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NON-INVASIVE CARDIAC OUTPUT BY TRANSTHORACIC ELECTRICAL BIOIMPEDENCE IN POST-CARDIAC SURGERY PATIENTS: COMPARISON WITH THERMODILUTION METHOD

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ABSTRACT. Objective. Thoracic electrical bioimpedance (TEB) cardiac output (CO) is being explored increasingly as a non-invasive alternative to the pulmonary artery catheter (PAC). This study compared TEB-CO measured using a new instrument – NICOMON (Larsen & Toubro Ltd. India) with thermodilution (Td) CO in post-cardiac surgery patients. **Methods.** Postoperative cardiac surgical patients requiring a PAC for their management were studied. TEB-CO was measured by passing a 4 mA RMS alternating current across the chest and measuring the analog bioimpedence across the thorax. Kubicek equation was used to estimate TEB-CO. Td-CO was measured using a PAC. Bland-Altman analysis was used to compare paired data. **Results.** One hundred and ninety-seven pairs of CO measurements were made by the two methods among 35 patients. Mean TEB-CO was 5.15 ± 1.27 l/min and mean Td-CO was 5.22 ± 1.28 l/min. Pearson correlation coefficient (r) for these measurements was 0.856 ($P < 0.01$), with bias −0.0651 l and precision: ±1.37 l/min. The percentage error of measurement of this precision was 26.44%. Cardiac index also correlated among the two methods ($r = 0.789$; $P = 0.01$). **Conclusions.** Thoracic electrical bioimpedance cardiac output compares favorably with thermodilution method among post-cardiac surgery patients. Further studies are indicated with this instrument to validate its efficacy in various clinical situations and utility in monitoring hemodynamic interventions.

KEY WORDS. Thoracic electrical bioimpedance, Bioimpedance cardiac output, Cardiac output, Noninvasive cardiac output.

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INTRODUCTION

The ability to measure cardiac output (CO) greatly advances hemodynamic management in the intensive care unit (ICU). The major limitation of reliable methods of measuring CO hitherto has been invasiveness and their lack of adaptability to the non-ICU environment. This has resulted in a paucity of empirical experience and knowledge pertaining to cardiac output in various physiologic states as well as in disorders where the patient is not eligible to be in an ICU environment. Using the pulmonary artery catheter (PAC) for measuring CO by the thermodilution (Td) method, hitherto considered a 'gold standard', is associated with limitations. Apart from the high cost, variable accuracy and complications such as catheter related infections, arrhythmias and hemorrhage can occur with the use of PAC. Recent studies have indeed shown no evidence favouring the use of PAC in cardiac failure [1]. A recent meta-analysis of 13 studies addressing the efficacy and safety of PAC concluded that use of the catheter neither improved outcomes in critically ill patients, nor altered the mortality or days in hospital [2].

In the recent past, transthoracic electrical bioimpedance (TEB) has been increasingly explored for its ability to measure CO non-invasively. It has been examined extensively over the last three decades, both in animal models as well as in various clinical conditions. Barin et al. [3] evaluated the accuracy and precision of a thoracic bioimpedance cardiac monitor by comparing it with conventional thermodilution. A total 80 simultaneous pairs of cardiac output measurements were made by TEB and Td methods among 47 patients undergoing routine cardiac catheterization for suspected cardiac disease. They observed a mean difference of 0.31 l/min between two methods with a standard deviation of the differences being 0.76 l/min with a correlation coefficient r^2 of 0.72 ($P < 0.001$). They concluded that TEB compared favourably with Td CO and that it could be used in a cardiac catheterization laboratory for non-invasive continuous measurement of cardiac output. Similar observations were made by Shoemaker et al. [4] using a different model in a multicenter trial. Appel et al. [5] compared cardiac output measurements by bio-impedance and thermodilution methods in severely ill surgical patients and reported good correlation. Ziegler et al. [6] compared 100 simultaneous measurements of TEB cardiac output with intermittent bolus Td-CO in 52 patients requiring mechanical ventilation and reported a good correlation (r^2 = 0.89; mean bias = −0.446 l/min).

