Original Article

# Comparison of Cardiac Output and Stroke Volume Calculated by Pulse Wave Transit Time at the Fingertip Versus at the Toe

Makoto Hasegawa[1,2)*] Ryoichi Ochiai[2)] and Yoshifumi Kotake[1,3)]

[1)]Department of Anesthesiology, Toho University Graduate School of Medicine, Tokyo, Japan
[2)]Department of Anesthesiology, Toho University Omori Medical Center, Tokyo, Japan
[3)]Department of Anesthesiology, Toho University Ohashi Medical Center, Tokyo, Japan

**ABSTRACT**

***Introduction***: The estimated continuous cardiac output (esCCO), which is a noninvasive way of measuring cardiac output, enables the measurement of vital parameters to evaluate the oxygen supply/demand balance of organs and tissues. The esCCO is optimized for measurement using a fingertip pulse oximeter; however, in some instances, various conditions prevent attaching a probe to the fingertip. Thus, the cardiac index (esCI) and stroke volume index (esSVI) at the fingertip and toe were simultaneously measured and examined to determine whether the values measured at the toe could be used as an alternative to estimate those parameters and predict fluid responsiveness.

***Methods***: In total, 31 otorhinolaryngology surgery cases under general anesthesia were examined. We statistically analyzed the compatibility and trending ability of the SVI and CI values between at the fingertip and toe. Further, we were able to examine fluid responsiveness during hypotension. These data were then used to create a receiver operating characteristic curve and determined cutoffs of stroke volume variation (SVV) at the toe in order to predict greater than 10% increase in esSVI at the fingertip.

***Results***: As per out findings, esSVI and esCCI measured at the fingertip and toe exhibited significantly high compatibility and trending ability. Further, the cutoff value for greater than 10% increase in esSVI at the fingertip was toe SVV of 7.0%.

***Conclusions***: esSVI and esCI measured at the toe have exhibited high compatibility and trending ability with the data obtained at the fingertip; concurrently, they enabled the evaluation of fluid responsiveness. We confirmed that even when physical limitations prevent the attachment of a pulse oximeter probe to the fingertip, the SVI and CI can be well estimated at the toe.

**Toho J Med 7 (1): 39–47, 2021**

**KEYWORDS: estimated continuous cardiac output (esCCO), cardiac output, cardiac index, stroke volume index, stroke volume variation**

## Introduction

Improvement and maintenance of the oxygen supply/demand balance of organs and tissues has been the primary goal of general management during anesthesia and intensive care, but directly measuring the oxygen supply/

*Corresponding Author: Makoto Hasegawa, 6-11-1, Omori-nishi, Ota-city, Tokyo 143-8541, Japan, tel: +81–3–3762–4151
e-mail: makoto.01.hasegawa@med.toho-u.ac.jp
DOI: 10.14994/tohojmed.2020-022

Received Oct. 29, 2020: Accepted Nov. 25, 2020
Toho Journal of Medicine 7 (1), Mar. 1, 2021.
ISSN 2189–1990, CODEN: TJMOA2

demand has remained to be a challenge in clinical settings; the main point of patient care is therefore to maintain the perfusion pressure within the autoregulatory range. Thus, it is essential to identify the cause of hypotension in order to avoid systemic/local ischemia. Particularly, it is crucial to elucidate whether the depression of myocardial contractility is due to a decrease in cardiac preload or myocardial dysfunction itself, and thus, it is important to confirm the left ventricular preload first. As the classical Frank-Starling curve[1] can be applied to evaluate cardiac preload by determining the increment of stroke volume in response to a fixed-volume "fluid challenge," measurement of this so-called "fluid responsiveness," is currently considered as the most reliable method in determining cardiac preload.[2] However, fluid challenge is not a continuous parameter, and stroke volume variation (SVV), which is defined as the respiratory variation in stroke volume during positive pressure ventilation, has been highlighted as a continuous alternative of fluid responsiveness.[2–4]

While a number of invasive and noninvasive methods have already been developed to monitor cardiac output, we opted to use the estimated continuous cardiac output (esCCO). esCCO can be calculated using the pulse wave transit time (PWTT), i.e., the interval between the R wave of electrocardiogram and the arrival of the plethysmographic wave of pulse oximetry at the fingertip.[5, 6] The PWTT is inversely proportional to stroke volume;[7] thus, esCCO enables us to noninvasively determine the stroke volume using standard parameters during general anesthesia. The PWTT has been determined to consist of three components: the pre-ejection period (PEP) of the heart, PWTT1, i.e., the time required for the pulse wave to propagate through the large blood vessels, and PWTT2, i.e., the time required for the pulse wave to propagate through the peripheral blood vessels, which can be easily affected by the autonomic nervous system.[7] Currently, the esCCO is optimized for measurement at the fingertip; however, there are certain factors that might prevent the attachment of a pulse oximeter to the fingertip, such as the type of surgery, site of trauma, or other physical conditions.

