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Research Article

Comparison of Estimated Continuous Cardiac Output and Transoesophageal Echocardiography Cardiac Output for Noninvasively Measuring Cardiac Output in Paediatric Patients Undergoing Kidney Transplant Surgery: A Pilot Study

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Abstract

Objective: Estimated continuous cardiac output (esCCO), a noninvasive technique for continuously measuring cardiac output, is based on modified pulse wave transit time (m-PWTT), which in turn is determined by pulse oximetry and electrocardiography (ECG). However, its trending ability has never been evaluated in paediatric patients. Therefore, this study examined esCCO's ability to detect the exact changes in cardiac output (CO), compared with transoesophageal echocardiography, in patients undergoing kidney transplantation.

Methods and Results: The cardiac index was determined simultaneously using both the estimated continuous cardiac output and transoesophageal echocardiography in 11 paediatric kidney transplant patients. After the initial calibration measurement, cardiac index was measured using transoesophageal echocardiography before and after volume loading, and before surgery completion. The cardiac index determined using transoesophageal echocardiography increased significantly between the pre- and post-volume loading measurements (P<0.05), but decreased significantly between volume loading and surgery completion (P<0.05). The correlation coefficient between cardiac indexes using the two devices was 0.75 (P<0.001) and the difference in the cardiac index, between the methods, was 0.21 ± 1.01 L/min/m2 (95% confidence interval, -1.77 to 2.19). The percentage error was 43.6%. The change in cardiac index, determined using transoesophageal echocardiography, of >15% from before volume loading to after volume loading or between volume loading and the completion of surgery was 16 points; this lead to a change of >15% in the cardiac index determined using continuous cardiac output, in the same direction, in 100% cases. The sensitivity and specificity

for cardiac index determination, using estimated continuous cardiac output compared to transoesophageal echocardiography, were 87.5% and 100%, respectively.

Conclusions: Although there was poor agreement between the cardiac indexes determined by estimated continuous cardiac output and transoesophageal echocardiography, the trends determined by both methods were in good agreement. This method may be sufficient for trend monitoring.

Keywords

Children; Cardiac output; Circulatory management; Kidney transplant

Introduction

The standard technique for measuring cardiac output in paediatric circulatory management involves the use of a pulmonary artery catheter. However, these devices are highly invasive, and are, therefore, reserved for use during cardiac and non-cardiac surgeries in patients with severe heart disease when the assessment of systemic oxygen delivery is required. A non-invasive or minimally invasive and continuous estimation of cardiac output would be an effective method for circulatory management [1]. Such methods include transthoracic bioimpedance, oesophageal Doppler, transthoracic echocardiography, transoesophageal echocardiography [1], and more recently electrocardiogram - pulse oximetry estimated continuous cardiac output.

Other noninvasive and minimally invasive devices can be used in paediatric patients [1]. The LiDCO (LiDCO, Cambridge, United Kingdom) transpulmonary method involves the injection of a small dose of lithium chloride, via a central catheter or large bore peripheral cannula, and the measurement of the resultant lithium concentration time curve via a sensor attached to a peripheral arterial cannula. In this method can be used frequently, is accurate, and minimally invasive. However, the use of the LiDCO device is not permitted in Japan. Pulse contour and bioimpedance methods can also be used, but they are inaccurate [1].

The estimated continuous cardiac output system can estimate cardiac output using an electrocardiogram and a pulse oximetry pulse wave [2]. Thus, cardiac output is estimated using only general cardiac monitoring systems, without the need for special probes or sensors. The cardiac output is estimated according to the time between the electrocardiogram R-wave and the arrival of the pulse wave at the pulse oximeter.

We previously reported on the agreement between estimated continuous cardiac output monitoring and other types of non-invasive equipment for paediatric patients [3]. In that study, we established a reference cardiac output using a dye dilution method and dye densitography-cardiac output. However, the dye-based method does not permit continuous measurement because subsequent measurements cannot be made until the indocyanine green dye has been excreted. In the present study, we assessed the trending ability of estimated continuous cardiac output in paediatric patients using transoesophageal echocardiography as the reference method. This method for determining cardiac output can be frequently performed, is accurate, minimally invasive, and can be used in paediatric

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patients [1]. In particular, this observational, blinded study evaluated the agreement between cardiac output measurements made using transoesophageal echocardiography and the estimated continuous cardiac output system.

