COMPARISON OF THORACIC ELECTRICAL BIOIMPEDANCE AND THERMODILUTION FOR THE MEASUREMENT OF CARDIAC INDEX IN PATIENTS WITH SEVERE SEPSIS

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SUMMARY
Cardiac index was measured using thoracic bioimpedance (Clbi) and thermodilution (Cltd) in 19 patients with proven sepsis, undergoing artificial ventilation of the lungs. There was a poor correlation between the techniques (r = 0.36, 242 data sets, regression line Clbi = 0.16 Cltd + 2.56 litre min^{-1} m^{-2}). The overall bias (Cltd - Clbi) was 1.69 litre min^{-1} m^{-2} with limits of agreement (precision) of +4.17 to -0.79 litre min^{-1} m^{-2}. In individual patients the bias was from -0.46 to 4.56 litre min^{-1} m^{-2} with the limits of agreement from +0.29 to +2.55 litre min^{-1} m^{-2} around the bias values. The two techniques cannot be used interchangeably in this group of patients. (Br. J. Anaesth. 1993; 70: 58-62)

KEY WORDS

Variations in the electrical impedance of the thorax to an alternating current (Z) which occur synchronously with the cardiac cycle were observed nearly 40 years ago [1]. The first use of this phenomenon to measure stroke volume and cardiac output was described by Nyboer [2] and developed by Kubicek and colleagues [3, 4]. The method uses the maximum rate of change of thoracic bioimpedance, (δZ/δt)max during systole to calculate stroke volume. The original equation used by Kubicek and colleagues was modified by Bernstein [5] to remove assumptions about body morphology. This equation is used to calculate stroke volume in a commercially available impedance cardiograph, the NCCOM-3 (BoMed Medical Manufacturing Ltd), which also measures heart rate and then calculates cardiac output and index. It is non-invasive, requiring only the application of 10 electrodes to the neck and chest, and provides a continuous estimate of cardiac index. The device has many potential applications, for example a continuous measure of cardiac output combined with a pulse oximeter and a mixed venous oximetry pulmonary artery catheter would allow continuous monitoring of oxygen delivery and consumption. However, during initial assessment of this device in our Intensive Care Unit, it became apparent that in patients with severe sepsis the cardiac indexes determined by thermodilution and by bioimpedance often differed. We report a comparative study of the NCCOM-3 and thermodilution for measurement of cardiac index in patients with severe sepsis.

PATIENTS AND METHODS
The study was approved by the institutional Ethics Committee. Patients were selected for study if they already had a pulmonary artery catheter placed for haemodynamic assessment and clinical signs consistent with systemic sepsis [6], with either microbiological evidence of a source of sepsis or positive blood cultures. All patients were undergoing mechanical ventilation of the lungs using intermittent mandatory ventilation or controlled ventilation. No alterations in therapy were made for the purpose of the study.

We studied 19 patients, usually twice daily whilst they were clinically septic. Five patients had a perforated viscus, two had pancreatitis, four had pulmonary infection, four had sepsis following trauma, two had infection following aortic aneurysm surgery, one patient had toxic shock syndrome and one had an infected hip arthroplasty. A total of 242 pairs of measurements were made.

Cardiac index was determined from thoracic bioimpedance changes using the NCCOM-3 device (revision 6 software [7]). Eight current injection and voltage sensing electrodes were placed on the neck and thorax and two additional electrodes were placed on the right sternal border and over the apex beat to provide a high-quality ECG signal. All the electrodes were placed according to the manufacturer’s instructions, and electrodes were left in place between measurements unless they interfered with the patient’s care. Neck dressings for internal jugular catheters were removed to allow electrode positioning where required. The ECG and bioimpedance (δZ/δt) signals were taken from the analog output port on the NCCOM-3 to a twin-channel chart recorder (Lectromed Ltd) to allow a visual check on the signal quality. The NCCOM-3 digital output often differed. We report a comparative study of the NCCOM-3 and thermodilution for measurement of cardiac index in patients with severe sepsis.

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port was connected to a "Thinkjet" printer (Hewlett-Packard Ltd) to provide a permanent printed record. The patient's sex, height and weight were introduced into the NCCOM-3 keyboard, and the calculated body surface area recorded. Cardiac index was taken as the average during 60 heartbeats accepted by the NCCOM-3 recorded at the same time as the thermodilution measurements.