Thus, in this study, we examined whether the PWTT measured using a pulse oximeter at the toe could be used as an alternative to measure the estimated stroke volume index (esSVI) and estimated continuous cardiac index (esCCI), i.e., the product of the esSVI and heart rate, in cases where a pulse oximeter could not be attached to the fingertip. Furthermore, we determined the cutoff values to estimate SVV (esSVV) measured at the toe when the cutoff for fluid responsiveness was set at greater than the 10% value for the fingertip esSVI.[8, 9]

## Methods

### Patients

The protocol used in this study has been approved by the Toho University Omori Medical Center Research Ethics Committee (M19229). It was also uploaded to the UMIN Clinical Trials Registry before the study began (UMIN: 000041020). Informed consent was obtained from all patients prior to participation. Patients who underwent otorhinolaryngology surgeries for benign illnesses under general anesthesia at our facility between June and August 2020 were included in this study. All included patients were adults and determined to have either Class I or Class II American Society of Anesthesiologists physical status (ASA-PS) fitness. Preoperative examinations excluded patients with arrhythmias, pacemakers, arteriosclerosis obliterans, arterial bifurcation abnormalities, and arterial disease. Further, because hydroxyethyl starch 13000 (6% Voluven) was to be used for fluid challenge, patients with contraindications and other at-risk diseases listed on the drug package insert were excluded (pulmonary edema, congestive heart failure, renal failure with oliguria or anuria, and dialysis) from analysis.

### Methods

*Monitoring*

Patients were fitted with a pulse oximeter on the finger ipsilateral to their IV port and another on an arbitrarily selected toe prior to being placed under general anesthesia. Further, a blood pressure cuff was affixed to the opposite upper arm, a three-lead ECG was fitted, and esCCO monitors (both HDM-3000 bedside monitors, Nihon Kohden, Tokyo, Japan) were then put in place. The blood pressure data measured at the upper arm were used in calibrating for the fingertip and toe esCCO calculation. Anesthesia was then induced after calibration. Measurements were collected from the end of calibration to the end of anesthesia.

*Anesthesia management*

Propofol (1-2 mg/kg), fentanyl (1-2 mcg/kg), remifentanil (0.05-0.25 mcg/kg/min), and rocuronium (0.6-0.9 mg/kg) were utilized to induce anesthesia. Mechanical ventilation was initiated after tracheal intubation. Intraoperative maintenance was performed using desflurane (4-6%), re-

mifentanil (0.05-0.2 mcg/kg/min), and rocuronium (0.1-0.2 mg/kg).

*Ventilator setting*

The intraoperative ventilator settings were observed as follows: FiO2 0.4-0.5, tidal volume 7-10 mL/kg (ideal body weight), breathing rate 12 times/min, and PEEP 5-8 $cmH_2O$.

*Fluid challenge*

The systolic blood pressure obtained during the first blood pressure measurement was used as the control value. Once anesthesia was induced and the patient was on mechanical ventilation, a 10% or greater decrease in systolic blood pressure relative to the control value was obtained as the starting point of the fluid challenge. Then, a 6% Voluven solution was used as the challenge agent. The rate and quantity of the fluid challenge was 300 mL over 15 min, and an infusion pump was used.[10]

*Data sampling*

Patient's age, sex, height, weight, and underlying illnesses were recorded. The following hemodynamic parameters were also recorded: heart rate (once per min), upper arm blood pressure (once every 5 min), and esSVI, esCCI, and PWTT, each measured at both the fingertip and toe. Further, blood pressure, esSVI, esCCI, PWTT, and esSVV before and after the fluid challenge were also recorded. It should be noted that sampling rate of the waveform of electrocardiogram was 250 Hz, whereas the plethysmographic waveform was sampled at 125 Hz, and 64 beats were then averaged to improve the accuracy of pulse wave transit time.

*Statistical analysis*

Microsoft Excel (Redmond, WA) and EZR (version 3.6.1, Saitama Medical Center, Jichi Medical University) were used to perform the statistical analyses.[11]

Compatibility and agreement

A regression line and Bland-Altman analysis were used to evaluate the compatibility and agreement between the esSVI and esCCI values measured at the fingertip and toe. The percent error in the toe esSVI and toe esCCI values was calculated as (2×precision)/(mean fingertip esSVI or fingertip esCCI), while compatibility was determined to be present if an error within ±30% was found.[12, 13] It should be noted, Bias is a means of evaluating agreement. The average value of the differences between the methods. Precision is an evaluation of the degree of dispersion. In other words, it means the standard deviation of the differences between the methods. Percent error is a means of evaluating compatibility.

