NON-INVASIVE MEASUREMENT OF CARDIAC OUTPUT BY THORACIC ELECTRICAL BIOIMPEDANCE: A STUDY OF REPRODUCIBILITY AND COMPARISON WITH THERMODILUTION

C. JEWKES, J. W. SEAR, F. VERHOEFF, D. J. SANDERS AND P. FOËX

SUMMARY

The performance and reproducibility of the BioMED NCCOM3 thoracic electrical bioimpedance cardiograph (TEB) has been evaluated in volunteers and patients. In resting supine volunteers, we determined the coefficient of variability over short time periods (30 min) and over several days, and examined the effects of differences in electrode type and electrode placement. The mean (range) intra-subject coefficients of variation (CV) for thoracic fluid index (TFI) and stroke volume (SV) were 1.0% (0.4–1.8%) and 4.7% (2.1–8.5%), respectively over a 30-min period. The corresponding CV were 5.6% (2.3–10.9%) and 10.9% (6.1–14.8%) for measurements made at rest on four separate occasions. Use of different electrode types (RedDot and Medicotest) resulted in differences in TFI (P < 0.01), but not in mean values for SV or cardiac output (Q); their use in individual subjects revealed differences of up to 20% in SV and Q. Alterations in electrode placement by 5 cm in the horizontal and diagonal planes produced no significant changes in TFI, SV or Q; changes in the longitudinal plane produced a graded change. Increases of 5 cm and 10 cm in thoracic length produced mean increases in TFI of 9.8% and 39.8%, respectively, and mean decreases in Q of 8.4% and 16.7% and SV of 7.5% and 15.8%. TEB measurements of Q and SV were compared with thermodilution (TD) in 16 intensive care patients. Mean (SEM) Q by TEB was 5.63 (1.10) litre min⁻¹ compared with TD 4.38 (0.72) litre min⁻¹ (P < 0.01). The correlation coefficient for Q (r) was 0.72, producing the equation $Q_{TEB} = 0.835 \times Q_{TD} + 1.13$; that for SV was $r = 0.83$, $SV_{TEB} = 1.009 \times SV_{TD} + 6.84$. Bias between the two methods revealed a mean difference of $-0.86$ litre min⁻¹ (95% confidence limits $-2.6$ to $+0.89$) for Q, and $-13$ ml ($-35.2$ to $+9.2$) for SV. Analysis of individual patient bias plots revealed two different trends. If the range of Q values was < 1.0 litre min⁻¹, there was a variable bias of magnitude similar to that seen in the volunteer studies. If values of Q had a range of > 1.0 litre min⁻¹, there tended towards a constant bias for that individual patient, indicating that TEB is able to follow trends.

KEY WORDS

Measurement techniques, cardiac output, thoracic electrical bioimpedance.

The technique of thoracic electrical bioimpedance (TEB) was introduced into clinical practice by Kubicek and colleagues [1] in 1966. Since then, several studies have reported comparisons of the method with various other techniques for measuring cardiac output (Q) [2–8]. These studies have reported different correlation coefficients, varying from good ($r = 0.97$ [4]), to poor ($r = 0.41$ [8]). The original Kubicek formula for stroke volume (SV) was:

$$SV = \rho (L^2/Z_0^2) \cdot (dZ/dr)_{max} \cdot LVET$$

where $\rho$ = resistivity of blood; $L$ = distance between the two inner electrodes; $Z_0$ = mean basal


Correspondence to C. J.
thoracic impedance; \( \frac{dZ}{dt} \) = first derivative of impedance; LVET = left ventricular ejection time.

A new impedance cardiograph, the BoMED NCCOM3 (Irvine, CA) has improved on several disadvantages of the original Minnesota Impedance Cardiograph. It has replaced the band electrodes with pairs of standard ECG electrodes, which improves patient acceptance. It also has an integrated computer using a new algorithm based on the Bernstein-Sramek formula [9] which allows on-line calculation of SV and \( Q \). There have been several studies comparing the NCCOM3 with thermodilution (TD) [8, 10-13] and these have shown reasonable correlation coefficients. However, apart from incidental reports, there has been no evaluation of the variability and reproducibility of the NCCOM3, or study of the effects of different electrode types and positions.