In contrast to the above reports, Hirschl et al. [7] compared TEB and arterial pulse wave form analysis with simultaneous Td-CO in critically ill patients and observed a poor correlation with the latter method. They observed a discrepancy of >0.5 l/min/m^2 among 39% of arterial pulse waveform analysis and 56% of TEB-CO measurements as compared to Td-CO. The magnitude of these discrepancies correlated significantly with age. They concluded that both these methods – TEB and arterial pulse waveform analysis – failed to be a substitute for the Td method because of substantial inaccuracy.

Few attempts at meta-analysis of the available studies on TEB to extract meaningful conclusions have been made [8, 9]. Raaijmakers et al. [9] conducted an extensive meta-analysis of the 154 available studies in different categories (animal studies, studies in healthy human subjects and those involving patients in different clinical conditions). They also looked at the influence of the reference method used. They observed an overall pooled correlation coefficient r^2 of 0.67 (95% CI – 0.64–0.71) between TEB-CO and that measured by other methods. The correlation was better in repeated measurement designs. Further, they observed a significant influence of the reference method used on the correlation coefficient. The correlation was significantly better in animal studies than in cardiac patients. Subgroup analysis revealed that TEB correlated better with indirect Fick method than echocardiography in healthy subjects. They concluded that TEB might be useful for trend analysis of different groups of patients but not for diagnostic interpretation. They also cautioned that differences between TEB and reference methods could also be due to inaccuracies in the reference method rather than in TEB.

This study was undertaken to compare the accuracy and precision of measurement of cardiac output by transthoracic electrical bioimpedance (TEB) using a novel instrument (NOCOMON, Larsen & Toubro Ltd., Mysore, India) in comparison with thermodilution method.

PATIENTS AND METHODS

Adult subjects between 18 and 80 years of age admitted to the cardiac ICU following elective cardiac surgery were recruited. The study was approved by the ethics committees of the two participating institutions. Informed consent was obtained from the patient for invasive monitoring. Patients with generalized edema, pulmonary edema, pleural effusion, overt cardiac failure, cardiac arrhythmias, pacemakers, valvular disease and hemodynamic instability (e.g. shock, fluctuating blood pressure) – conditions which may interfere with interpretation of either of the two methods of cardiac output measurement, were excluded from the study. Height, weight, chest circumference and body surface area were noted for each subject.

TEB-CO was measured using NICOMON – an instrument developed by M/S Larsen & Toubro India Ltd. (developed and standardized by Jindal et al. [10]). CO measurements were made in the supine, resting state. Two pairs of surface electrodes were applied on the sides of the neck and two pairs on the sides of the trunk along the mid-axillary line. The outer two pairs of electrodes injected an alternating current of 48 kHz, 4 mA RMS alternating current while the inner two pairs sensed the impedance changes. The analog bioimpedence signal was documented from the inner pairs of electrodes and was displayed as a graph against time. An adaptive filter was used to remove signals outside the 'cardiac' frequency, such as those due to respiration and movement. After calibrating the instrument, the basal impedance (Zo) is measured across the thorax. The signal is the sampled at 256 Hz over 25–40 consecutive cardiac cycles; a time derivative of the sequential impedance (dZ/dt) is

