

# Comparison of parameter types for the calibration of noninvasive continuous cardiac output monitoring of patients undergoing lumbar spinal surgery in the prone position

Seung Cheol Lee, Gang Hyun Lee, Tae Young Lee and Sang Yoong Park\*

*Department of Anesthesiology and Pain Medicine, College of Medicine, Dong-A University, Busan, Korea*

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## Abstract.

**BACKGROUND:** Cardiac output (CO) decreases on reversing the patient's position to the prone position. Estimated continuous cardiac output (esCCO) systems can noninvasively and continuously monitor CO calibrated by patient information or transesophageal echocardiogram (TEE).

**OBJECTIVE:** To compare the accuracy, precision, and trending ability of two calibration methods of CO estimation in patients in prone position.

**METHODS:** The CO estimates calibrated by TEE (esT) and patient information (esP) of 26 participants were included. CO was collected at four time points. The accuracy and precision of agreement were evaluated using the Bland-Altman method. A four-quadrant plot was used for trending ability analysis.

**RESULTS:** The bias between esP and TEE and between esT and TEE was 0.2594 L/min (95% limits of agreement (LoA):  $-1.8374$  L/min to  $2.3562$  L/min) and  $0.0337$  L/min (95% LoA:  $-0.7381$  L/min to  $0.8055$  L/min), respectively. A strong correlation was found between  $\Delta$ esP and  $\Delta$ TEE ( $p < 0.001$ , CCC = 0.700) and between  $\Delta$ esT and  $\Delta$ TEE ( $p < 0.001$ , CCC = 0.794). The concordance rates between  $\Delta$ esP and  $\Delta$ TEE and between  $\Delta$ esT and  $\Delta$ TEE were 91.9% and 97.1%, respectively.

**CONCLUSION:** Despite limited accuracy and precision, esP showed acceptable trending ability. The trending ability of esCCO calibrated by the reference TEE value was comparable with that of TEE.

Keywords: Calibration, cardiac output, prone position, pulse wave analysis, echocardiography, transesophageal

## 1. Introduction

An increase in age-related diseases, such as degenerative diseases of the lumbar spine [1], has been observed with the increase in the number of elderly individuals, resulting in an increase in the number of candidates requiring lumbar spine surgery. Nearly 180,000 general spine surgeries were performed in South Korea in 2020 [2]; lumbar spine surgery is one such surgery that is performed in the prone position. A significant decrease in cardiac output (CO) occurs on changing the position of the patient from the

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\*Corresponding author: Sang Yoong Park, Department of Anesthesiology and Pain Medicine, College of Medicine, Dong-A University, 26 Daesingongwon-ro, Seo-gu, Busan 49201, Korea. E-mail: parksy@dau.ac.kr.

supine to the prone position due to a decrease in preload, resulting in decreased arterial pressure and tissue perfusion [3]. Perioperative cardiac complications are the main cause of mortality after noncardiac surgery, and 1.5% of patients undergoing noncardiac surgery die in the subsequent 30 days [4]. The overall incidence of cardiac complications ranges from 0.2–13% in lumbar spine surgery [5]. Therefore, the optimization of hemodynamic variables, including CO, is an integral part of perioperative care that reduces postoperative mortality and morbidity during lumbar spine and other surgeries that require patients to be placed in the prone position [6].

Many noninvasive hemodynamic monitoring techniques, such as impedance cardiography, arterial pressure-based CO (APCO), volume clamp method, and pulse wave transit time (PWTT) method, have been developed and studied recently [7–9]. Among these methods, the estimated continuous cardiac output (esCCO) system, a technique based on the PWTT method, can noninvasively and continuously monitor CO. The esCCO system determines a reference value for calibration by measuring and entering the basic vital sign parameters using electrocardiogram (ECG), pulse wave oximetry, and arterial blood pressure (ABP) and by entering patient information, such as age, gender, height, and weight [9]. Other cardiac output measurement devices, such as a transesophageal echocardiogram (TEE), can also be used for initial calibration [10].