Materials and Methods

Patients

This study involved paediatric patients who underwent kidney transplant surgery at our hospital between March 2010 and April 2011. To obtain a sufficient renal blood flow volume prior to the reperfusion of the renal artery, a large volume of fluid was infused. Subsequently, there was a large haemodynamic change during the renal transplant surgery. Moreover, the cardiac output increased rapidly before reperfusion of the renal artery. Thus, this type of surgery was appropriate for examining the trending of the estimated continuous cardiac output method. Paediatric patients with arrhythmia were excluded because of the inability to accurately detect the R-wave. The subjects' parents provided written consent to participate in this study, which was approved by an appropriate ethics committee.

Anaesthetic management

In these paediatric patients, only general anaesthesia involving fentanyl, propofol, and rocuronium bromide was used. The anaesthetic state was maintained by sevoflurane inhalation (1.0-2.0%) and continuous administration of remifentanil hydrochloride (0.05-0.5 μg $\bullet$ kg^{-1} $\bullet$ min^{-1}).

Fluid and cardiovascular management

To obtain sufficient renal blood flow volume prior to the reperfusion of the renal artery, carperitide (0.025 μg $\bullet$ kg^{-1} $\bullet$ min^{-1}) and dopamine (2 μg $\bullet$ kg^{-1} $\bullet$ min^{-1}) were administered. Normal saline was administered to achieve a targeted central venous pressure of 15 mmHg, and the administration rate of dopamine was adjusted to maintain a systolic blood pressure of 130 mmHg.

Electrocardiogram, pulse oximetry, and end-tidal carbon dioxide assessments were used to monitor cardiac function and respiratory status, whereas rectal temperatures were used for temperature management.

Data sampling

After the haemodynamic state of the patients had been stabilized following the initiation of the surgery, we connected the estimated continuous cardiac output system to a pulse oximeter and electrocardiogram unit (Table 1). Electrocardiograms, pulse oximetry wave data, arterial blood pressure, and pulse wave transit time were obtained using a BSM-9101 Bedside Monitor (Nihon Kohden, Tokyo, Japan) and transmitted to a personal computer with a pre-compiled C-language program for estimated continuous cardiac output calculations.

We also measured the cardiac output by transoesophageal echocardiography. The first measurement obtained was used for calibration, and the estimated continuous cardiac output was subsequently measured. After the initial calibration cardiac indexes calculation using the estimated continuous cardiac output and transoesophageal echocardiography methods were performed three times simultaneously (before volume loading, after volume loading, and before completion of surgery).

*p<0.05 Between before volume loading and after volume loading
**p<0.05 Between after volumen loading and before surgery completion

Table 1: Hemodynamic data.

	Before Volume Loading	After Volume Loading	Before Surgery Completion
HR (beats/min)	94±26	109±25*	99±26**
MAP (mmHg)	72±14	88±18*	92±10
CVP (mmHg)	8±5	10±4*	7±4**
SVRI (dynes×sec/cm²/m²)	1427±536	1154±342*	1809±653**
TEECI (L/min/m²)	3.85±1.1	5.67±1.49*	4.12±1.11**
esCCI (L/min/m²)	4.02±1.32	5.64±1.47*	4.60±1.02**

Transoesophageal echocardiography determination of cardiac output

The transoesophageal echocardiography measurements were obtained by an investigator blinded to the estimated continuous cardiac output measurements. The transoesophageal echocardiography measurements were performed using a multiplane echocardiograph (Sonos 550, Philips, Amsterdam, Netherlands). The Doppler estimated cardiac output by transoesophageal echocardiography [1] was derived from the Doppler-estimated stroke volume using the velocity-time integral of flow through the left ventricular outflow tract, the cross-sectional area of left ventricular outflow tract, and the heart rate recorded during the imaging study, according to the following formula:

Cardiac output by transoesophageal echocardiography = the velocity - time integral of flow through the left ventricular outflow tract × cross-sectional area of left ventricular outflow tract × heart rate

The left ventricular outflow tract velocity-time integral and cross-sectional area were recorded simultaneously by pulsed-wave Doppler from an apical long-axis view by placing a Doppler sample volume in the left ventricular outflow tract at the level of the aortic valve. The left ventricular outflow tract cross-sectional area was measured using the following formula:

Cross sectional area = 3.14 × (left ventricular outflow tract diameter/2) × (left ventricular outflow tract diameter/2).

Statistical analysis

The correlation and linear regression of the different cardiac index values were calculated. P-values < 0.05 were considered statistically significant.

To examine the correlations between the cardiac indexes determined by transoesophageal echocardiography and estimated continuous cardiac output, a regression analysis was performed using the least squares method. Bland-Altman plots were used to evaluate the bias and standard deviation for both cardiac index estimations. We also calculated the 95% limits of agreement for both determinations (bias ± 1.96 standard deviations) and the percentage of the mean for the cardiac index determined using transoesophageal echocardiography (percentage error). This percentage error was considered clinically acceptable if it was <30%, in accordance with the report of Critchley and Critchley [4].

For a further trend analysis we confirmed whether a change in the cardiac index direction of transoesophageal echocardiography and estimated continuous cardiac output method was same or not. We initially analysed all data, and thereafter, assessed only the changes

in the transoesophageal echocardiography cardiac index that were greater than 15%; in addition, the sensitivity and specificity were calculated using a receiver operating characteristic curve analysis.

Results

The 11 paediatric subjects were included in this study comprised 6 boys and 5 girls. Their mean age was 8.27 ± 4.34 years (mean ± standard deviation), with a mean height of 115.86 ± 28.96 cm, and a mean weight of 22.68 ± 12.48 kg.

A total of 33 pairs of cardiac index values, determined using either transoesophageal echocardiography or estimated continuous cardiac output, were analysed; there were 3 sample points for each subject. The cardiac index, determined using transoesophageal echocardiography, increased after volume loading, compared to before volume loading, and decreased before surgery completion, compared to after volume loading (Table 1).

A regression analysis indicated that the correlation coefficient between the cardiac index values, determined by both methods, was 0.75 (Figure 1). The Bland-Altman analyses revealed that the mean bias was 0.21 ± 1.01 (Figure 2). The percentage error for the determinations of the cardiac index was 43.6%.
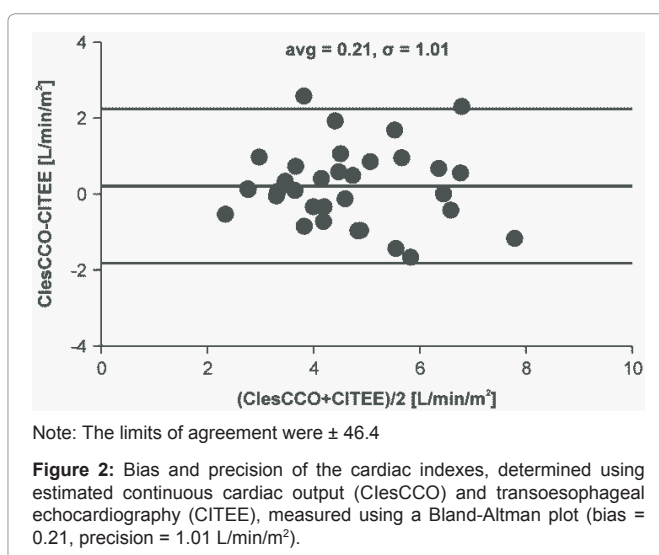
Changes in cardiac index, determined using transoesophageal echocardiography, of >15% from before volume loading to after volume loading or between volume loading and surgery completion were 16 points, and those leading to a change in the estimated continuous cardiac output determination of the cardiac index, in the same direction, was 100%. The sensitivity and specificity of the cardiac index determination, using estimated continuous cardiac output compared with transoesophageal echocardiography, were 87.5% and 100%, respectively. The area under the receive operator characteristic curve was 0.958, with a confidence interval of 0.881-1.036.

