34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

The Comparison of a Novel Continuous Cardiac Output Monitor Based on Pulse Wave Transit Time and Echo Doppler during Exercise

Yoshihiro Sugo, Tomoyuki Sakai, Mami Terao, Teiji Ukawa, Ryoichi Ochiai

Abstract— **A new technology called estimated continuous cardiac output (esCCO) uses pulse wave transit time (PWTT) obtained from an electrocardiogram and pulse oximeter to measure cardiac output (CO) non-invasively and continuously. This study was performed to evaluate the accuracy of esCCO during exercise testing. We compared esCCO with CO measured by the echo Doppler aortic velocity-time integral (VTIao_CO). The correlation coefficient between esCCO and VTIao_CO was r = 0.87 (n = 72). Bias and precision were 0.33 ± 0.95 L/min and percentage error was 31%. The esCCO could detect change in VTIao_CO larger than 1 L/min with a concordance rate of 88%. In polar plot, 83% of data are within 0.5 L/min, and 100% of data are within 1 L/min. Those results show the acceptable accuracy and trend ability of esCCO. Change in pre-ejection period (PEP) measured by using M-mode of Diagnostic Ultrasound System accounted for approximately half of change in PWTT. This indicates that PEP included in PWTT has an impact on the accuracy of esCCO measurement. In this study, the validity of esCCO during exercise testing was assessed and shown to be acceptable. The result of this study suggests that we can expand its application.**

I. Introduction

We previously reported about a non-invasive continuous cardiac output (CO) monitoring method which utilizes electrocardiogram (ECG) and a pulse oximeter wave. It calculates an estimate of CO based on hemodynamic analysis combined with pulse wave transit time (PWTT) [1]. The esCCO is inexpensive and easy to use, requiring no consumable items such as catheters, and thus constitutes a useful noninvasive technique in cardiovascular monitoring. A multicenter study involving seven university hospitals in Japan was performed to test the accuracy of the esCCO, mostly during and after cardiac surgery [2]. The results supported the clinical relevance of the esCCO not only in the ICU, but also during surgical procedures. In previous studies, the esCCO was evaluated mainly in invasive manner, for example, using CO measurement by thermodilution catheter and invasive blood pressure value to get pulse pressure (PP) for calibration [2]. The advantage of the esCCO is that it provides stroke volume (SV) and CO non-invasively and continuously. Monitoring during exercise testing is usually limited to measurement of electrical activity of the heart and heart rate (HR) with electrocardiography, and intermittent blood pressure (BP). So, we suggest that continuous SV and CO during exercise should provide with valuable clinical information. In this report, we describe the performance of estimated stroke volume (esSV) and esCCO by comparing them with echo Doppler aortic velocity-time integral method during exercise testing. Pre-ejection period (PEP) can be measured with M-mode of Diagnostic Ultrasound System and synchronized ECG recording, so we also analyzed relation between PWTT and PEP to confirm the impact of including PEP in PWTT.

Manuscript received March 15, 2012. This work was supported in part by Nihon Kohden Corporation. Y. Sugo, T. Sakai, M. Terao and T. Ukawa are with Nihon Kohden Corp., 1-31-4 Nishi-Ochiai, Shinjuku-ku, Tokyo, Japan (corresponding author to provide phone: +81-3-5996-8063; fax: +81-3-5996-8652; e-mail: Yoshihiro_Sugo@ mb4.nkc.co.jp). R. Ochiai is with the Dept. of Anesthesiology, Toho University, Tokyo, Japan.

II. Method

A. Measurement

The study was approved by the Institutional Review Board of Nihon Kohden. Fifteen healthy male volunteers gave written informed consent were enrolled in this study. Age, height, weight, and body surface area of the subjects were 37.2 ± 10.3 years, 173.5 ± 2.9 cm, 65.0 ± 7.3 kg and 1.78± 0.10 m^2, respectively.

Aortic valve area (AVA) and aortic velocity-time integral measurement by the echo Doppler was done during exercise testing by a well trained clinical technologist. We used a supine position protocol in 10 subjects and a lateral position protocol in five subjects. In the supine position protocol, the measurement was done during leg raising and exercise testing in supine position. Five out of fifteen subjects were not able to be measured in supine position, so in these subjects we used a lateral position protocol and the measurement was done during leg raising in lateral position.

The study protocols were as follows:

- Lateral position protocol

SV and CO measured by the echo Doppler aortic velocity-time integral (VTIao_SV and VTIao_CO) were obtained at rest, and esCCO was calibrated with VTIao_CO. We compared esSV to VTIao_SV and esCCO to VTIao_CO during leg raising exercise.