Previous studies have demonstrated the accuracy, precision, and trending ability of esCCO, and several studies [9,11,12] have examined the use of esCCO calibrated using patient information and noninvasive basic vital sign parameters for the initial calibration. Terada et al. [9] studied the ability of the esCCO system to measure the trends during laparotomy without postural change and reported that esCCO has a reasonable trending ability. Magliocca et al. [11] compared esCCO with the thermodilution CO (TDCO) method in patients undergoing orthotopic liver transplantation and concluded that although esCCO has no interchangeability, it has an acceptable trending ability. Terada et al. [12] compared the ability of esCCO and APCO to detect the stroke volume index and demonstrated that the accuracy, precision, and dynamic trend of esCCO are better than those of APCO.

Some studies [13,14] have used reference CO values for the initial calibration of esCCO and adopted the TDCO or APCO methods for reference CO measurement. The results of both studies indicated that esCCO has limited interchangeability in terms of accuracy and precision. Suzuki et al. [13] compared esCCO with APCO in patients undergoing cardiovascular surgery and showed that the trending ability of esCCO was almost acceptable. Tsutsui et al. [14] also assessed the trending ability of esCCO and reported that it is comparable with that of the TDCO method.

To the best of our knowledge, no study has measured CO using the PWTT method in patients undergoing surgery in the prone position. We aimed to compare the accuracy, precision, and trending ability of esCCO obtained using two different calibration methods with that of the TEE-measured CO values obtained from patients in the prone position during lumbar spine surgery.

## 2. Methods

This prospective study was conducted at the Dong-A University Hospital in accordance with the principles of the Declaration of Helsinki. We obtained approval from the Institutional Review Board of the Dong-A University Hospital. The study is registered with the Clinical Research Information Service of the Republic of Korea (no. KCT0006164; Available at: <https://cris.nih.go.kr>).

Twenty-six patients scheduled to undergo elective lumbar spinal surgery in the prone position who were between the ages of 30 and 80 years and with a physical status of 1, 2, or 3 according to the American Society of Anesthesiologists classification were enrolled in this study after obtaining written informed

consent. Patients younger than 30 years or older than 80 years and patients with an ejection fraction less than 35% on preoperative echocardiography, severe valvular heart disease, preoperative hemodynamic instability, respiratory failure, persistent cardiac arrhythmia, permanent pacemaker, and/or an intra-aortic balloon pump were excluded. Patients with swallowing difficulties; any history of esophageal diseases, such as strictures, diverticula, and tumors; or recent gastroesophageal surgery were also excluded from the study.

Based on the PWTT method, esCCO can be calculated using ECG, ABP, and pulse wave oximetry according to the following formula:

$$\text{esCCO} = K \times (\alpha \times \text{PWTT} + \beta) \times \text{HR} = \text{Stroke Volume(SV)} \times \text{HR}$$

The pulse wave transit time is the duration between the ECG R-wave peak to the rise point of the pulse wave oximeter. The rise point is defined as the time taken by the pulse wave to reach 30% of the maximum amplitude. The pulse wave transit time is correlated with SV, and K is calculated by the arterial pulse pressure. Experimental constants,  $\alpha$  and  $\beta$ , were derived from the demographic data of the patients. The EsCCO value was determined by averaging the PWTT for 64 consecutive heartbeats.

Two bedside monitors (BSM-6701K, Nihon Kohden, Tokyo, Japan) were connected to the patient to assess and monitor each esCCO. Two sets of electrodes were used to monitor the ECG (lead II), and two pulse oximeter probes were placed on the second and fourth fingertips of the same hand. The blood pressure was monitored noninvasively every 5 minutes until the insertion of the radial arterial catheter and every 15 minutes thereafter. The radial arterial and central venous catheters were placed under sevoflurane-induced (1.0–2.0%, end-tidal) general anesthesia, and a 2–7 MHz TEE transducer (Philips, X7-2t, MA, USA) was inserted to the depth of the lower esophagus. The position of the participant was then reversed from the supine to the prone position. The participants were positioned on a convex saddle frame, with their heads on the prone position foam headrest to prevent compression of the endotracheal tube and TEE. CO was evaluated through TEE, and the value was entered for the initial calibration of esCCO (esT). The reference CO value was calculated according to the modified Simpson's method (biplane method of discs) using a portable ultrasound device (CX50, Philips, MA, USA) as it is the only recommended method that is known to fare well in the prediction of ventricular volume, CO, and ejection fraction even with abnormal ventricles [15]. The average of three sequential measurements of CO was used to improve precision and minimize the interventricular differences. The CO measurement with TEE was performed by an anesthesiologist who had performed this technique at least 200 times and had sufficient experience in monitoring cardiac function using TEE during cardiovascular surgery. Concurrently, another esCCO calibrated by patient information (esP) was also assessed. The CO measurements of esT, esP, and TEE were collected at four time points (T1: 10 minutes after reversing the patient to the prone position; T2: 10 minutes after skin incision; T3: mid-time of the surgery; and T4: at the time of placing the last suture).