Trending ability

A polar plot analysis was used in determining and interpreting the trending ability of the toe esSVI and esCCI relative to the fingertip esSVI and esCCI, respectively. Polar points were noted on the 10-min change in toe esSVI and esCCI (Δt_esSVI or Δt_esCCI) relative to the 10-min change in fingertip esSVI and esCCI (Δf_esSVI and Δf_esCCI). Furthermore, the mean values of Δf_esSVI, Δt_esSVI, Δf_esCCI, and Δt_esCCI, which were not within the 15% of the mean values of the fingertip esSVI and fingertip esCCI, respectively, were excluded. Trending ability was determined to be present if the bias was ±5° and the concordance rate at 30° was ≥90%.[14, 15] It should be noted that concordance rate is the percentage of the number of points whose directions match to the number of points to be analyzed.

Fluid responsiveness

Patient heart rate, esSVI, esSVV, and esCCI were continuously recorded for 5 min immediately prior to the beginning of the fluid challenge and after the end of the fluid challenge. First, to determine whether significant changes have occurred in these values before and after the fluid challenge, the Shapiro-Wilk test was performed in order to confirm normality, after which, paired Student's t-test was used. Next, patients were then separated into two groups, i.e., a responder group and a non-responder group. This was based on the presence or absence of fluid responsiveness (whether or not a 10% increase in the fingertip esSVI was observed after the fluid challenge). Paired Student's t-test was then used within the responder and non-responder groups to determine whether significant differences were present in the pre- and post-challenge values of each parameter. Finally, in cases where a ≥10% increase in the fingertip esSVI was observed, we used the area under the receiver operating characteristic curve (ROC-AUC) to determine the cutoff values for esSVV measured at the toe predictive of fluid responsiveness. The threshold of statistical significance for all tests was $p < 0.05$.

## Results

**Patient characteristics**

In total, 31 individuals from whom informed consent was obtained have formed the subject population for this study. Patients' characteristics and the surgery times and anesthesia times have been summarized in Table 1. We

Table 1 Patient Characteristics

| | Overall (n = 31) | Responder (n = 15) | Non-responder (n = 16) |
|---|---|---|---|
| Age (years) | 49.7 ± 17.5 | 41.2 ± 16.2 | 56.1 ± 16.2 * |
| Height (cm) | 172.2 ± 6.58 | 173.8 ± 4.12 | 171.1 ± 7.95 |
| Weight (kg) | 69.3 ± 12.1 | 70.1 ± 4.29 | 68.7 ± 15.8 |
| BMI (kg/m$^2$) | 23.3 ± 3.5 | 22.8 ± 1.9 | 23.7 ± 4.6 |
| Operation time (min) | 134.5 ± 39.2 | 128.8 ± 44.5 | 139.9 ± 34.2 |
| Anesthesia time (min) | 182.6 ± 45.6 | 175.4 ± 49.8 | 189.4 ± 41.6 |
| Infusion amount (mL) | 1134.5 ± 327.3 | 1040 ± 283.6 | 1223.1 ± 349.1 |

* $p < 0.05$

Test methods: unpaired two-sided Student's t-test

Table 2 Parameter of Compatibility and Agreement and Trending Ability

| | Regression line | | Bland-Altman analysis | | | Polar plot analysis | |
|---|---|---|---|---|---|---|---|
| | r = | Y = | Bias | Precision | %Error | Bias | Concordance rate at 30° |
| esSVI (mL/beats/m$^2$) | 0.78 | 1.01x − 14.58 | − 14.04 | 5.98 | 24 | 13.9 | 97.5 |
| esCCI (L/min/m$^2$) | 0.86 | 0.92x − 0.62 | − 0.89 | 0.39 | 24 | 2.5 | 100 |
| PWTT (msec) | 0.69 | 1.25x + 67.87 | 125.34 | 35.39 | 31 | 15.8 | 82.4 |
| HR (bpm) | 0.99 | 0.99x + 0.32 | − 0.03 | 1.41 | 4 | — | — |

esSVI, stroke volume index by esCCO; esCCI, cardiac index by esCCO; PWTT, pulse wave transit time; HR, heart rate

were able to determine that 14 patients belonged to ASA-PS Class I, whereas 17 belonged to Class II. In addition, 22 patients underwent nasal and sinus surgery, 5 underwent tonsil surgery, and 4 underwent cervical surgery.

**Results**

*Compatibility, agreement, and trending ability of the esSVI measured at the fingertip and toe (Table 2)*

In total, 830 data points were obtained for use in the esSVI regression line and Bland-Altman analysis. The correlation coefficient was r = 0.78 ($p < 0.001$), whereas the linear regression equation was y = 1.01x − 14.58 (Fig. 1). In the Bland-Altman analysis, bias and precision were determined to be −14.04 mL/beat/m$^2$ and 5.98 mL/beats/m$^2$, respectively. Meanwhile, the percent error was 24% (Fig. 2).

