

# Are Noninvasive Continuous Cardiac Output Monitoring Interchangeable with Esophageal Doppler?

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**Objective:** To compare the trending ability, accuracy, and precision of non-invasive stroke volume (SV) measurement based on a bioreactance technique and measurement of the pulse wave transit time (PWTT) versus the esophageal Doppler monitoring (EDM).

**Materials and Methods:** Two hundred twenty-seven paired measurements from 10 patients who underwent abdominal surgery under general anesthesia were included for SV measurements. Pearson's correlation coefficient was calculated, and Bland-Altman analysis was performed to evaluate the agreement between EDM and bioreactance (EDM-bioreactance) and between EDM and PWTT (EDM-PWTT).

**Results:** EDM-bioreactance had a correlation coefficient of 0.75 (95% confidence interval [CI] 0.62 to 0.78;  $p < 0.001$ ), bias of 0.28 ml (limits of agreement -30.92 to 31.38 ml), and percentage error of 46.82%. EDM-PWTT had a correlation coefficient of 0.48 (95% CI 0.44 to 0.72;  $p < 0.001$ ), bias of -0.18 ml (limits of agreement -40.28 to 39.92 ml), and percentage error of 60.17%. A subgroup analysis of data from patients who underwent crystalloid loading was performed to detect the trending ability. The four-quadrant plot analysis between EDM-bioreactance and EDM-PWTT demonstrated concordance rates of 70.00% and 73.68%, respectively.

**Conclusion:** SV measurement based on bioreactance technique and measurement of PWTT are not interchangeable with EDM.

**Trial registration:** Thai Clinical Trials Registry, TCTR 20181217003

**Keywords:** Stroke volume, Cardiac output, Doppler, Perioperative care, Pulse, Time

Received 2 Jul 2019 | Revised 14 Oct 2019 | Accepted 17 Oct 2019

J Med Assoc Thai 2020;103(6):541-7

Website: <http://www.jmatonline.com>

Perioperative goal-directed hemodynamic management using cardiac output measurement is being used more often. Evidence shows that perioperative goal-directed hemodynamic management is associated with better outcomes in patients with a moderate to high surgical risk<sup>(1-4)</sup>. In the past, the gold standard of cardiac output measurement was the thermodilution technique performed by pulmonary

artery catheter insertion. However, the complications of invasive cardiac output monitoring outweigh the benefits<sup>(5)</sup>. The role of less invasive or non-invasive cardiac output monitoring techniques throughout the perioperative period has been receiving more attention.

Early evidence of perioperative goal-directed hemodynamic management was largely obtained by esophageal Doppler monitoring (EDM)<sup>(6-8)</sup>. However, the use of EDM is limited in some groups of patients, such as those undergoing regional anesthesia and those undergoing facial or esophageal surgery. Newer devices based on non-invasive techniques have been developed. These devices can minimize the anesthetic time and reduce catheter-related complications. Furthermore, they do not require special skills for their use. Additionally, the new concept of enhanced recovery after surgery (ERAS) supports the use of non-invasive devices<sup>(9)</sup>. The purpose of the present study was to demonstrate the interchangeability between non-invasive hemodynamic monitoring and

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## How to cite this article:

Pisitsak C, Luetrakool P, Pisalayon M, Thamjamrassri T. Are Noninvasive Continuous Cardiac Output Monitoring Interchangeable with Esophageal Doppler? J Med Assoc Thai 2020;103:541-7.

[doi.org/10.35755/jmedassocthai.2020.06.10413](https://doi.org/10.35755/jmedassocthai.2020.06.10413)

EDM. Therefore, the authors performed the test to compare the trending ability, accuracy, and precision of the two non-invasive methods of stroke volume (SV) measurement [i.e., a bioactance technique and measurement of the pulse wave transit time (PWTT)] with EDM.

## Materials and Methods

The Ethics Committee of the authors' institution approved the study, and informed consent was obtained from all patients. The present study included 10 adult patients that underwent gastrointestinal surgery under general anesthesia in December 2018. The exclusion criteria were patients with contraindications to EDM, bioactance, and PWTT measurement (i.e., patients with coagulopathy, nasal or esophageal disease, skull base fracture, acute heart failure, myocardial infarction, arrhythmia, and intra-aortic balloon pump insertion).

For each patient, induction of anesthesia was performed using a technique based on the anesthesiologist's preference and the patient's condition. All patients were intubated and underwent controlled ventilation. After induction of anesthesia, three monitors for EDM, bioactance, and PWTT were applied. Crystalloid fluids were infused at a rate of 500 ml in 15 minutes. Extra fluid boluses of similar amounts were infused when the mean arterial pressure was less than 65 mmHg, the systolic blood pressure was less than 90 mmHg, or the urine output was less than 1 ml/kg/hour. The SV before and after administration of the fluid bolus was recorded for trending analysis.