Details regarding the demographic characteristics of the participants and types of surgery are shown in Table 1. The hemodynamic data of the participants at all time points (T1–T4) are presented in Table 2. The differences between esT, esP and TEE were evaluated at each of the four time points using one-way analysis of variance (ANOVA) with Bonferroni's post-hoc test or Kruskal-Wallis test with Dunn's post-hoc test for multiple comparisons. Pearson correlation coefficients with 95% confidence intervals (Cis) for esT, esP, and TEE were calculated, and repeated measurements were conducted to correct the correlation coefficients [16]. The accuracy and precision of the agreement between esT and esP with TEE were evaluated using the Bland-Altman method [17]. The mean bias represents the systemic error between the two methods. When the estimated bias is small and near zero, and the 95% CI is narrow, it indicates that the agreement between the two measurements is accurate and precise. The results of the Bland-Altman

Table 1  
Patient and surgery characteristics ( $n = 26$ )

Characteristic	
Male, $n$ (%)	9 (35)
Age, y	72 (52–80)
Height, cm	157.8 $\pm$ 8.6
Weight, kg	62.3 $\pm$ 11.6
BMI, kg/m <sup>2</sup>	25.1 $\pm$ 3.6
ASA score (I/II/III), $n$	2000/12/14
Comorbidity	
Hypertension	14
Diabetes mellitus	12
Congestive heart failure	3
Angina	2
Chronic kidney failure	5
Cerebrovascular accident	3
Parkinson disease	2
Aortic stenosis	1
Asthma	1
Surgery time, min	188 (176–229)
Diagnosis	
Spinal stenosis	10
Herniated nucleus pulposus	1
Spine fracture	4
Spine metastatic cancer	1
Post-operation complication	4
Spondylodiscitis	3
Spondylolisthesis	3
Fluid balance management, mL	
Input	1800 (1500–2450)
Output including EBL	525 (377–950)
Transfusion, RBC	
Patients, $n$ (%)	5 (19)
Phenylephrine, $n$ (%)	19 (61)
Ephedrine, $n$ (%)	7 (27)

Age is presented as median (range), and the other values are presented as mean  $\pm$  standard deviation, median (interquartile range) or number of patients (% of total). BMI = body mass index; ASA = American Society of Anesthesiologists score; EBL = estimated blood loss; RBC = red blood cell;  $n$  = number.

analysis were presented as percentage error (PE) by dividing the limit of agreement (LoA) by mean CO. A PE cut-off of  $\pm 30\%$  of the measurement technique can be interpreted as pragmatic guidance for clinicians that is comparable with the reference measurement value [18]. A four-quadrant plot was used for the trending ability analysis. Four-quadrant plots with the concordance rate (CR) and concordance correlation coefficient (CCC) were presented. The trending ability is considered reliable when the CR is 90% to 95% [19]. The CCC ranges from 0 to 1; a higher value indicates stronger agreement, whereas a value lower than 0.9 can be interpreted as poor agreement. CCC can determine the accuracy and precision of the measurement techniques.

The sample size was calculated by estimating the mean bias and LoA of esCCO [17]. Based on accuracy, the expected mean bias of the CO value between esCCO and TEE was assumed to be 0.39 L/min. The expected precision between esCCO and TEE was  $\pm 1.16$  L/min; thus, it was concluded that 26 participants would be sufficient for the study [20].