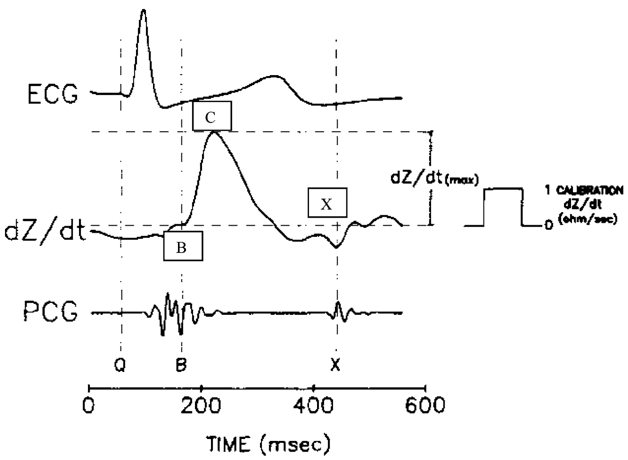

Fig. 1. Time plot of the first derivative of impedance changes (dz/dt) to transthoracic electrical transmission recorded during a cardiac cycle (middle trace) shows waveforms which are related to events on ECG and phonocardiogram (PCG). B point on the dz/dt graph corresponds to first heart sound; X corresponds to second heart sound. BX = left ventricular ejection time (LVET). (dz/dt) max is measured as the height of the curve from B to the peak of the systolic wave (C).

computed and plotted against time. This graph (Figure 1) shows important features related to the cardiac cycle, which are of significance for computing stroke volume. The various phase reversal points in this waveform are labeled as A, B, C, X, Y, O and Z. The complex BCX (called C wave) corresponds to the ventricular systole and BX, left ventricular ejection time (LVET). The amplitude BC represents the maximum rate of change of impedance (dZ/dt max) [10].

Stroke volume is then estimated using the Kubicek formula [11]:

$$\text{Stroke volume} = \text{k p}(\text{L}/\text{Z}_0)^2[\text{LVET (dZ/dt) max}]$$

where k is a constant which accounts for variation in body composition based on age, gender, relative fat content, chest circumference; L is the inter-electrode distance; p is the blood specific resistivity computed using hematocrit (13.5 + 4.29 × Hematocrit). For the purpose of this study, 'p' was calculated for a hematocrit of 45% and this was used as a constant for all subjects.

The entire measurement process was repeated thrice to ensure consistency. At each attempt, measurements which varied from the previous one by >10% were rejected; repeat measurements were obtained till consistent stroke volume values were obtained. The mean value of the three accepted stroke volume measurement was used as the 'stroke volume' for further computations. Cardiac output was then computed as the product of heart rate and stroke volume. Cardiac index was calculated for each subject as the ratio of CO and body surface area (BSA).

For measuring Td-CO, a multi-lumen PAC (Edwards, 16F) with a thermistor mounted on the tip and equipped with a 10 cm thermal filament located 15–25 cm proximal to the catheter tip was introduced into the pulmonary artery by conventional method, with all precautions. The catheter-mounted thermistor and temperature sensor ports were connected externally to a Baxter system (Irvine, CA, USA) for measuring cardiac output continuously. Low energy heat pulses are generated by the thermal element in the proximal part of the PAC (in the region of the right atrium and ventricle). This increase in blood temperature is diluted by the blood flow and is sensed sequentially by the thermistor. A thermodilution curve is generated for the cardiac cycles and the averaged cardiac output from 3 to 8 cycles is measured from the area under the curve. Stable cardiac output values over a period of 3 min of observation in a hemodynamically stable patient were documented.

Measurement of CO by the each of the two methods was performed for all subjects by two investigators independently. All CO measurements were made when the patient was hemodynamically stable in a restful state, within 2–5 min of each other. Care was taken to observe that the patient's clinical state had not changed between the paired measurements. Several pairs of measurements were made on each patient over a period of 1–4 h.

It was estimated that, to recognize a cardiac output difference of 300 ml/min (SD 1.25 l) between the two methods with a power of 0.80, at least 140 paired samples need to be compared. This study was designed to have a 95% probability (alpha=0.05) of finding a 10% difference between the two with a 10% chance of a type II error. All values are presented as mean and SD or 95% limits as appropriate. Pearson correlation coefficient (r) was determined for the pairs of cardiac output measurements. Mean cardiac output, bias (measured as the mean difference between the cardiac outputs from the pairs of methods), precision (±2 SD of the difference between the cardiac outputs from the pairs of methods) and percentage error of measurement (ratio of precision to mean cardiac output of the two methods) were computed for each pair as recommended by Bland and Altman [12] and Critchley and Critchley [13]. A $P < 0.05$ was considered to be significant. Statistical analysis was performed using SPSS 11.0 statistical package.