- Supine position protocol

esSV, VTIao_SV, esCCO and VTIao_CO were obtained by the same protocol as the lateral position protocol at rest and during leg raising protocol. Supine ergometer exercise was started with stepwise changes in load as follows: 0 -> 25 -> 50 -> 75 -> 50 -> 25 -> 0 [Watts]. We compared esSV to

VTIao_SV and esCCO to VTIao_CO when data is stable in each step.

PWTT and non-invasive blood pressure (NIBP) were obtained by BSM-9101 bedside monitor (Nihon Kohden, Tokyo, Japan) and these values were transmitted to a personal computer equipped with a c-compiled program to calculate esCCO. ECG monitoring was performed using lead II, and a pulse oximeter probe was placed on a fingertip. NIBP was measured at the brachial artery on the side contralateral to the pulse oximeter probe. Reference CO and SV were measured by the Diagnostic Ultrasound System Xario XG (SSA-680A) (Toshiba Medical System Corporation, Tokyo, Japan). In Diagnostic Ultrasound System, AVA was measured on the B mode and aortic velocity-time integral was calculated on the Doppler mode. VTIao_SV was calculated by multiplying AVA and velocity-time integral value. VTIao_CO was calculated by multiplying VTIao_SV and HR which was displayed on the BSM-9101 screen. Another ECG monitoring was performed on Diagnostic Ultrasound System. We measured the interval from ECG R-wave to the aortic valve opening point on M-mode screen as PEP.

B. Calculation of PWTT

The sampling interval of ECG wave and oximetry pulse wave were 4 ms and 8 ms, respectively. The time from the ECG R-wave to the rise point of the oximetry pulse wave was defined as PWTT. According to the other previous study [3], required time resolution of PWTT was thought to be 1 ms, so error of PWTT was -7 ms to 3 ms. Because PWTT data of 64 consecutive heart beats were averaged, error of PWTT was declined to 1 / (square root of average number). Finally the temporal resolution was -0.875 ms to 0.375 ms.

C. esSV and esCCO calculation

esSV was calculated by using the formula:

$$esSV = K \times (\alpha \times PWTT + \beta) \quad (1)$$

Each parameter was calculated according to the methods described by Sugo et al. [1] by using the formulas below for only first time after the start of the measurement in each case.

$$K = iSV/PP \quad (2)$$

PP measured by NIBP should be corrected to compensate the difference between NIBP and radial invasive blood pressure. [Personal communication with Dr. Ochiai] PP was calculated based on the following formula:

$$PP = (NIBP\_SYS - NIBP\_DIA) \times (a + b \times NIBP\_SYS + c \times NIBP\_DIA) \quad (3)$$

where NIBP_SYS: systolic pressure of NIBP, NIBP_DIA: diastolic pressure of NIBP: a, b, c are constants.

$$\beta = VTIao\_SV/K - \alpha \times PWTT \quad (4)$$

esCCO was calculated as follows:

$$esCCO = esSV \times HR \quad (5)$$

D. Data Analysis

The 1SD value was defined as precision. The Microsoft Excel (Microsoft Office XP Professional) and SPSS II for Windows ver. 11.0.1J (SPSS Inc., Chicago, IL, USA) software programs were used to perform the statistical analysis. The following statistical analysis was performed. The significance level was set at $p < 0.05$.

・Correlation analysis and Bland-Altman plot

The calibrated points were excluded and the remaining 72 pairs of esSV and VTIao_SV, esCCO and VTIao_CO were analyzed.

・Trend ability.

One in 72 points could not be measured due to a significant body movement, so 70 pairs of sequence change in esCCO and change in VTIao_CO were analyzed. The concordance rate [4] and polar coordinate [5] were analyzed as for the trend ability.

・Change in each time component from calibration points

PWTT and PEP at the calibration point were defined as the reference value and change in PWTT and change in PEP were calculated. Correlation analysis between the change in PWTT and change in PEP was performed.

III. Results

A. Correlation analysis and Bland-Altman plot

The correlation coefficient between VTIao_SV and esSV was $r = 0.82$ ($p < 0.01$, $n = 72$), Bias and precision were 3.43 ± 9.91cc. Percentage error (2 × precision/average SV) was 28% (Figure 1 A). The correlation coefficient between VTIao_CO and esCCO was $r = 0.87$ ($p < 0.01$, $n = 72$), bias and precision were 0.33 ± 0.95 L/min. Percentage error (2 × precision/average CO) was 31% (Figure 1 B).

B. Trend ability

1) Concordance rate

Changes in VTIao_CO larger than 1 L/min were detected in 34 data points. esCCO could track these directional changes in 30 of these data points with a concordance rate of 88.4%.

2) Polar coordinate

Polar plots are shown in Figure 2. 100% of the data points are within the 1.0 L/min lines and 83% of the data points are within the 0.5 L/min.