All three monitors were calibrated using the same data of body weight, height, age, and gender for each patient. Only one investigator set up the monitors, inserted the EDM catheter, and obtained the data; therefore, there was no inter-rater variability. The SV, cardiac output, blood pressure, and heart rate were recorded at 5-minute intervals. The authors chose to analyze the SV instead of the cardiac output to avoid the influence of other factors on the heart rate. The operative data analyzed in the present study were blood loss, fluid intake, and urine output. Patient characteristics were also recorded.

### EDM measurements

After endotracheal intubation, an EDM catheter (CardioQ; Deltex Medical, Chichester, England) was placed nasally with sufficient lubricating gel. The depth of the catheter in Asian patients is between the second and third markers, and this depth was used in

the present study. The probe was rotated to obtain the waveform of the thoracic aorta. A good signal was characterized by the sharpest sound with the highest peak waveform amplification and a sharp, well-defined outline with a predominantly black center. The stroke distance was measured and then converted to the SV by the software of the monitor. The analysis was performed every five cardiac cycles.

### Bioreactance measurements

The device used for bioreactance measurements was the Starling SV monitor (Cheetah Medical, Tel-Aviv, Israel). Four double-electrode sensors were applied on the patient's chest wall before anesthesia as recommended by the manufacturer. All electrode sensors were single-use sensors. The alternating current was transmitted between the outer and inner pairs of the electrode sensors. Blood in the thoracic cavity absorbs electrical currents, resulting in a delayed signal in relation to the SV; this delayed signal is called the phase shift. The phase shift created a Cheetah waveform, which then was converted to the SV by the Cheetah algorithm. The analysis averaged 30 to 60 seconds.

### PWTT measurements

The PWTT was calculated from continuous electrocardiography and pulse oximetry data obtained from an estimated continuous cardiac output monitor (esCCO; Nihon Kohden, Tokyo, Japan). The PWTT is defined as the duration of time from the electrocardiographic R-wave peak to the rise point of the pulse oximetry pulse wave. A multivariate analysis based on patient information, pulse pressure, and initial PWTT was performed by the software to obtain the cardiac output for the calibration. The pulse pressure was chosen from the non-invasive blood pressure monitoring. The esCCO software continuously calculated the SV after the calibration had finished. Completion of the calibration took four minutes. The principle of SV calculation is based on an inverse relationship between the SV and PWTT.

Data from all three devices were recorded only when the signals were of good quality.

### Statistical analysis

A sample size of eight achieved 80% power to detect a difference of 0.84 between the null hypothesis correlation of 0 and the alternative hypothesis correlation of  $-0.84$  using a two-sided hypothesis test with a significant level of 0.05. Finally, we increased the sample size to 10 cases<sup>(10)</sup>.

**Table 1.** Patient characteristics

| Variables                                   | All patients (n=10)<br>Mean±SD |
|---|--------------------------------|
| Age (year)                                  | 64.5±15.9                      |
| Sex: male; n (%)                            | 9 (90)                         |
| Body mass index (kg/m <sup>2</sup> )        | 22.9±3.0                       |
| ASA physical status; n (%)                  |                                |
| II  | 4 (40)                         |
| III   | 5 (50)                         |
| IV  | 1 (10)                         |
| Primary diagnosis; n (%)                    |                                |
| Gastrointestinal malignancy                 | 10 (100)                       |
| Surgery; n (%)                              |                                |
| Hepatectomy                                 | 1 (10)                         |
| Gastrectomy                                 | 1 (10)                         |
| Low anterior resection                      | 6 (60)                         |
| Colectomy                                   | 2 (20)                         |
| Duration of surgery (minute)                | 164.5±49.6                     |
| Intraoperative fluid intake (ml)            | 2,110.0±1,393.1                |
| Estimated blood loss (ml)                   | 530.5±895.7                    |
| Baseline mean arterial pressure (mmHg)      | 82.8±17.8                      |
| Baseline heart rate (beats/minute)          | 74.2±18.1                      |
| Baseline cardiac output from EDM (L/minute) | 4.2±0.9                        |
| Baseline oxygen saturation (%)              | 97.9±2.0                       |

EDM=esophageal Doppler monitoring; ASA=American Society of Anesthesiologists; SD=standard deviation