Table 2  
Hemodynamic values at four time points

	T1	T2	T3	T4
sABP (mmHg)	117 ± 22	121 ± 19	119 ± 18	127 ± 21
dABP (mmHg)	61 ± 15	63 ± 12	64 ± 14	63 ± 14
mABP (mmHg)	82 ± 18	85 ± 15	84 ± 15	86 ± 16
HR (beats/min)	80 ± 14	75 ± 12	70 ± 12	71 ± 11
esCCO (esT, L/min)	4.04 ± 1.11	3.79 ± 1.04	3.32 ± 1.03	3.64 ± 1.17
esCCO (esP, L/min)	4.24 ± 0.99	3.94 ± 0.77	3.57 ± 0.87	3.95 ± 1.21
CO (TEE, L/min)	4.09 ± 1.14	3.66 ± 1.08	3.43 ± 1.05	3.49 ± 1.00
CVP (cmH <sub>2</sub> O)	11 (8–14)	12 (7–15)	10 (6–12)	10 (6–13)

Data are presented as the mean ± standard deviation or median (interquartile range). sABP = systolic arterial blood pressure; dABP = diastolic arterial blood pressure; mABP = mean arterial blood pressure; HR = heart rate; esCCO = estimated continuous cardiac output; esT = esCCO calibrated by TEE; esP = esCCO calibrated by patient information; CO = cardiac output; TEE = transesophageal echocardiogram; CVP = central venous pressure; T1 = 10 minutes after reversing patients to the prone position; T2 = 10 minutes after skin incision; T3 = middle time of the surgery; T4 = at the time of last suture.

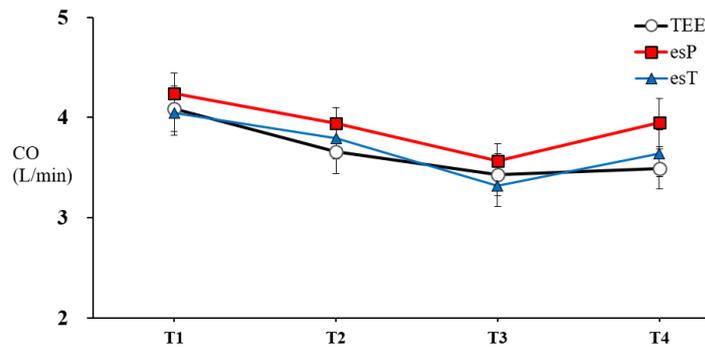


Fig. 1. TEE cardiac output (CO) measurements (circles, black line) esCCO calibrated by patient information (esP) (squares, red line), and esCCO calibrated by TEE (triangles, blue line). Data are presented as mean ± SEM (standard error of measurement). T1: 10 minutes after reversing to the prone position. T2: 10 minutes after skin incision. T3: mid-time of surgery. T4: time of placing the last suture.

Statistical analyses were performed using SPSS v26.0 (IBM Corp., Armonk, NY, USA), MedCalc Statistical Software v20.009 (MedCalc Software Ltd., Ostend, Belgium) and R v4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

### 3. Results

Both esP and esT showed no significant differences compared with TEE at any time point during anesthesia and surgery (Fig. 1).

Pearson correlation coefficient ( $r$ ) with 95% confidence intervals (CIs) of esP, esT and TEE were calculated, and repeated measurements were conducted to correct the correlation coefficients. The correlation coefficients between esP and TEE and between esT and TEE were 0.713 ( $p < 0.001$ , 95% CI, 0.582–0.808) and 0.814 ( $p < 0.001$ , 95% CI, 0.722–0.878), respectively.

The Bland-Altman analysis that was corrected for repeated measurements (26 measurements repeated four times) and included all time points (T1–T4) showed that the bias between esP and TEE was