On the other hand, 71 points were obtained for use in the polar plot analysis, bias was 13.9°, and the concordance rate at 30° was 97.5% (Fig. 3).

*Compatibility, agreement, and trending ability of the esCCI measured at the fingertip and toe (Table 2)*

In total, 829 points were obtained for use in the esCCI regression line and Bland-Altman analysis. The correlation coefficient was r = 0.86 ($p < 0.001$), whereas the linear regression equation was y = 0.92x(Table 2)0.62. In the Bland-Altman analysis, bias and precision were determined to be 0.89 L/min/m$^2$ and 0.39 L/min/m$^2$, respectively. The percent error was 24%.

In total, 135 points were obtained for use in the polar plot analysis. Bias was observed to be 2.5°, and the concordance rate at 30° was 100%.

**Fluid responsiveness**

*Patient characteristics*

Characteristics of the 15 patients in the responder group and the 16 in the non-responder group have been summarized in Table 1. Patients in the non-responder group were found to be significantly older ($p < 0.05$). No other significant differences were observed.

*Changes in hemodynamic parameters after fluid challenge (Table 3)*

The fluid challenge was able to produce a significant increase in the fingertip esSVI ($p < 0.05$). Concurrently, the mean blood pressure was observed to decrease ($p < 0.05$), together with the fingertip esSVV ($p < 0.05$). No significant changes were observed for any other parameters.

*Changes in hemodynamic parameters after fluid challenge in responders and non-responders (Table 4)*

In the responder group, fluid challenge has resulted in a

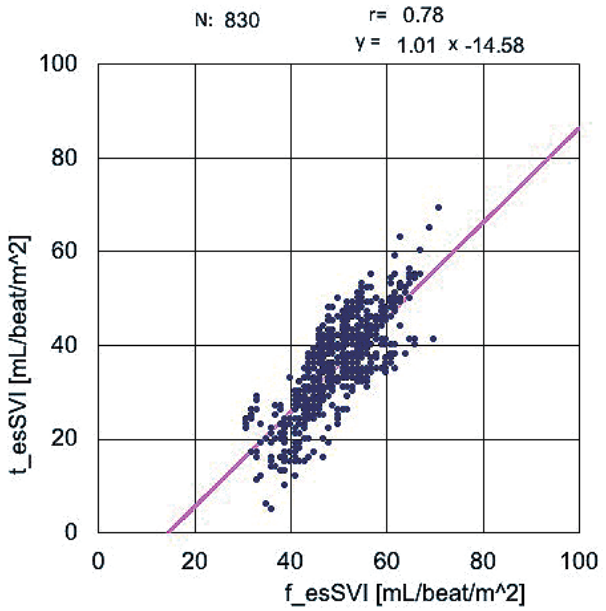


Fig. 1 Correlation between fingertip esSVI (f_esSVI) and toe esSVI (t_esSVI).
The correlation coefficient was r = 0.78 ($p < 0.001$).
f_esSVI, fingertip esSVI; t_esSVI, toe esSVI

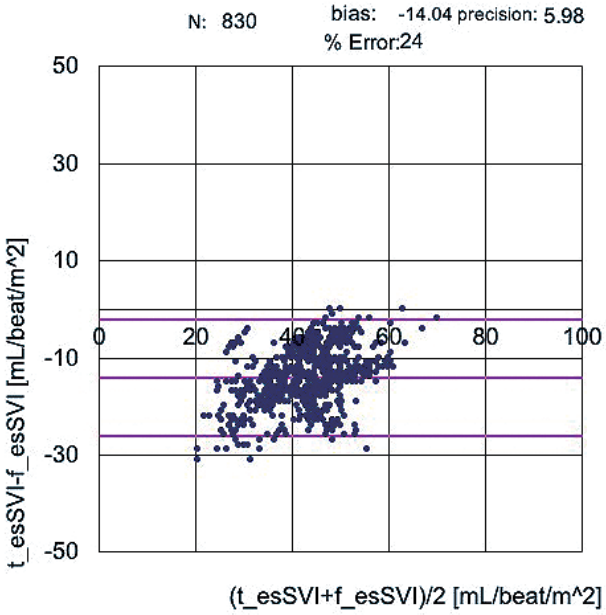


Fig. 2 Bland-Altman analysis of esSVI between f_esSVI and t_esSVI
The difference in the esSVI values between t_esSVI and f_esSVI was −14.04 ± 5.98 mL/beats/m².
The percent error was 24%
f_esSVI, fingertip esSVI; t_esSVI, toe esSVI