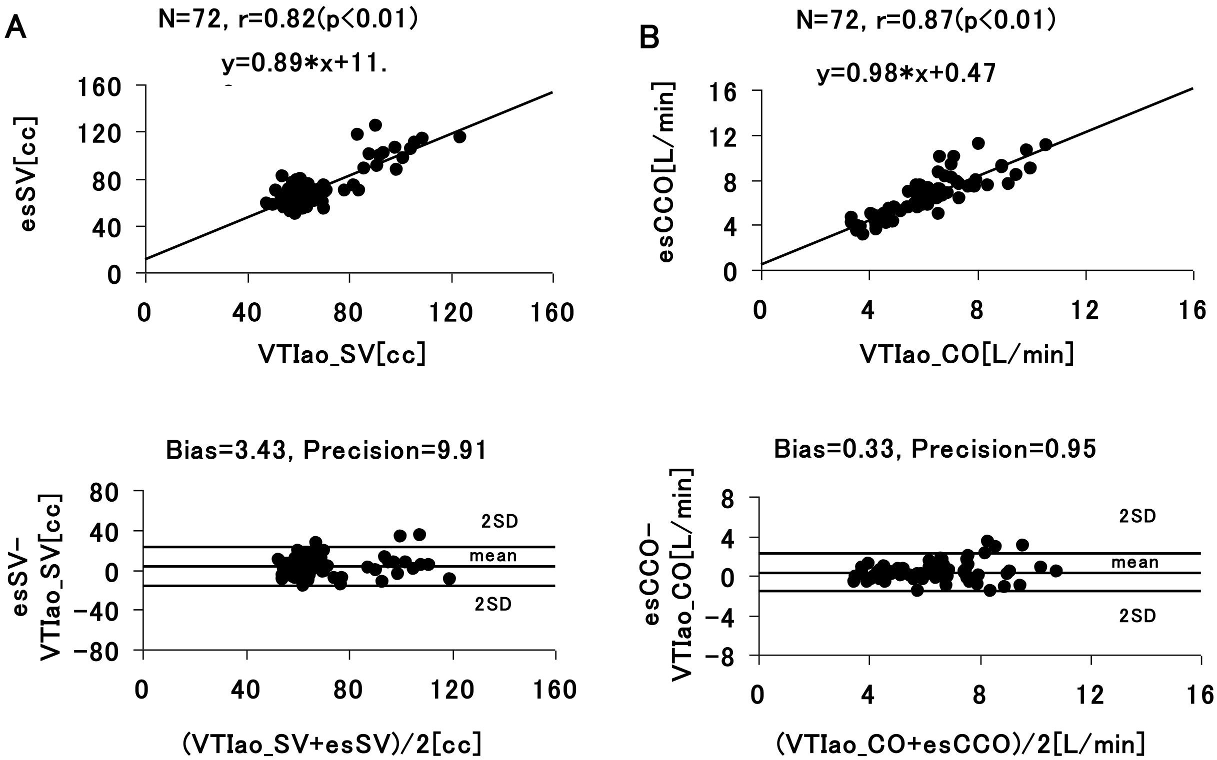

Figure 1 Correlation analysis of esSV and VTIao_SV (A top) and Bland and Altman plot (A bottom), correlation analysis of esCCO and VTIao_CO (B top) and Bland and Altman plot (B bottom)
2SD is twice the calculated precision.
esSV: estimated stroke volume, esCCO: estimated continuous cardiac output,
VTIao_SV and VTIao_CO: Stroke volume and cardiac output measured by the echo Doppler aortic velocity-time integral

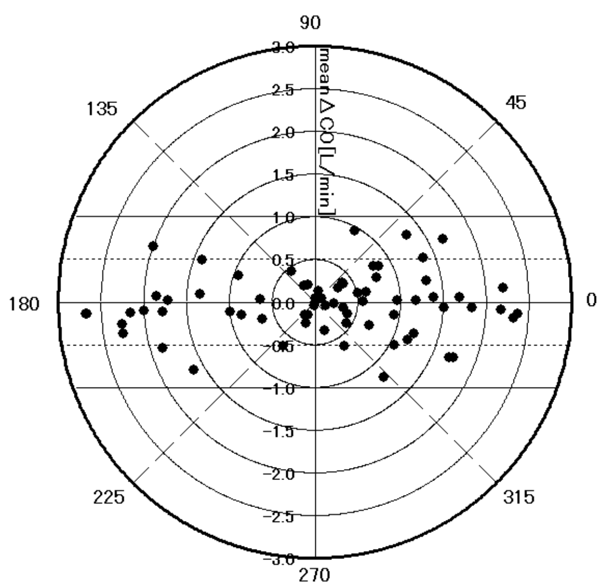

Figure 2 Polar plots showing trending ability of the esCCO system (n=72). The dashed lines represent the limits of good agreement (± 0.5L/min), and straight lines represent the limits of acceptable agreement (± 1L/min).