The data distributions were evaluated by the Shapiro-Wilk test. Non-normally distributed data were reported as median and interquartile range. Pearson's correlation coefficient was used to assess individual associations of the SV between EDM and bioreactance (EDM-bioreactance) and between EDM and the PWTT (EDM-PWTT) at 5-minute intervals from all 10 patients. The accuracy and precision between EDM-bioreactance and EDM-PWTT were demonstrated using scatter plots and Bland-Altman analysis. Bias was assessed as the mean difference between SV measurements from each pair of devices. The limits of agreement were calculated as the bias ±1.96 standard deviation of the bias. The percentage error was calculated as the ratio of 1.96 standard deviation of the bias to the mean SV of the reference method. The clinically acceptable percentage error is less than 30%<sup>(11)</sup>. A four-quadrant plot analysis was performed using the percentage change of the SV before and after 500-ml crystalloid loading to analyze the trending ability of EDM-bioreactance

and EDM-PWTT. The concordance rate was defined as the percentage of data points in the upper right and lower left quadrants of the plot. An acceptable concordance rate is greater than 92% as described by Critchley et al<sup>(12)</sup>. The exclusion zone in the present study was defined as the area of percentage change in the SV of less than 10%<sup>(13)</sup>.

Statistical analysis was performed using IBM SPSS Statistics software, version 24.0 (IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

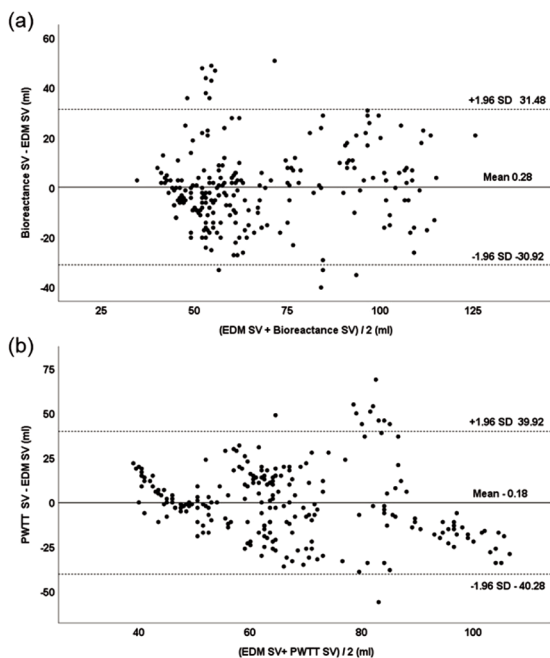
## Results

Two hundred twenty-seven paired measurements were obtained for the analyses. The patient characteristics are shown in Table 1. The baseline SV of EDM, bioreactance, and PWTT was 59.40±17.35, 64.10±16.07, and 56.80±10.84 ml, respectively. The mean SV of EDM, bioreactance, and PWTT was 66.64±21.72, 66.93±23.29, and 66.46±17.77 ml, respectively.

The authors performed a Bland-Altman analysis to identify the accuracy and precision of SV measurement by bioreactance and PWTT versus that by EDM. The bias or mean difference of EDM-bioreactance was 0.28 ml (limits of agreement -30.92 to 31.38 ml) with a percentage error of 46.82% (Figure 1a). The bias of EDM-PWTT was -0.18 ml (limits of agreement -40.28 to 39.92 ml) with a percentage error of 60.17% (Figure 1b). Both EDM-bioreactance and EDM-PWTT had a higher percentage error than the clinically acceptable range, which is less than 30%<sup>(11)</sup>. No significant difference was found in the bias of SV between EDM-bioreactance and EDM-PWTT (p=0.762).

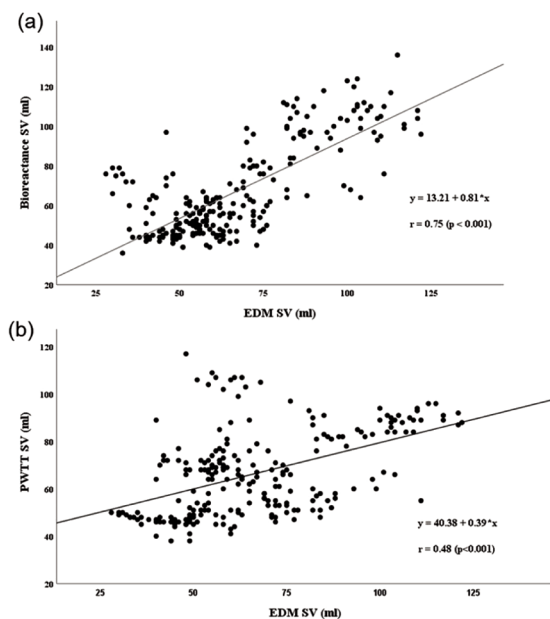
For EDM-bioreactance, the correlation coefficient was 0.75 (95% confidence interval [CI] 0.62 to 0.78; p<0.001) (Figure 2a). For EDM-PWTT, the correlation coefficient was 0.48 (95% CI 0.44 to 0.72; p<0.001) (Figure 2b).