Thermodilution determinations of cardiac output were performed using a COM-1 cardiac output computer (Edwards Laboratories) with a closed injectate delivery system and in-line temperature sensor ("CO-set" system, Edwards Laboratories). Injectate temperatures were always less than 10 °C, and injections were made manually during expiration. Measurements were always made by one of the authors; the average of three measurements was used. Cardiac output was converted to cardiac index using the body surface area calculated by the NCCOM-3 thoracic bioimpedance computer.

The results were analysed using linear regression analysis and by the method described by Bland and Altman [8] for comparing two methods of measurement, which allows bias and precision to be assessed numerically and graphically.

The NCCOM-3 calculates cardiac output by using the formula:

\[ \dot{Q} = HR \times V_{EPT} \times VET \times \delta Z / \delta \text{max} / Z^0 \]

where \( \dot{Q} \) = cardiac output (litre min\(^{-1} \)); HR = heart rate (beat min\(^{-1} \)); VET = ventricular ejection time (s); \( Z^0 \) = baseline thoracic impedance (Ω); \( \delta Z / \delta \text{max} \) = maximum rate of change of thoracic impedance during systole (Ω s\(^{-1} \)). \( V_{EPT} \) is the volume of electrically participating tissue, calculated as:

\[ V_{EPT} = d \times (0.17 \times H)^{3/4} / 4.25 \]

where \( H \) = height (cm); \( d \) = ratio of actual to ideal weight multiplied by the ratio of the calculated thoracic blood volume to the calculated ideal thoracic blood volume [5].

The cardiac output is scaled with the body surface area calculated from height and weight (body surface area = [height in cm]\(^{0.726} \) x [weight in kg]\(^{0.418} \) x 0.00718) to obtain cardiac index. To determine if one factor caused the difference or ratio between cardiac index measured by the two techniques, both the difference and ratio of the two stroke volume measurements were regressed against the values for heart rate, height, weight, \( Z^0 \) and ventricular ejection time (determined by the NCCOM-3) using multiple linear regression. The ventricular ejection time was also computed from the heart rate using the formula described by Weisssler and Garrard [9] and compared with the ratio and difference of the two stroke volume measurements using linear regression. The stroke volume was used for the regressions to minimize mathematical linkage of the values being regressed.

RESULTS

The scatter plot of cardiac index measured by bioimpedance against cardiac index measured by thermodilution is shown in figure 1. The regression line is \( y = 0.16x + 2.56 \); the correlation coefficient 0.36. There is a large scatter in the results.

If the data are presented as the difference between simultaneous cardiac index estimates plotted against the mean of the values, a plot as shown in figure 2 [8]. This accentuates what the regression line revealed: there is generally an increasing error with increasing cardiac index. The bias is 1.69 litre min\(^{-1} \) m\(^2\) with limits of agreement of ±2.48 (+4.17 to -0.79) litre min\(^{-1} \) m\(^2\). The limits of agreement represent the 95% confidence limits for the estimate of a value of cardiac index that would be recorded by bioimpedance for a given value of cardiac index determined by thermodilution in the range 2-8 litre min\(^{-1} \) m\(^2\).

The linear regression line for cardiac index measured by the NCCOM-3 on cardiac index measured by thermodilution has a large offset (2.56 litre min\(^{-1} \) m\(^2\)) and a low gradient (an increase of 0.16 litre min\(^{-1} \) m\(^2\) in the NCCOM-3 reading for every litre min\(^{-1} \) m\(^2\) increase in the thermodilution value). If this is regarded as a "calibration" error in the NCCOM-3, this can be corrected mathe-
in critical care units has facilitated comparison of cardiac output measured by thermodilution and bioimpedance in seriously ill patients [23–30]. These comparisons showed regression lines with gradients less than 1 (0.28–0.98) and positive intercepts (0.35–2.61 litre min⁻¹). Thus the bioimpedance technique would be expected to indicate a cardiac output that exceeds the output measured by thermodilution at low cardiac outputs, but would underestimate at higher cardiac outputs. The correlation coefficients for these studies ranged from 0.41–0.91. All these studies with the exception of that by Donovan and colleagues [29] used the NCCOM-3 impedance cardiograph.