Discussion

Several convenient and minimally invasive continuous cardiac output monitoring systems have been developed [5], such as oesophageal Doppler monitoring, partial carbon dioxide rebreathing, and chest cavity impedance [6,7]. However, none of these systems is currently in general use [8]. The accuracy of the estimated continuous cardiac output system, in adults, has been reported during cardiac
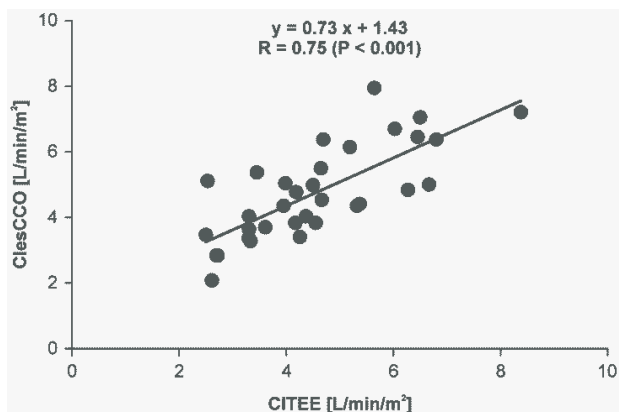
Figure 2: Bias and precision of the cardiac indexes, determined using estimated continuous cardiac output (ClesCCO) and transoesophageal echocardiography (CITEE), measured using a Bland-Altman plot (bias = 0.21, precision = 1.01 L/min/m²).

surgery [9] and in multicentre studies [2]. Ishihara et al. [9] compared a total of 981 paired sets of data (89.9%) among 1093 measurements in the absence of displacement of either pulse-oximetry or electrocardiogram probes and/or inaccurate detection of R waves, finding a difference between the estimated continuous cardiac output and the pulmonary artery catheter cardiac output values of - 0.06 ± 0.82 L/min, with a linear correlation (r = 0.80, P<0.0001).

Yamada et al. [2] analysed 587 datasets (213 patients) from among 588 estimated continuous cardiac output and pulmonary artery catheter cardiac output value datasets (excluding the calibration points). The results indicated a correlation coefficient of 0.79 (P<0.0001; 95% confidence interval, 0.756-0.819), a bias (mean difference between estimated continuous cardiac output and thermodilution cardiac output) of 0.13 L/min (95% confidence interval of bias, 0.04-0.22 L/min), and a precision (1 standard deviation) of 1.15 L/min (95% prediction interval, -2.13 to 2.39 L/min). These results indicate the potential of estimated continuous cardiac output for clinical use in adults.

In a previous study, we evaluated whether estimated continuous cardiac output could be effectively used in children in clinical settings. Our findings indicated no differences in the accuracy, correlation coefficient, or percentage error when comparing the reference cardiac output (dye dilution method) and estimated continuous cardiac output between children and adults [3]. In the present study, we compared the agreement and trending ability between cardiac output measurements using a new non-invasive technique (estimated continuous cardiac output), derived from pulse wave transit time, and reference values obtained using transoesophageal echocardiography. Transoesophageal echocardiography is accepted as a reliable method for clinical cardiac output measurements in children [1], with a high accuracy [10-13]. The thermodilution measurement of cardiac output using a pulmonary artery catheter is considered a gold standard; however, the value obtained using the pulmonary artery catheter method has been questioned in recent years, and its influence on outcomes is controversial. To avoid the limitations associated with pulmonary artery catheter use, alternative techniques have been developed for routine cardiac output monitoring.