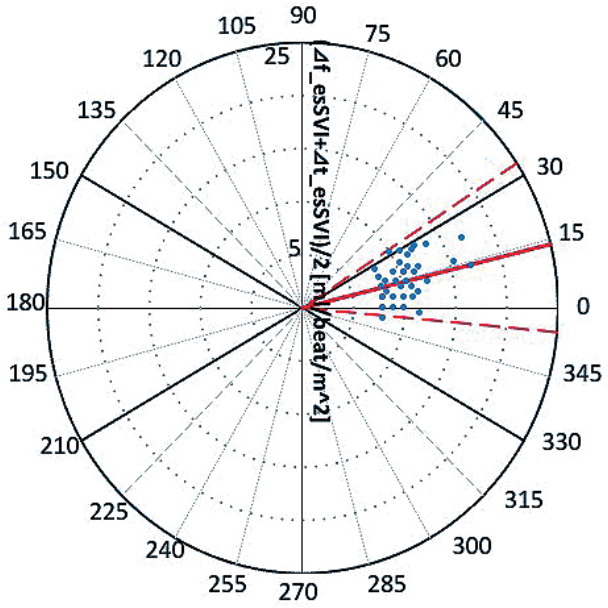


Fig. 3 Polar plot analysis of esSVI
The radial limit of agreement between SVI from t_esSVI and f_esSVI was ±13.9. And the concordance rate at 30° was 97.5%
(exclusion zone 7.52 ml/beats/m² (15% of average f_esSVI), concordance 70, disconcordance 1)
f_esSVI: fingertip esSVI, t_esSVI: toe esSVI

significant increase in the fingertip esSVI and esCCI ($p < 0.05$). Conversely, esSVV was observed to have significantly decreased ($p < 0.05$). Significant increases in the toe esSVI and esCCI were also observed ($p < 0.05$).

On the other hand, in the non-responder group, the mean blood pressure has been noted to decrease ($p < 0.05$). However, no other significant changes in the fingertip hemodynamic parameters were observed. In contrast, the toe esSVI and esCCI significantly decreased ($p < 0.05$).

*Estimation of fluid responsiveness based on the toe esSVV (Fig. 4)*

In order to predict fluid responsiveness using the toe esSVV values, we drew a receiver operating characteristic curve, and the AUC values were then calculated. We found that the AUC was 0.785 (0.6199-0.951, $p < 0.05$) and that the cutoff value was a toe esSVV of 7.0% to predict greater than 10% increase in the fingertip esSVI.

## Discussion

### Study findings

esCCO technology, which has been optimized for measurement of the PWTT at the fingertip, provides both non-invasive and continuous measurements of stroke volume and cardiac output.[16, 17] As the accuracy and precision of esCCO are highly dependent on the accuracy and feasibil-

Table 3 Changes in hemodynamic parameters after fluid challenge

| | | Overall (n = 31) | |
|---|---|---|---|
| | | Control | Fluid challenge |
| | mBP (mmHg) | 74.7 ± 12.7 | 68.8 ± 11.7 * |
| | HR (bpm) | 64.7 ± 13.9 | 64.1 ± 12.0 |
| Fingertip | esSVI (mL/beat/m$^2$) | 48.4 ± 8.03 | 51.6 ± 8.17 * |
| | esCI (L/min/m$^2$) | 3.11 ± 0.77 | 3.29 ± 0.66 |
| | esSVV (%) | 5.59 ± 2.59 | 3.86 ± 1.66 * |
| Toe | esSVI (mL/beat/m$^2$) | 37.1 ± 9.84 | 36.8 ± 8.87 |
| | esCI (L/min/m$^2$) | 2.39 ± 0.78 | 2.33 ± 0.60 |
| | esSVV (%) | 7.17 ± 3.55 | 6.86 ± 3.80 |

*$p < 0.05$
mBP, mean blood pressure; HR, heart rate;
esSVI, stroke volume index by esCCO;
esCI, cardiac index by esCCO;
esSVV, stroke volume variation by esCCO

Table 4 Changes in hemodynamic parameters after fluid challenge in responder and non-responder

