactive agents. Further studies are required to prove that CO and systemic oxygen delivery are also maintained by other inotropic or vasoactive agents when they are administered at compression of the nondependent lung. Last, no patients with severe hypotension or severe hypoxemia were included in the present study and our results therefore cannot be translated to that population.

In conclusion, although arterial oxygenation was not significantly improved by nondependent lung compression, the addition of intravenous ephedrine to nondependent lung compression prevented the decrease in systemic oxygen delivery without deterioration of arterial oxygenation during OLV. Intravenous ephedrine may be an effective option to mitigate the hemodynamic impairment caused by application of the lung retractor in patients undergoing esophagectomy.

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Conflict of interest None.

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