PATIENTS AND METHODS

Variability

This phase of the evaluation comprised four parts. In each part, normal volunteers were studied in the supine position at rest and recordings made after a 20-min stabilization period. The BoMED NCCOM3 was used to measure cardiac output, stroke volume, heart rate (HR), and basal impedance \( (Z_0) \) or thoracic fluid index (TFI).

Two "sensing" electrode pairs were placed on the thorax at the level of the xiphisternum in the mid-axillary line and on the lateral aspect of the neck immediately above the clavicles. The other two pairs of the "current injecting" electrodes were placed 5 cm above the cervical and below the thoracic sensing electrodes. The current injecting electrodes deliver a 2.5-mA, 70-kHz, alternating current. The NCCOM3 calculates SV from the Bernstein—Sramek formula [9]:

\[
SV = \text{VEPT} \times \text{VET} \times \frac{(dZ/dt_{\text{max}})}{Z_0}
\]

where VEPT is volume of electrically participating tissue (calculated as \( d[(0.17H)\text{P}]/4.25 \), where \( d \) is a scaling factor proportional to the ratio observed: ideal weight, \( H = \) height in cm), VET is the ventricular ejection time, \( dZ/dt_{\text{max}} \) is the rate of change of impedance during systole, and \( Z_0 \) (or TFI) is the basal thoracic impedance. The NCCOM3 was set to average 16 beats and all digital output were recorded on a Thinkjet Printer (Hewlett-Packard). The analogue output from the NCCOM3 was recorded also on a chart recorder, to permit examination of the \( dZ/dt \) waveform.

In the first group of subjects, the electrodes were placed in the position recommended by the manufacturer and a non-invasive arterial pressure cuff was applied to the upper arm. After the 20-min stabilization period, recordings were made of TFI, SV, \( Q \), HR and systolic, diastolic and mean arterial pressures (Dinamap 845XT, Critikon) every 5 min for 30 min. For TEB data, three readings were averaged over the time taken to record the arterial pressure. Reproducibility for each subject was calculated as the coefficient of variability for each cardiovascular variable.

In the second group of subjects, variability was studied over several days. The electrodes were placed in the manufacturer recommended positions, and after a 20-min stabilization period TFI, SV, \( Q \) and HR were recorded for 10 readings. The subjects repeated this procedure on four occasions with an interval between tests of at least 12 h.

In a third group of subjects, the effect of different electrode types was studied. The initial electrodes were Medicotest (Olstakkke, Denmark), which were replaced by RedDot (3M, Canada) and TFI, SV, \( Q \) and HR re-recorded. Ten readings for each variable and for each electrode type were averaged and the reproducibility was expressed as the coefficient of variability.

In a fourth group of subjects, the influence of alteration of electrode position was studied. Electrodes were placed initially in the recommended positions and moved sequentially by 5-cm increments in the frontal, sagittal and diagonal planes. TFI, SV and \( Q \) were recorded with each electrode configuration, and an average of six consecutive readings compared with those measured with electrodes in the recommended positions.

Comparison of TEB with thermodilution

The second part of the evaluation consisted of a comparison of simultaneous measurements of SV and \( Q \) by thoracic electrical bioimpedance (TEB) and thermodilution (TD) methods. Local Hospital Ethics Committee approval was obtained.

The patients investigated were admitted to the Intensive Care Unit (ITU) and had pulmonary
artery (PA) catheters inserted and cardiac output measurements made for clinical indications. Patients were excluded if they were in septic shock, had severe arrhythmias, or were too unstable. Thermodilution measurements were made using ice cold saline 10 ml at end-expiration. Cardiac output was calculated using the standard commercially available American Edwards Cardiac Output Computer (COM-1). All measurements were taken as the average of three consecutive readings, and the data used only if there was less than 10% variation between the readings. Thoracic electrical bioimpedance (TEB) measurements were made using the BoMED NCCOM3 as described earlier, with the electrodes placed in the recommended positions. TEB measurements were made as an average of 16 beats, and the readings were made simultaneously with the TD readings. Thus three TEB readings were averaged (giving 3 x 16 = 48 beats) to correspond to one TD reading.

Data were analysed to determine the correlation coefficient between the two methods by estimating SV and Q, and the presence of bias was assessed by the method described by Bland and Altman [14]. In addition, an assessment of the ability of TEB to follow haemodynamic trends was made by examining the bias plots for individual patients.