A subgroup analysis of patients who received 500-ml crystalloid loading was performed to detect the trending ability of bioreactance and PWTT measurement compared with EDM. Twenty-four paired measurements were obtained for the analysis. The mean SV obtained by EDM, bioreactance, and PWTT measurement before fluid loading was 62.12±15.95, 63.20±20.65, and 65.87±18.17 ml, respectively, and that after fluid loading was 72.70±21.77, 71.62±24.63, and 71.83±19.08 ml, respectively. The four-quadrant plot with an exclusion zone of less than 10% of the percentage change in



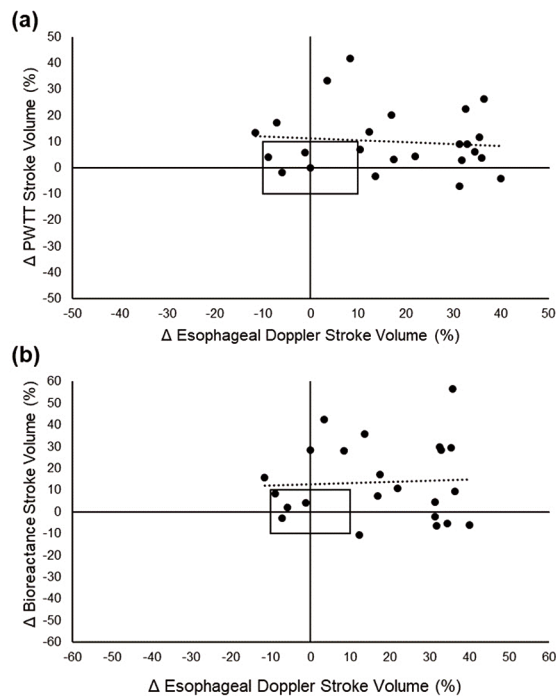
**Figure 1.** Bland-Altman analysis of SV measurement. (a) Bioreactance technique and EDM. (b) PWTT and EDM. Solid line indicates mean bias, and dashed line indicates 95% limits of agreement.

SV=stroke volume; EDM=esophageal Doppler monitoring; PWTT=pulse wave transit time; SD=standard deviation



**Figure 2.** Linear regression analysis of SV measurement between each pair of devices. (a) Bioreactance technique and EDM. (b) PWTT and EDM.

SV=stroke volume; EDM=esophageal Doppler monitoring; PWTT=pulse wave transit time



**Figure 3.** Concordance proportions between each pair of devices after fluid loading. (a) PWTT and esophageal Doppler monitoring concordance rate=73.68%. (b) Bioreactance technique and esophageal Doppler monitoring concordance rate=70.00%.

PWTT=pulse wave transit time

the SV after fluid loading between EDM-PWTT and EDM-bioreactance demonstrated a concordance rate of 70.00% (Figure 3a) and 73.68% (Figure 3b), respectively, which were lower than the acceptable value of more than 92%<sup>(12)</sup>.

No adverse event related to the cardiac output monitoring in the present study was reported.

The agreement between bioreactance and PWTT (bioreactance-PWTT) was also compared. The correlation coefficient between these two techniques was 0.38 (95% CI 0.34 to 0.66;  $p < 0.001$ ), the bias was 0.46 ml (limits of agreement  $-45.05$  to  $-45.97$ ), and the percentage error was 68.48%.

## Discussion

The decrease in postoperative complications secondary to the implementation of perioperative goal-directed hemodynamic management has resulted in the increased use of hemodynamic monitoring devices. Perioperative non-invasive hemodynamic monitoring is gaining more interest because of improvements in technology, and thus, higher accuracy of the devices. The major advantages of

these devices are their simplicity and high safety profile. However, there have been few data comparing these devices with the former technology.