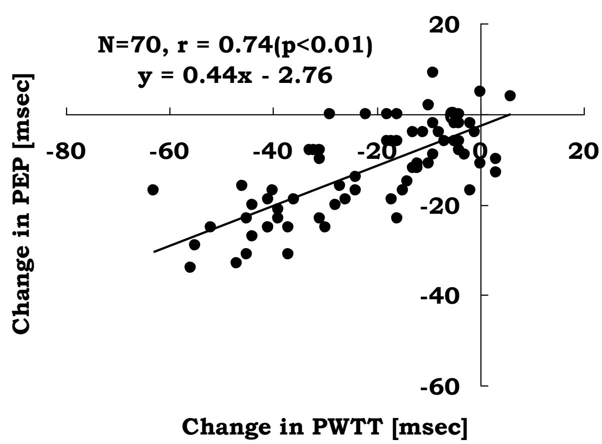

Figure 3 Correlation analysis of change in PWTT and change in PEP.
PWTT and PEP at the calibration point were defined as the reference value and change in PWTT and change in PEP were obtained.
PWTT: pulse wave transit time, PEP: pre-ejection period

C. Change in each time component from calibration points

PWTT and PEP at rest were 199 ± 15 ms, 41 ± 12 ms, respectively. Change in PWTT was – 21.8 ± 17.1 ms, and change in PEP was – 12.9 ± 10.1 ms. The correlation coefficient between the change in PEP and change in PWTT was 0.74 with the slope of 0.44 (Figure 3).

IV. DISCUSSION

A. Comparison of previous study

The findings of this study show a good correlation between esCCO and VTIao_CO, which is in agreement with the correlation coefficients of $r = 0.79$ ($p < 0.001$, $n = 587$) shown in a previous study in OR and ICU [2]. Reference method in the previous study was the thermodilution cardiac output (TDCO) measurement. The bias of 0.33 shown in this study was larger than that reported in the previous study [2], but the precision of 0.95 was smaller than that reported in the previous study [2]. The percentage error of 31% was much smaller than the previous study (54%) [2]. This could be mainly because the average CO (6.10L/min) was higher than the previous study (4.24L/min).

B. Comparison of other study

The percentage errors of esCCO (31%) and esSV (28%) were almost within an acceptable percentage error, which suggests that esCCO could be substituted for the compared CO as for the reference. Critchley et al. [6] reported the allowable error of 30% was determined based on the estimation of 20% TDCO error. In this study, the echo Doppler was used as a reference method. If the error of the echo Doppler was the same as TDCO (20%), it can be suggested that esCCO is interchangeable with the echo Doppler method. A concordance rate was higher than 90% to 95% when using the exclusion zones of 0.5 to 1.0 L/min or 15%, indicating a reliable trending ability [5]. So the concordance rate of 88.4% in this study is almost acceptable. The trending ability of changes in CO was assessed by using polar coordinates proposed by Critchley et al [5]. If most of the trending points lie within the 0.5L/min boundaries, a change in CO of > 0.5 L/min would have a high chance of predicting a true change in CO (80%-90% with low chance of type II error) [4]. In this study 100% of the data points are within the 1.0 L/min lines and 83% of the data points are within the 0.5 L/min, which therefore suggest that the trend ability of esCCO is acceptable for clinical use.

C. Impact of inclusion of PEP

The good relationship between change in PWTT and change in PEP was observed. In this study, the slope between the change in PWTT and change in PEP was 0.44, which cannot be neglected. Chan et al. [3] performed simultaneous measurements of PWTT and PEP in healthy subjects during a head-up tilt test. They reported that PEP reflects progressive central hypovolemia. Feissel et al. [7] reported that the respiratory change in PEP was useful for guiding the initial phase of volume therapy in septic patients undergoing mechanical ventilation. Moreover, Bendjelid et al. [8] reported that in patients receiving mechanical ventilation after undergoing cardiac surgery, the change in PEP can be used to predict fluid responsiveness. The impact of PEP for predicting change in preload was confirmed by these previous studies. In this study, we confirmed the impact of PEP included in PWTT in regard to exercise testing.

D. Limitation of this study

In this study, we evaluated esCCO in the supine ergometer exercise. Other exercise such as bicycle ergometer and treadmill was not suitable to do the evaluation because these exercise method can produce a significant artifact. However, further evaluation is needed to assess the performance of esCCO in various settings.

V. CONCLUSIONS

We confirmed the acceptable accuracy of esSV and esCCO by comparing them with the echo Doppler aortic velocity-time integral method during exercise only by using non-invasive parameter. The result of this study suggests the possibility of expanding its application.

ACKNOWLEDGMENT

We are grateful to Naoki Fukushima for technical assistance and Nami Setoguchi for valuable comments.

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