Data handling. Data measured by the different techniques were compared using the correlation analysis and the Wilcoxon matched pairs signed ranks test; data recorded using different electrodes in the same subjects were compared using the sign test and Wilcoxon test. Data are presented as mean (sd) or mean (range), unless otherwise indicated.

Statistical significance was assumed at P < 0.05.

RESULTS

Volunteer Studies

Individual variability

Reproducibility during supine period at rest. Sixteen healthy volunteers (age 19–55 yr; weight 51–81 kg) were studied. Resting heart rates (HR) and mean arterial pressures (MAP) varied between 51 and 88 beat min⁻¹ and 76 and 104 mm Hg, respectively.

The mean resting thoracic fluid indices (TFI) for all subjects was 26.2 (sd 0.26) Ω. The range of individual coefficients of variation (CV) for TFI was 0.4–1.8%. Resting mean stroke volumes (SV) and cardiac outputs (Q) varied between 66 and 180 ml, and 4.7 and 10.5 litre min⁻¹. The average coefficients of variation (calculated as the mean of the individual CV when determined from the seven sets of observations collected over the 30-min study period) are shown in table I. There were no differences in the magnitude of the CV for any of the four haemodynamic variables.

Reproducibility during supine period at rest on four different occasions. Nine male subjects (age 28–42 yr; weight 60–87 kg) were studied at rest on four occasions to assess variability in TFI, HR, SV and Q with time. All measurements were made using Medicotest ECG electrodes. The average values for each subject, calculated from the mean of each of the four separate occasions, were calculated; each individual data set being the mean of 10 bioimpedance readings. The intrapatient average for TFI over the four occasions varied between 22.5 and 29.3 Ω; the average CV was 5.6% (range 1.9–13.1%).

The inter-day coefficients of variation for the other variables were: HR, average CV 7.5%, range of individual CV 4.6–11.0%; SV, average CV 10.9%, range 6.1–14.8%; Q, average CV 8.7%, range 2.1–17.5%.

Influence of electrode type on TFI and SV

The influence of electrode type on TFI (and calculated SV) was assessed in 10 subjects on 44 occasions; for each data set TFI and SV were the mean of 10 readings following a period of 20 min resting supine.

There was a significant difference between values for TFI (mean values for TFI were 26.9 (sd 2.4) Q and 25.3 (2.2) Q, respectively, for RedDot and Medicotest electrodes (P < 0.001)); the mean

| TABLE I. Mean values for each haemodynamic variable, average coefficient of variation (CV) and range of CV for all 16 subjects studied on a single occasion over a 30-min period at rest. MAP = Mean arterial pressure (calculated as systolic pressure + 2 diastolic pressure/3); HR = heart rate; SV = stroke volume; Q = cardiac output |
|-----------------------------------------------|----------------|---------------|
| MAP (mm Hg)                                  | 88.5           | 3.4           |
| HR (beat min⁻¹)                              | 65             | 4.8           |
| SV (ml)                                      | 110            | 4.7           |
| Q (litre min⁻¹)                               | 7.0            | 5.1           |

Mean | CV (%) | Range of CV (%)
Influence of electrode position

In six volunteers (age 20–42 yr; weight 54–78 kg), the influence of changing the position of the sensing and current injecting electrodes was studied (fig. 1). Alterations in electrode position in either the diagonal or frontal planes resulted in less than 5% changes in TFI and SV. Likewise, changes of electrode position such that the effective inter-electrode position was increased by 5 cm by movement of the cervical electrodes also resulted in less than 5% changes in TFI and SV.

When the inter-electrode distance was increased by 5 cm by movement of the thoracic electrodes, there was a mean increase in TFI of 9.8% (P < 0.05), and decrease in SV of 7.5% (ns). These changes were of the same magnitude as those of the coefficients of variation found in the first group of subjects studied. However, when the inter-electrode distance was increased by 10 cm, there was a mean increase in TFI of 39.8% (P < 0.05) and mean decreases in SV of 15.8% (P < 0.05).

Patient Studies

Comparison of bioimpedance with thermodilution

Sixteen patients in the ICU were studied during controlled ventilation after aortic surgery, after abdominal surgery or for acute respiratory failure. No patient had clinical signs of systemic sepsis. The data collected provided 160 simultaneous measurements of cardiac output (Q) and stroke volume (SV).