| | | Responder (n = 15) | | Non-responder (n = 16) | |
|---|---|---|---|---|---|
| | | Control | Fluid challenge | Control | Fluid challenge |
| | mBP (mmHg) | 71.5 ± 7.96 | 73.7 ± 13.1 | 77.7 ± 15.7 | 64.2 ± 8.14 * |
| | HR (bpm) | 62.3 ± 12.7 | 64.1 ± 11.6 | 67.0 ± 15.0 | 64.1 ± 12.9 |
| Fingertip | esSVI (mL/beat/m$^2$) | 46.1 ± 6.55 | 52.7 ± 7.12 * | 50.6 ± 8.85 | 50.6 ± 9.16 |
| | esCCI (L/min/m$^2$) | 2.80 ± 0.60 | 3.40 ± 0.63 * | 2.77 ± 0.81 | 2.32 ± 0.64 |
| | esSVV (%) | 6.97 ± 2.24 | 4.11 ± 1.34 * | 4.30 ± 2.25 | 3.62 ± 1.91 |
| Toe | esSVI (mL/beat/m$^2$) | 32.7 ± 8.21 | 36.7 ± 9.68 * | 41.3 ± 9.75 | 37.0 ± 8.36 * |
| | esCCI (L/min/m$^2$) | 1.98 ± 0.48 | 2.33 ± 0.59 * | 2.77 ± 0.81 | 2.32 ± 0.64 * |
| | esSVV (%) | 8.77 ± 3.19 | 7.59 ± 4.20 | 5.67 ± 3.29 | 6.17 ± 3.17 |

*$p < 0.05$
mBP, mean blood pressure; HR, heart rate;
esSVI, stroke volume index by esCCO;
esCI, cardiac index by esCCO;
esSVV, stroke volume variation by esCCO

ity of the PWTT measurement, any factors affecting the PWTT measurement can render esCCO inaccurate. Thus, under conditions such as cardiac arrhythmia and cardiac shock, a stable and reliable PWTT measurement is not deemed possible.[18–20] Additionally, esCCO has been developed and optimized for measurement at the fingertip, and the accuracy and precision of esCCO have not been tested on other body parts such as the toe and earlobe. It has been assumed that measurement at locations other than the fingertip may not be as accurate because the length of vasculature, physical properties of the vascular wall, and physiological control of the vascular system may differ from those at the fingertip.

Thus, in this study, we calibrated the PWTT obtained at the fingertip using pulse pressure values measured at the upper arm to calculate the fingertip and toe esCCO and esSVI from PWTTs; thereafter, their correlation was examined. As a result, we found that both parameters exhibited high compatibility and trending ability; thus, it is clear that the data collected at the toe can also be used to estimate stroke volume and cardiac output. Further, using a first-order regression analysis, we were able to determine that the values measured at the toe were lower than those measured at the fingertip, confirming that estimation of the esCCI and esSVI was comparatively feasible at the toe. Based on the results of this study, we can conclude that f_

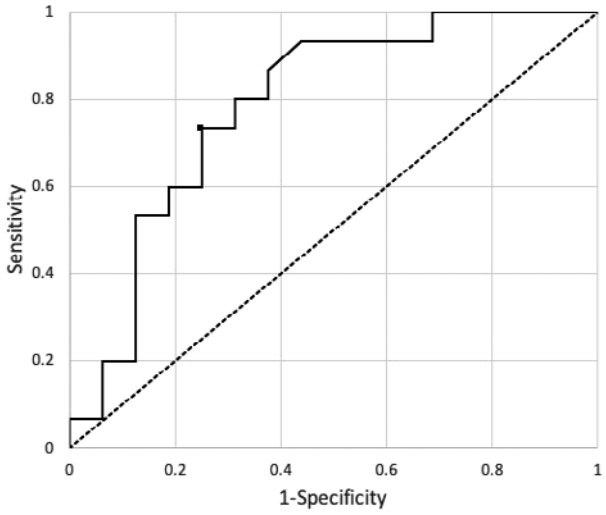


Fig. 4 The prediction of fluid responsiveness by t_esSVV
The AUC was 0.785 (0.6199–0.951, $p<0.05$), and the cutoff value was t_esSVV of 7.0% to predict greater than 10% increase in f_esSVI. Sensitivity, 0.7333; specificity, 0.7500
f_esSVI, fingertip esSVI; t_esSVI, toe esSVI

esSVI was linearly correlated with t_esSVI. In other words, it would be feasible to estimate f_esSVI by using the following formula: f_esSVI = t_esSVI + 14.04. It would also be possible to estimate f_esCCI by using the formula f_esCCI = t_esCCI + 0.89.

After the introduction of general anesthesia, the PWTT measured at the fingertip (calibrated using upper arm blood pressure) can be used to determine the esSVI and esCCI. When a probe cannot be fitted to a fingertip, it can instead be fitted to a toe, and a conversion equation is then used to obtain the correct esSVI and esCCI values, enabling proper general management.

Fluid management can become exceedingly challenging during very long surgeries or those with substantial blood loss or in cases with cardiac complications as cardiac preload becomes harder to evaluate. Although central venous pressure and pulmonary artery wedge pressure have been used as representatives of cardiac preload, numerous clinical studies have reported otherwise. Fluid responsiveness has been identified as an important parameter to evaluate the cardiac preload and circulating blood volume.[21–24] In this study, we found that a 7% value of the esSVV measured at the toe was the cutoff value for 10% or higher responsiveness in the esSVI of the upper arm. We can thus conclude that these results are practically applicable.