RESULTS

Forty two patients admitted to the cardiac ICU were considered for this study between December 2004 and March 2005. Of these seven were excluded due to presence of arrhythmias (n = 4) or pulmonary or systemic edema (n = 3). A total of 35 patients (mean age 53 ± 8.7 years; M:F::29:6) underwent paired TEB and TD CO measurements during either first or second post-operative day. Thirty-four of these had undergone coronary artery bypass surgery while one patient had mitral valve surgery. Twenty patients were on ventilator; 11 were on intra-aortic balloon pump and 22 were on vasopressors at the time of the study. None of these patients had ongoing arrhythmias, pulmonary or systemic edema, pneumothorax or pacemaker placement.

A total of 197 pairs of CO measurements with TEB and Td were made among these 35 patients. Three patients had single pairs of measurements available while the rest had 3–14 paired measurements made over 1–4 h of observation. Table 1 summarizes the comparison of these measurements. The mean TEB-CO was 5.15 ± 1.27 l/min and Td-CO was 5.22 ± 1.28 l/min. Pearson correlation coefficient (r) for these cardiac outputs was 0.856 ($P < 0.01$). The bias was −0.0651 l/min (TEB-CO was lower than Td-CO by a mean of 65 ml/min). Ninety-five percent limits of agreement were between +1.3 and −1.44 l/min. Ten measurements (5%) fell outside the 95% limits of agreement. The precision was ±1.37 l/min. The percentage error of measurement of this precision as compared to the average to the two methods of cardiac output was 26.44%. Figure 2 shows the correlation of the two measures and Bland Altman analysis. The regression line on the graph plotting the difference in cardiac output against the average cardiac output was horizontal, suggesting that there was no effect of magnitude of measurement on the difference between the two methods. Paired cardiac output values did not differ among patients with or without ventilation, vasopressor support or aortic balloon pump placement. Cardiac index also correlated among the two methods (r = 0.789; P = 0.01).

Table 1. Comparison of Cardiac output (CO) measured by Thoracic electrical bioimpedance (TEB) and Thermodilution (Td) among 35 post-cardiac surgery patients

	TEB-CO	Td-CO
n^*	197	197
Minimum (L/min)	2.78	2.90
Maximum (L/min)	8.60	8.90
Mean (L/min)	5.1537	5.2188
Std. deviation	1.27270	1.27935
Correlation coefficient	0.856 ($P < 0.01$).	
Bias	0.0651	
Precision	1.37	
% Error	26.44%	

n^* = 197 paired measurements obtained from 35 patients.

DISCUSSION

Advancing technology has generated a strong drive towards developing non-invasive tests for revealing the structure and function of the body. In particular, cardiac physiologic studies, though recognized to be vital in managing critically ill patients, have been slow to yield to non-invasive methods of study. The use of the pulmonary artery catheter, till recently considered the standard method, is now recognized to have no advantage in varied situations. This, together with the advancing technology has been an impetus to develop noninvasive methods of measuring cardiac physiologic parameters. This study was performed to evaluate a novel instrument designed to measure CO using principles described by Kubicek et al. [11].

This study of paired TEB and Td CO measurement in 35 post-cardiac surgery patients showed a good correlation between the two methods. This observation is consistent with other recent reports where TEB has been studied with improved methodology. This study used the Kubicek equation for estimating stroke volume. Attempts at improving the estimation of stroke volume using the Kubicek equation have led to development of at least three additional modifications. Very few studies have compared the Kubicek equation and its modifications, with variable claims as regards accuracy. A meta-analysis of articles addressing accuracy of TEB by Raaijmakers et al. [9] concluded that the Kubicek equation for estimating CO was superior to Srameck-Bernstein equation, particularly in critically ill patients. A more recent study by Van De Water et al. [14] compared four different modifications of the Kubicek equation with TD-CO among post-coronary artery surgery patients and concluded that the most recent version – a proprietary modification of Sramek-Bernstein (ZMARC impedance-modulating aortic compliance) – to be most accurate. However, in view of the absence of any consensus, the original Kubicek equation was chosen for estimating stroke volume in this study. Also, a constant resistivity value was used for all subjects rather than one that is computed for each individual based on measured hematocrit, as both these methods have been shown to be comparable [9].