The mean (SEM) Q by bioimpedance was 5.63 (1.10) litre min⁻¹, compared with a mean of 4.38 (0.72) litre min⁻¹ for thermodilution. The correlation of the two methods for cardiac output yielded the equation $Q_{\text{TEB}} = 0.853 \times Q_{\text{TD}} + 1.13$ and a correlation coefficient $r = 0.72$ ($P < 0.001$). The mean (SEM) SV by bioimpedance was 68.8 (18.9) ml compared with a mean of 55.8 (16.3) ml measured by thermodilution. The corresponding equation for stroke volume was $SV_{\text{TEB}} = 1.009 \times SV_{\text{TD}} + 6.84$, with a correlation coefficient $r = 0.83$ ($P < 0.001$). However, the correlation coefficient describes only the association of one method with another; not the agreement of the results. Therefore the difference between measurements (TD minus TEB) was plotted

\[ \text{RedDot minus Medicotest} \]

the range of differences was -2.0 to 4.5 $\Omega$. This resulted in a mean difference for SV of 4.0 ml (range of differences -39 to 38 ml).
Fig. 3. Individual bias plots for two representative patients. 
A: Constant bias found in most patients; B: variable bias as a result of the intrinsic variability found in a given individual for repeated determinations of a constant cardiac output. CO = cardiac output (average value of thermodilution and thoracic electrical bioimpedance); Difference = (thermodilution minus thoracic electrical impedance).

against the corresponding means of the two methods [(TD + TEB)/2] together with the 95% confidence limits (fig. 2). The mean difference for cardiac output was $-0.86 (-2.6$ to $+0.89)$ litre min$^{-1}$ and that for stroke volume $-13 (-35.2$ to $+9.2)$ ml.

Figures 3A and B show individual bias plots representative of two different groups of patients. Most patients showed a constant bias for both $\dot{Q}$ and SV (fig. 3A). Here the patient has a bias of $-0.15$ litre min$^{-1}$ over a range of $\dot{Q}$ values between 5.7 and 7.4 litre min$^{-1}$. However, in a few patients there was an apparent variable bias (fig. 3B). In these patients, the range over which cardiac output measurements have been recorded was narrow.

**DISCUSSION**

The major advantage of the thoracic electrical bioimpedance (TEB) method for measuring cardiac output ($\dot{Q}$) and stroke volume (SV) is the ease with which it can be learnt and applied by the clinician. The NCCOM3 also has the advantage of on-line analysis and the provision of beat-to-beat information.

Our results showed that for normal subjects the variability of TEB measurement of $\dot{Q}$ and SV was of the same magnitude as for other cardiovascular variables (e.g. HR and MAP). Similar estimates for variability have been reported by Veigl and Judy using the earlier Minnesota Impedance Cardiograph [15] and Wong and colleagues [16]. Dye dilution and thermodilution methods of measuring cardiac output give comparable estimates of variability: Fischer and colleagues [17] reported a variability of $7\%$ for $\dot{Q}$ measured by dye dilution and while Sleeper and colleagues [18] showed a variability of $6\%$ for dye dilution if the same arterial site was used for sampling, but a variability of $20\%$ if different arteries were used for sampling. The variability of thermodilution depends on several factors, including volume and temperature of injectate and relationship to the ventilatory cycle. Stevens and colleagues [19] reported a coefficient of variation of $4\%$ for thermodilution measurements when they were timed to peak inspiration or end-expiration; but $10\%$ if the injections were made randomly throughout the ventilatory cycle. Runciman, Ilsley and Roberts [20], in a detailed examination of the factors affecting variability of thermodilution, concluded that, despite attention to detail, a $10\%$ variability in cardiac output measurement existed when compared with dye dilution techniques. Stetz and colleagues [21] investigated the reproducibility of commercially available thermodilution devices, and concluded that there must be a minimum difference of $12-15\%$ between triplicate determinations of $\dot{Q}$ to suggest a change of clinical significance. Our coefficients of variation were $4.7\%$ for SV and $5.1\%$ for $\dot{Q}$ over a single 30-min study period.