**Issues and solutions**

*Reasons for underestimation of the esSVI at the toe*

Our results indicated an esSVI bias of 14.04 mL/beat/$m^2$ between the fingertip and toe measurements. Thus, we examined the compatibility and trending ability of the PWTT (a component of the esSVI) at the fingertip and toe as well as the compatibility of the heart rate (HR, Table 2).

As per our findings, compatibility was preserved for HR, confirming that the observed bias was not the result of measurement errors at the fingertip and toe. Further, we postulated that one reason that PWTT increased at the toe was due to the differences in the length of the vessels at the fingertip and toe. In particular because the esSVI at the fingertip has been standardized for age, height, weight, and sex and because the fingertip and toe data exhibited high compatibility, we can surmise that the length of the vessels in the foot is also correlated with patient data. Therefore, we can conclude that the underestimation of the esSVI at the toe could be attributed to the fact that the absolute values of the PWTT were longer at the toe and that the PWTT and esSVI are inversely proportional.

*Changes in toe hemodynamic parameters before and after fluid challenge*

In this study, patients whose fingertip esSVI changed by more than 10% in response to the fluid challenge were categorized into the responder group. In this responder group, the hemodynamic parameters of the esSVI and esCCI were observed to have significantly increased at the toe. Namely, one of the noted results of this study was that the effects of the fluid challenge could be estimated using the measurements collected at the toe.

In contrast, in the non-responder group, the toe esSVI was observed to have significantly decreased. The changes in the toe esSVI after the fluid load in the non-responder group were unique, as the fluid load resulted in no change in the esSVI at the fingertip but in a reduction in the esSVI at the toe. It is not deemed possible to identify the mechanism for the esSVI only decreasing at the toe, but it is possible that the fluid load resulted in simultaneous vasodilation at the lower extremities. Reports have indicated that a decrease in vascular resistance can also decrease the accuracy of esCCO measurements.[25] We believe that here, because the patients in the non-responder group entered a deeper state of anesthesia, among other reasons, the fluid challenge resulted in vasodilation in the non-responder group.

Why, then, was the precision of values measured at the

toe poorer than those measured at the fingertip? Normally, vasodilation shortens the PEP, lengthens PWTT1, and shortens PWTT2. Furthermore, reports have indicated that PWTT1 is dependent on the changes in blood pressure.[26] It is possible that, in this study, vasodilation has introduced changes in these three parameters, resulting in PWTT1 and PWTT2 being larger for the toe than for the fingertip, decreasing the toe esSVI. The mechanism of such a unique response of the toe esSVI after fluid load remains to be unclear, but one possibility is that the shortened PEP and lengthened PWTT1 and PWTT2 due to vasodilation at the lower extremities resulted in the reduction of the toe esSVI.

As the proportions of the PEP, PWTT1, and PWTT2 at the fingertip and toe remain unknown, further investigation is warranted to elucidate the mechanism inducing hemodynamic changes in non-responders.

## Conclusion

This study has showed that the esSVI and esCCI values measured at the toe exhibit good compatibility and trending ability and that they also enable the evaluation of fluid responsiveness. As a result, even when surgical procedures or complications prevent the attachment of a pulse oximeter to the fingertip, cardiac output can still be measured at the toe, and general management can still be safely performed.