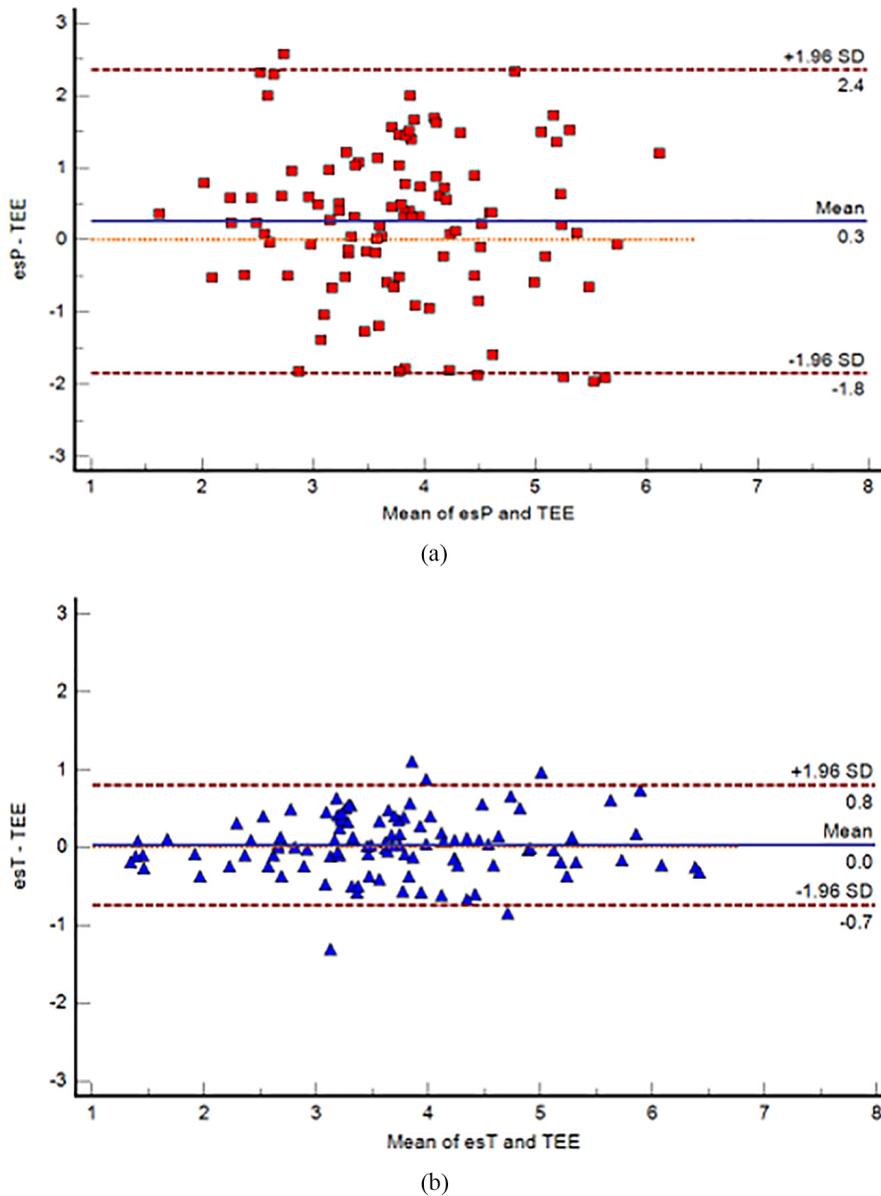


Fig. 2. Bland-Altman plots for the agreement analysis between esP and TEE (a), and esT and TEE (b). The blue continuous lines show the mean difference (bias), and the red dashed lines show the upper and lower 95% limits of agreement (LoA). TEE = transesophageal echocardiogram; esP = esCCO calibrated by patient information; esT = esCCO calibrated by TEE; SD = standard deviation.

0.2594 L/min (95% CI of LoA:  $-1.8374$  L/min to  $2.3562$  L/min) (Table 4 and Fig. 2a). The bias between esT and TEE was  $0.0337$  L/min (95% CI of LoA:  $-0.7381$  L/min to  $0.8055$  L/min) (Table 3 and Fig. 2b).

A strong correlation existed between  $\Delta$ esP and  $\Delta$ TEE ( $p < 0.001$ , CCC =  $0.700$ , 95% CI:  $0.431$ – $0.854$ ) and between  $\Delta$ esT and  $\Delta$ TEE ( $p < 0.001$ , CCC =  $0.794$ , 95% CI:  $0.566$ – $0.908$ , Fig. 3). CR between  $\Delta$ esP and  $\Delta$ TEE and between  $\Delta$ esT and  $\Delta$ TEE were  $91.9\%$  and  $97.1\%$ , respectively (Table 4 and Fig. 3).

Table 3  
Agreement analysis

Method A	esP	esT
Method B	TEE	TEE
Mean	0.2594	0.0337
Lower limit	-1.8374	-0.7381
95% CI	-2.6347 to -1.2967	-0.9158 to -0.6096
Upper limit	2.3562	0.8055
95% CI	1.8155 to 3.1536	0.6769 to 0.9831
PE	56%	21%

esP = esCCO calibrated by patient information; esT = esCCO calibrated by TEE; TEE: transesophageal echocardiography; CI: confidence interval; PE: percentage error.

Table 4  
Four-quadrant analysis

	N	Concordant	Disconcordant	Concordance rate [%]	CCC (95% CI)
esP	37	34	3	91.9%	0.700 (0.431–0.854)
esT	34	33	1	97.1%	0.794 (0.566–0.908)

N = number; CCC = concordance correlation coefficient; CI = confidence interval; esP = esCCO calibrated by patient information; esT = esCCO calibrated by TEE.