The design of this study confirms to that expected of one aimed at comparing performance of different devices measuring a single parameter. Most patients received multiple paired measurements with the two methods (TEB and Td) over time, in standardized settings. The same two operators were involved in obtaining the measurements during the entire study. Interventions such as ventilation, vasopressors, intra-aortic balloon pump, etc did not significantly influence the measurements. Comparison of the two methods was performed using

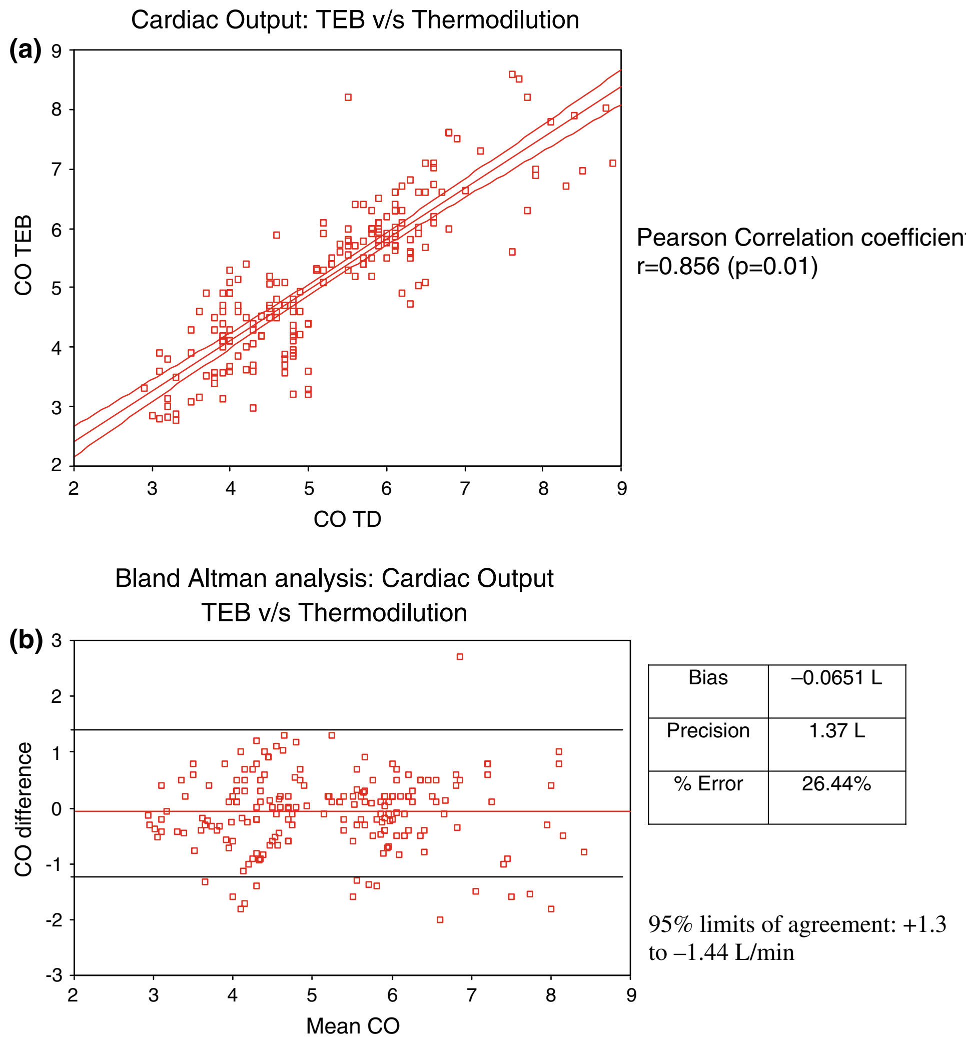

Fig. 2. Comparison of 197 paired cardiac output measurements by TEB and Td methods from 35 post-cardiac surgery patients monitored in ICU. (a) Correlation of cardiac outputs measured by TEB-CO and Td-CO. X & Y axes: Cardiac ouput in l/min. (b) Bland Altman analysis of the data. X: Mean of TEB and TD CO for each pair of data. Y: CO difference.

recommended methods [12, 13]. Interventions such as mechanical ventilation, intercostal drainage and vaso-pressor administration, though used in a significant proportion of patients, were observed not to influence comparability of CO measurements in this study.

The mean difference in cardiac output measured by TEB and thermodilution in this study was small – about 65 ml/min (TEB-CO being lesser). This difference was not influenced significantly by the magnitude of cardiac output measured. Further, repeated measurements did not result in increased variation between the two methods. It was estimated that with the present 197 paired measurements showing a mean difference of 0.065 l/min between the two methods, at a significance level of 0.05, the statistical power achieved was about 90%. The percentage error of measurement of the precision in this study as compared to the average to the two methods of cardiac output was 26.44% – which is within the acceptable limit of 30% [13].

Van de Water et al. [14] recently reported a study comparing TEB and thermodilution cardiac output among 54 post cardiac surgical patients in whom 210 paired measurements were made. They observed an overall correlation coefficient of 0.811 with a bias of −0.17 l/min and precision of 1.09 l/min. These observations are comparable to those in the present study. Both these studies substantiate the conclusion that TEB is a reliable method for monitoring cardiac output among post – cardiac surgical patients. Discrepant reports, however, do exist. For example, Thomas et al. [15] observed that