Inter-day variability was greater. This reflects, in part, normal physiological variations for which it is virtually impossible to standardize (e.g. factors such as the time of day, relationship to ingestion of food and emotional state affect basal or resting cardiac output). Coefficients of variation for SV and $\dot{Q}$ of $10.2\%$ and $8.5\%$, respectively, again compare well with those reported by Veigl and Judy [15].

One of the main sources of observer error of the TEB method relates to the placement of the electrodes and the electrode type. Alteration of
electrode type in normal healthy volunteers gave changes of 19%, 22% and 19%, respectively, for TFI, SV and Q. One explanation may be that different electrode types change the skin-electrode interface which would, in turn, affect the dynamic component of the impedance signal.

Any alteration in electrode position should alter \( Z_0 \) as this is proportional to \( L \)—the length of the volume conductor through which the impedance changes are measured. The NCCOM3 uses the Bernstein–Sramek formula [9], where SV is proportional to VEPT, and inversely proportional to \( Z_0 \). VEPT is proportional to \( H^2 \) which is proportional to \( L^2 \). Therefore SV and \( Q \) are proportional to \( L^2 \). If the normal inter-electrode distance is assumed to be 30 cm, an increase in the distance by 5 cm should increase SV (and hence \( Q \)) by 26%, and an increase of 10 cm should result in an increase in SV of 40%. These are much larger than the changes of 8% and 16% we recorded with changes in electrode position. This is caused by the internal algorithm in the NCCOM3 [9] which includes the factor \( \delta \)—a correction factor for changes in the body habitus from ideal. The magnitude of \( \frac{dZ}{dr_{max}} \) is dependent also upon the sensing electrode distance and the value of \( Z_0 \) [9, 22, 23].

Other studies have compared the TEB method for determining \( Q \) and SV with TD [6, 8, 10–13, 24], dye dilution [3, 4], the direct Fick method [7, 25], the indirect Fick (carbon dioxide rebreathing) method [26] and Doppler ultrasound [8, 13, 25, 27]. There has been wide variation in the reported correlation coefficients for TEB against TD— from 0.41 [28] to 0.93 [6]. These differences can be attributed, in part, to the different populations studied.

Another factor contributing to the variation in correlation coefficients is the different reference techniques used for comparison. These all have their own variability and sources of inaccuracy [17, 19–21]. Even the direct Fick method has been shown to have a variability of around 8% [29]. These sources of variability and inaccuracies are not necessarily the same as those of the technique being investigated and thus, in comparisons, differences may be compounded. None of the reference techniques is therefore a true "gold standard", while the correlation coefficient reflects only a measure of association between two methods, not agreement.

A more relevant way to assess agreement is to construct a bias plot examining the variability between the two methods over the whole range of results [14]. Our data show a variable bias for \( Q \), with 95% confidence limits of \(-2.6 \) to \(+0.89 \) litre \( \text{min}^{-1} \). This is a larger range than that reported by Northridge and colleagues [27] for spontaneously breathing patients after infarction, but similar to the values of Wong and colleagues [8] and Siegel and colleagues [13].

Wong noted the best agreement between bio-impedance and thermal dilution in patients who had not undergone aortic or open heart surgery [18]. In these patients, errors may occur because of intrathoracic fluid shifts, aortic manipulation or changes in PCV. Wong also noted that mechanical ventilation (as in all of our patients) had no effect on the agreement between the measurement techniques. In comparison with the study by Northridge and colleagues [27], the greater variability in our study reflects the larger number of comparisons (160 vs 25 data points) and a greater range of cardiac output (\( Q \)) values (2.6–8.5 litre \( \text{min}^{-1} \) compared with 1.1–6.2 litre \( \text{min}^{-1} \)).

Our results suggest that TEB overestimates at low and underestimates at high values of cardiac output, despite the NCCOM3 having an internal algorithm which is designed to compensate for these changes in \( \frac{dZ}{dr_{max}} \) at low cardiac outputs. An explanation for this phenomenon may be the alteration in distribution of blood flow in the thorax at low and high cardiac outputs, which in turn may lead to alterations in the relative contributions of the various impedance changes making up the global impedance change measured by the NCCOM3 [9]. These discrepancies between the two methods for cardiac output measurement may further lie in the different physical principles utilized by the techniques; and hence a good correlation under one set of physiological circumstances (e.g. IPPV) may not be seen under another (e.g. spontaneous ventilation).

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