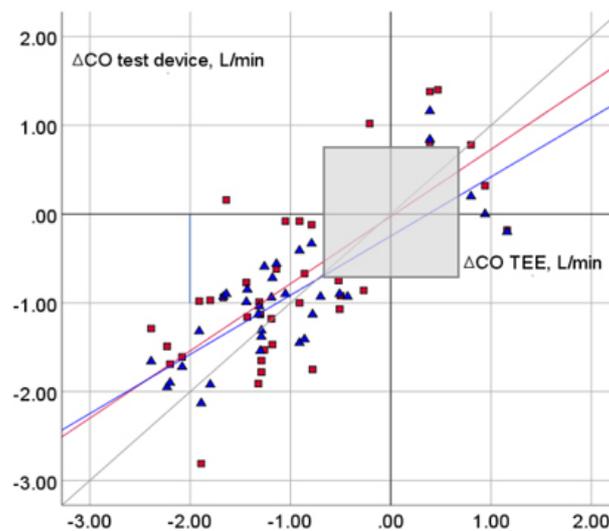


Fig. 3. The four-quadrant plot shows the changes in the cardiac output (CO),  $\Delta$ esP (red squares) and  $\Delta$ esT (blue triangles) compared to  $\Delta$ TEE. The central exclusion zone, set at  $\Delta$ CO < 0.75 L/min, is represented by a gray square. Regression lines for  $\Delta$ esP (red line) and  $\Delta$ esT (blue line) are represented by the identity line (gray line). TEE = transesophageal echocardiogram; CO = cardiac output.

The trending abilities of esP and esT were expressed using the four-quadrant plot and CCC (Fig. 3). An exclusion zone of 0.75 L/min was applied based on previous literature [11].

#### 4. Discussion

This clinical study is the first study that assesses the accuracy, precision, and trending ability of the

initial calibration methods of patient information and reference TEE value for estimating CO using esCCO in patients undergoing prone position lumbar spine surgery. We hypothesized that regardless of the calibration method, esCCO might have a reliable trending ability. We also hypothesized that performing the initial calibration with the reference TEE values would help improve the accuracy and precision of esCCO. The correlation between esP and TEE was moderately strong, and the correlation between esT and TEE was also strong at all time points (T1–T4). In the Bland-Altman plot, the bias between esP and TEE and between esT and TEE was 0.2594 L/min and 0.0337 L/min, respectively. Compared with that of esT, esP reported higher CO measurement than TEE. The PE of esP was 56%, which was high, indicating that interchangeability was not acceptable. In contrast, the PE of esT was 21%, suggesting that the esCCO system that was calibrated using the reference CO value has interchangeability. CCC between  $\Delta$ esP and  $\Delta$ TEE and between  $\Delta$ esT and  $\Delta$ TEE was 0.700 and 0.794, respectively, in the four-quadrant analysis. CR between  $\Delta$ esP and  $\Delta$ TEE and  $\Delta$ esT and  $\Delta$ TEE was 91.9% and 97.1%, respectively demonstrating that esP and esT have reliable trending ability as suggested by Critchley et al. [21].

Previous studies enrolled patients undergoing procedures such as open-heart surgery and transplantation surgery. Vasoactive drugs are often likely to be required during these types of surgeries since a significant change in the systemic vascular resistance (SVR) might occur. The arterial elasticity affects PWTT; thus, esCCO may not provide reliable measurements when significant changes in SVR occur [22]. By enrolling patients undergoing lumbar spine surgery, we ensured that only less potent inotropes, such as phenylephrine and ephedrine, were required; this difference may influence the result. We can hypothesize that esCCO has interchangeability in lumbar spine surgery and can play a role in similar circumstances. The distance from the heart to the fingertip might differ between patients of similar age, height, and weight. Moreover, the arterial pulse wave velocity, which is influenced by SVR, can change from the point of initial calibration. Thus, the demographic data implied in esCCO cannot be generalized due to the presence of individual differences, which might further influence the accuracy and precision of esCCO when calibrated by patient information. However, it may be useful if a CO monitoring device has an acceptable trending ability, even if it fails to provide an absolute value of CO [19]. In addition to the comparable trending ability of esCCO with that of TEE, esCCO is noninvasive and easily accessible. A recent study revealed an excellent correlation between the ECG parameters in the supine and prone positions when detecting the QRS axis, PR, RR, QRS, and QT intervals with electrodes placed on the torso and dorsal aspect [23]. In addition, since the distance from the heart to the fingertip, where the upstroke of pulse oximetry is detected, does not change according to the patient's position, the prone position does not influence the quality of PWTT and esCCO.