The thermodilution technique is currently considered the most accurate cardiac output measurement method and is generally used as a reference method. Peyton and Chong<sup>(14)</sup> conducted a meta-analysis to compare the accuracy and precision between EDM and thermodilution. They reported a bias of  $-0.77$  LPM with limits of agreement of  $-1.06$  to  $-0.48$  LPM and percentage error of 42.1% (95% CI 32.2 to 52.0)<sup>(14)</sup>. However, only two studies involving 57 patients were analyzed. The acceptable percentage error is 30% or less; therefore, in terms of accuracy and precision, EDM cannot replace thermodilution as a reference method. However, some evidence supports the use of EDM because of its excellent correlation with thermodilution<sup>(15,16)</sup>. Therefore, when using EDM, the trend of the cardiac output change should be used instead of the absolute values. Because EDM has been proven useful for perioperative hemodynamic management, currently, using only trends of hemodynamic data from EDM to guide management might be sufficient without the need to obtain correct data values. In the present study aimed to compare the performance of the two non-invasive techniques (bioreactance and PWTT) with EDM.

Bioreactance is safe because only four sensors are non-invasively applied on the front or back of the patient. The SV was calculated from the degrees of the phase shift of the electrical currents induced by the flow in the thorax. One systematic review and meta-analysis revealed unacceptable error between non-invasive cardiac output monitoring and thermodilution<sup>(17)</sup>. However, other evidence showed that bioreactance had a strong correlation with thermodilution ( $r=0.92$ ,  $p<0.001$ ) with a good concordance rate of 94%<sup>(18)</sup>. In the present study, bioreactance had a moderate correlation with EDM with unacceptable percentage error. This finding is similar to that of previous studies. De Pascale et al<sup>(19)</sup> showed that the percentage error between bioreactance and EDM was 50.6% with a concordance rate of 78.7%. Lamia et al<sup>(20)</sup> reported that the percentage error between bioreactance and EDM was 47% with good correlation ( $r=0.87$ ,  $p=0.001$ ). Conway et al<sup>(21)</sup> reported similar results that EDM was not interchangeable with bioreactance because of a percentage error of 57%; nevertheless, the concordance rate after fluid loading was 90.5%, which was almost acceptable with respect to the

trending ability. In the present study, the subset of data used for the trending analysis after fluid loading was obtained from only 24 data pairs; thus, it was too small to allow for a conclusion about the trending ability when comparing with EDM. In conclusion, bioreactance and EDM were not interchangeable in the present study. The concordance rate after treatment between the two methods need further investigation.

The PWTT is used to measure cardiac output based on the principle that the SV is inversely correlated with the PWTT. Smetkin et al<sup>(22)</sup> demonstrated that the PWTT had a percentage error of 40% compared with thermodilution when using invasive instead of non-invasive blood pressure measurement for calibration. However, another study showed that the PWTT had a good correlation with thermodilution ( $r=0.80$ ,  $p<0.001$ )<sup>(23)</sup>. The trending ability after treatment by the concordance rate was only 73% as reported by Smetkin et al<sup>(22)</sup>. The authors found that the PWTT had a large error when comparing with EDM. To the authors' knowledge, no previous study has compared the agreement between PWTT measurement and EDM. The authors conclude that PWTT measurement is not interchangeable with EDM. Also, PWTT is not interchangeable with bioreactance.

Although the present study failed to demonstrate acceptable accuracy and precision of EDM-bioreactance and EDM-PWTT, the authors cannot conclude that bioreactance and PWTT measurement have unacceptable errors for perioperative assessment of cardiac output, because EDM was not the gold standard of cardiac output measurement. The limitations of EDM include the use of electrocautery during surgery, the operator-dependent positioning, and the requirement for anesthesia in most situations. In those cases, the physicians might alternatively use bioreactance or PWTT measurement because of the acceptable trending ability with thermodilution from previous studies. Our study has limitation. Because of the ethical consideration, the physicians could not measure cardiac output in patients undergoing gastrointestinal surgery with thermodilution technique which is invasive procedure. Thus, the present study did not prove which monitoring provided the most accurate information comparing to the gold standard. Future study should compare these non-invasive techniques with EDM and thermodilution to fully elucidate the accuracy and precision of non-invasive devices against EDM.

## Conclusion

Non-invasive cardiac output monitoring based on



the bioreactance technique and PWTT measurement are not interchangeable with EDM.

### What is already known on this topic?

Non-invasive hemodynamic monitoring has some limitations about accuracy and precision comparing to more invasive devices. However, the trend monitoring to guide hemodynamic management is acceptable because of the safety profile.

### What this study adds?

The less invasive EDM cannot be used in awake patients under regional anesthesia. Non-invasive hemodynamic monitoring has been increasingly used in these group of patients. This study demonstrated that non-invasive hemodynamic devices are not interchangeable with EDM. Therefore, the benefits of perioperative goal directed hemodynamic management using EDM should be re-evaluated with non-invasive devices.

### Funding disclosure

This research was funded by Ramathibodi Hospital, Mahidol University.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

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