TEB-CO values obtained in the first 12 h after coronary artery bypass surgery were not reliable as compared to thermodilution in the ICU. Koobi et al. [16] note that whole-body impedance cardiography (which differs from conventional TEB method) reliably measured cardiac output among similar patients and that TEB had excellent repeatability, facilitating continuous monitoring of patients after the operation.

Most recent reports appear to reflect a good correlation between TEB and thermodilution methods in varied patient groups – ranging from acutely ill emergency room patients to post-operative ICU patients. Few studies, however, have compared TEB with another conventional method among non-ICU patients. A large multicenter study of TEB among patients with trauma, medical intensive care and surgical intensive care patients (n = 2192) by Shoemaker et al. [4] showed an overall good correlation coefficient of 0.85 with thermodilution method. This study supports the utility of TEB in a wide variety and severity of clinical disorders, particularly to follow trends. The observations in our study also matches the pooled correlation (r^2 = 0.67) of 112 studies reported in a meta-analysis by Raaijmakers et al. [9].

Some of the limitations of this study are rather short periods of comparison of methods in each patient, absence of blinding between the two methods, exclusion of some patients in whom TEB was expected to be difficult to interpret (e.g. pulmonary edema, arrhythmias, etc.), and lack of measurements tracking spontaneous hemodynamic changes during ICU observation or response to interventions.

In summary, TEB CO measured using this novel instrument correlates well with Td-CO measurements among post-cardiac surgical patients. Using TEB to monitor such patients in the postoperative period would be advantageous given its non-invasive nature and lower cost as compared to PAC. Studies to explore the reliability of this novel non-invasive method over extended periods of monitoring in the ICU appear warranted. These should address ability of TEB trends to accurately track changing hemodynamic parameters and response to therapeutic interventions so as to demonstrate its utility in the situations where it would be most useful. Having established the reliability of TEB in the ICU, future studies could also address its utility in hemodynamic monitoring in non-acute situations outside the ICU.

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