Judging from a previous study [23] and the principle of the esCCO system, the prone position itself may not interfere with the ability of esCCO to estimate CO. Further studies should determine the ability of esCCO under different circumstances as it may be useful and feasible for continuous monitoring CO in other noncardiac surgeries performed in the prone position.

Changing the position of the patient from supine to prone position under general anesthesia induces a significant decrease in CO (as high as 25%) caused by a decrease in preload [3]. Moreover, it increases the intrathoracic pressure and secondarily influences a decrease in systolic pulmonary venous flow, left ventricular compliance and venous return from the inferior vena cava [24]. Most patients scheduled for lumbar spine surgery are at an increased risk of developing cardiovascular disease including coronary artery disease, due to their advanced age and the presence of associated risk factors. Additionally, these patients cannot walk long distances due to pain and neurogenic claudication; they may be asymptomatic and have silent cardiovascular diseases [5]. There is a substantial risk of bleeding [25] and perioperative

cardiac complications, including death [4] in many types of lumbar spine surgery. Therefore, it is essential to perform continuous monitoring of hemodynamic variables, including CO, using accurate and precise measurement tools to minimize these complications.

Transesophageal echocardiography, a well-established clinical tool for circulatory evaluation, is a feasible, rapid, safe, and semi-invasive monitoring device suitable for use in patients undergoing surgery under general anesthesia and mechanical ventilation, regardless of the position [26]. Dessap et al. [27] reported that the feasibility, tolerance, and image quality of the standard views of TEE were good in the prone and supine positions. Corresponding to this previous study, the image quality of the four-chamber long-axis view and two-chamber long-axis view for calculating the stroke volume in this study were comparable between the supine and prone positions when measuring the CO with TEE to obtain a reference value. TEE is used widely and routinely at our hospital to monitor cardiac performance, as the TDCO method is invasive and has the risk of severe complications [28]. The TEE method has been validated in comparison with the TDCO method in a previous study [10] and is now accepted as a reliable CO measurement method. The meta-analysis by Zhang et al. [10] concluded that there was no significant difference between the CO estimated using TEE and TDCO (random effects model: mean difference, 0.00; 95% CI, -0.12 to 0.11). Based on these findings, we decided to adopt TEE as a reference method for comparison with esCCO.

The present study had some limitations. The small sample size cannot represent the hemodynamic variety of the population, and only patients undergoing lumbar spine surgery in the prone position were enrolled. The median age of the participants in our study was 72 years, and many of their diagnoses were age-related degenerative spine diseases. Further studies should be performed to determine the ability of esCCO to estimate CO in various noncardiac surgeries, circumstances, and age groups. It may also be suitable to measure esP and esT both before and after reversing the patient from supine to prone and vice versa and analyze the ability to detect the change in CO when the position of the patient changes as these two moments usually exhibit substantial hemodynamic changes. However, the patients were predominantly in the prone position during surgery. Situations, such as surgical incision, substantial bleeding, intraoperative hypotension and instituting vasoactive and inotropic support, which can happen often in lumbar spine surgery, were reflected in the results of our study.

## **5. Conclusion**

esP, which noninvasively measures the estimated CO using basic vital signs and patient information, showed an acceptable trending ability, despite limited accuracy and precision. The accuracy and precision of esT calibrated by TEE were comparable with those of the reference CO values measured by TEE. The trending ability of esT was also good for tracking changes in CO in patients undergoing prone position lumbar spine surgery. Therefore, we propose that esCCO, a completely noninvasive and continuous CO monitoring system, may be a suitable alternative to other monitoring techniques.

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## **Conflict of interest**

The authors declare that they have no conflict of interest.

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No funding was received to assist with the preparation of this manuscript.

## Data sharing availability

Due to the nature of this research, the participants did not agree to share their data publicly; hence, supporting data is not available. However, data are available from the authors upon reasonable request and with the permission of Dong-A University.

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