**Conflicts of interest:** None declared.

## References

1) Patterson SW, Starling EH. On the mechanical factors which determine the output of the ventricles. J Physiol. 1914; 48: 357-79.
2) Carsetti A, Cecconi M, Rhodes A. Fluid bolus therapy: monitoring and predicting fluid responsiveness. Curr Opin Crit Care. 2015; 21: 388-94.
3) Hofer CK, Senn A, Weibel L, Zollinger A. Assessment of stroke volume variation for prediction of fluid responsiveness using the modified Flotrac™ and PiCCOplus™ system. Crit Care. 2008; 12: R82.
4) Cannesson M, Musard H, Desebbe O, Boucau C, Simon R, Henaine R, et al. The ability of stroke volume variations obtained with Vigileo/Flotrac system to monitor fluid responsiveness in mechanically ventilated patients. Anesth Analg. 2009; 108: 513-7.
5) Ochiai R, Takeda J, Hosaka H, Sugo Y, Tanaka R, Soma T. The relationship between modified pulse wave transit time and cardiovascular changes in isoflurane anesthetized dogs. J Clin Monit Comput. 1999; 15: 493-501.
6) Sugo Y, Sakai T, Terao M, Ukawa T, Ochiai R. The comparison of a novel continuous cardiac output monitor based on pulse wave transit time and echo Doppler during exercise. Annu Int Conf IEEE Eng Med Biol Soc. 2012; 2012: 236-9.
7) Sato N. Non-invasive cardiac output monitoring using a technology of pulse oximetry -esCCO. Clin Anesthesiol. 2011-12; 35: 1825-30.
8) Critchley LA, Lee A, Ho AM. A critical review of the ability of continuous cardiac output monitors to measure trends in cardiac output. Anesth Analg. 2010; 111: 1180-92.
9) Marik PE, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. Ann Intensive Care. 2011; 1: 1.
10) Sakamoto N, Terada T, Ochiai R. Prediction of fluid responsiveness by means of stroke volume variation measured by pulse wave transit time -based cardiac output monitoring. Toho J Med. 2020; 6: 41-7.
11) Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013; 48: 452-8.
12) Kotake Y, Sato N. Bland-Altman analysis for the accuracy evaluation of the cardiac output monitor. J Jpn Intensive Care Med. 2009; 16: 263-72.
13) Sugo Y, Sakai T, Terao M, Ukawa T, Ochiai R. The agreement and trend ability of a non-invasive continuous cardiac output measurement method utilizing ECG and SpO2 pulse wave against echo Doppler during exercise. Iryou kikigaku (The Japanese journal of medical instrumentation). 2013; 83: 273-82.
14) Desebbe O, Henaine R, Keller G, Koffel C, Garcia H, Rosamel P, et al. Ability of the third-generation FloTrac/Vigileo software to track changes in cardiac output in cardiac surgery patients: A polar plot approach. J Cardiothorac Vasc Anesth. 2013; 27: 1122-7.
15) Cecconi M, Parsons AK, Rhodes A. What is a fluid challenge? Curr Opin Crit Care. 2011; 17: 290-5.
16) Biais M, Berthezene R, Petit L, Cottenceau V, Sztark F. Ability of esCCO to track changes in cardiac output. Br J Anaesth. 2015; 115: 403-10.
17) Fischer MO, Balaire X, Le Mauff de Kergal C, Boisselier C, Gerard JL, Hanouz JL, et al. The diagnostic accuracy of estimated continuous cardiac output compared with transthoracic echocardiography. Can J Anesth. 2014; 61: 19-26.
18) Ball TR, Tricinella AP, Kimbrough BA, Luna S, Gloyna DF, Villamaria FJ, et al. Accuracy of noninvasive estimated continuous cardiac output (esCCO) compared to thermodilution cardiac output: A pilot study in cardiac patients. J Cardiothorac Vasc Anesth. 2013; 27: 1128-32.
19) Wacharasint P, Kunakorn P, Pankongsap P, Preechanukul R. Clinical validation of pulse contour and pulse wave transit time-based continuous cardiac output analyses in Thai patients undergoing cardiac surgery. J Med Assoc Thai. 2014; 97: S55-60.
20) Smetkin AA, Hussain A, Fot EV, Zakharov VI, Izotova NN, Yudina AS, et al. Estimated continuous cardiac output based on pulse wave transit time in off-pump coronary artery bypass grafting: a comparison with transpulmonary thermodilution. J Clin Monit Comput. 2017; 31: 361-70.
21) Pearse R, Dawson D, Fawcett J, Rhodes A, Grounds RM, Bennett ED. Early goal-directed therapy after major surgery reduces complications and duration of hospital stay. A randomised, controlled trial. Crit Care. 2005; 9: R687-93.
22) Benes J, Giglio M, Brieza N, Michard F. The effects of goal-directed fluid therapy based on dynamic parameters on post-surgical outcome: a meta-analysis of randomized controlled trials. Crit Care. 2014; 18: 584.

23) Rinehart J, Le Manach Y, Douiri H, Lee C, Lilot M, Le K, et al. First closed-loop goal directed fluid therapy during surgery: a pilot study. Ann Fr Anesth Reanim. 2014; 33: e35-41.
24) Volkov PA, Sevalkin SA, Churadze BT, Volkova YT, Guryanov VA. Goal-target infusion therapy based on noninvasive hemodynamic monitoring esCCO. Anesteziol Reanimatol. 2015; 60: 19-23 [Article in Russian].
25) Magliocca A, Rezoagli E, Anderson TA, Burns SM, Ichinose F, Chitilian HV. Cardiac output measurements based on the pulse wave transit time and thoracic impedance exhibit limited agreement with thermodilution method during orthotopic liver transplantation. Anesth Analg. 2018; 126: 85-92.
26) Ochiai R, Takeda J, Hosaka H, Sugo Y, Tanaka R, Soma T. The relationship between modified pulse wave transit time and cardiovascular changes in isoflurane anesthetized dogs. J Clin Monit Comput. 1999; 15: 493-501.