The estimated continuous cardiac output percentage error of 43.6% is not considered clinically acceptable. However, estimated

Figure 1: Correlation between cardiac indexes determined using estimated continuous cardiac output (ClesCCO) and transoesophageal echocardiography (CITEE) (R = 0.75, P<0.001).

continuous cardiac output produced reliable cardiac output trending data, with a transoesophageal echocardiography concordance of 100%, which is higher than the acceptable level of 90% [10]. There are two reports describing the trending ability of estimated continuous cardiac output in adults. In a study of adult subjects (mean age, 65.3 ± 12.6 years), Ishihara et al. measured cardiac outputs with a new estimated continuous cardiac output system and compared the results with values obtained using intermittent bolus thermodilution cardiac output, utilising statistical methods including polar plot analyses. The percentage error was 69.6%, and a polar plot analysis indicated that the mean polar angle was -1.6°. The radial limits of agreement were ± 53.3° [11]. Moreover, Bataille et al. examined adult subjects having a mean age of 65 years (range, 20-85 years). The authors measured cardiac output with a new estimated continuous cardiac output system and compared the results with transoesophageal echocardiography results, also utilising statistical methods including polar plot analyses. The percentage error was 49%, and the polar concordance rate at an angle of 30° was 82%. Polar plot analysis indicated an angular bias of -9°, with radial limits of agreement from -54° to +36° and a concordance rate of 76% [12]. However, there are no reports regarding the trending ability of the new cardiac output device in paediatric patients. However, there is one such study, by Osthaus et al., that was performed on 5 piglets [13]. In their paper, the trending ability was verified using a receiver operating characteristic curve analysis of the changes of the new cardiac output values in relation to the first cardiac output measurement. They also examined the rate, in the same direction, that changes in the reference cardiac output (greater than 15%) led to a similar change measured using the new device's determined cardiac output. In the present study, the receiver operator characteristic curve analysis showed a sensitivity of 87.5% and specificity of 100% (area under the curve, 0.958; confidence interval, 0.881–1.036) and the concordance rate was acceptable (100%) in children; however, the estimated continuous cardiac output percentage error was unacceptable (43.6%).

The theory underlying estimated continuous cardiac output depends on pulse contour analyses, which can be used to measure the stroke volume and cardiac output from the arterial pressure and pulse rate. The stroke volume and cardiac output can be determined using the following formulae:

Stroke volume = K × pulse pressure ……… (1)

K is a constant.

Cardiac output = K × pulse pressure × Heart rate ……… (2)

The estimated continuous cardiac output method calculates cardiac output through estimation of modified-pulse wave transit time.

Pulse pressure = α × modified-pulse wave transit time + β …….. (3)

where α and β are constants

According to formula (3), α is determined by changes in both pulse pressure and modified pulse wave transit time. Furthermore, in humans, α is -0.30, according to unpublished preliminary data from 14 subjects, whereas β can be determined using formula (3) and individual data.

We found that the cardiac output measurement after volume loading was significantly larger than the measurement before volume loading, and that the measurement before the completion of surgery was significantly lower than the measurement after volume loading.

These observations suggest that kidney transplantation was a suitable procedure for examining the trending ability of estimated continuous cardiac output.

In our previous study, we did not observe differences in the accuracy, correlation coefficient, or percentage error when comparing the reference cardiac output (dye dilution method) and estimated continuous cardiac output between children and adults [3]. However, in this study, we found poor agreement between the two methods, although we found good trend agreement between the two methods. Thus, the estimated continuous cardiac output trending ability, in children.

One limitation of this study is the small population. We focussed on paediatric kidney transplant patients because there was a large haemodynamic change.

In conclusion, the standard technique for measuring cardiac output involves the use of a pulmonary artery catheter. However, since a pulmonary artery catheter is highly invasive, we used transoesophageal echocardiography in the current study. At present, none of the minimally invasive continuous cardiac output monitoring systems are generally used in adults [8]; moreover, these systems are not generally used without cardiac echocardiography in paediatric patients [1]. Based on the present study, we suggest that estimated continuous cardiac output measurement is an advantageous, non-invasive method, particularly in paediatric patients.

Compliance with Ethical Standards

Ethical Approval: All authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Informed Consent

Informed consent was obtained from all participants included in the study.

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