The use of correlation coefficients to compare two methods of measurement has been criticized as they do not give any indication of the error that can be expected when one method of measurement is substituted for another. To overcome this, the method of Bland and Altman [8] may be used to estimate the bias and precision of one method compared with another. Gotshall, Wood and Miles [24] and Wong and colleagues [26] used the technique to compare cardiac output measured by thermodilution and bioimpedance in critically ill patients. They showed bias values of −0.67 and −0.03 litre min⁻¹ and “limits of agreement” of +2.77 to −4.11 litre min⁻¹ and +3.24 to −3.30 litre min⁻¹, respectively. As a result, both groups urged caution in the use of bioimpedance as a monitor of absolute values of cardiac output.

The comparison of thermodilution and bioimpedance measurements of cardiac output in patients with sepsis has not been examined directly. Bernstein [27] observed that in vasodilated septic patients the bioimpedance method underestimated cardiac output, and suggested this was caused by shunting of the current via vasodilated skin and muscle, thus bypassing the lungs and great vessels. Wong and colleagues [26] analysed a subgroup of septic patients and found a correlation coefficient of 0.73 and a regression line close to the line of identity. The limits of agreement using Bland and Altman’s technique are very wide, implying the techniques are not interchangeable. Even if the bioimpedance results are mathematically corrected to cause the regression line to match the line of identity, the scatter of the results is such that it is impossible to replace thermodilution methods with bioimpedance.

In this study we found a very poor correlation between the cardiac index measured by bioimpedance and thermodilution. The bioimpedance method overestimated at low cardiac index and markedly underestimated at high cardiac index, with a large scatter in the results. The correlation coefficient is the smallest reported for any comparison of bioimpedance and thermodilution methods on any group of critically ill patients. The limits of agreement using Bland and Altman’s technique are very wide, implying the techniques are not interchangeable. Even if the bioimpedance results are mathematically corrected to cause the regression line to match the line of identity, the scatter of the results is such that it is impossible to replace thermodilution methods with bioimpedance.

We used accepted methods for measurement of cardiac index by thermodilution and tried to ensure that cardiac index determinations using bioimpedance and thermodilution were made over as many of the same cardiac cycles as possible. No patient had tricuspid incompetence as judged by the central
venous pressure trace. Cold injectate was used, to minimize errors. The thermodilution technique was identical to that used in other comparative studies of thermodilution and bioimpedance that have shown far better correlation. In a study performed just before this study in the same Intensive Care Unit using the same equipment and techniques on non-septic, artificially ventilated patients, Jewkes and colleagues [31] showed a correlation coefficient of 0.72 and limits of agreement of −2.6 to +0.89 litre min⁻¹ for cardiac output. Thus we attribute the large discrepancy in the two methods in this study partially to errors in the bioimpedance technique specific to septic patients. However, the accuracy of thermodilution measurements of cardiac output in patients with sepsis has not been investigated by comparison with other techniques except suprasternal Doppler flow measurement [26], so there is a small chance that errors in thermodilution measurements caused the discrepancy.

The mean thoracic bioimpedance (Z₀) of the patients in this study was small (12.4 Ω); a normal value for supine patients is 22.5–24 Ω, that in the presence of pulmonary oedema, 18 Ω [32]. The small value we attribute to non-cardiogenic pulmonary oedema (adult respiratory distress syndrome) and pulmonary atelectasis, which alter the air–fluid relationships in the lungs and hence the lung resistivity. A reduction in thoracic bioimpedance has been noted with pleural effusion, and an increase with pneumothorax, dehydration and chronic obstructive lung disease [33], which would support this hypothesis, and in general the patients with more severe lung infiltrates on chest radiographs had smaller Z₀ values. Alternatively, as Bernstein [5] has suggested, the reduced Z₀ in sepsis may be caused by muscle and cutaneous vasodilatation. The value of thoracic bioimpedance was not directly related to the difference or the ratio between the values for stroke volume from the two methods of measurement, as assessed by multiple linear regression. However, the maximum change in bioimpedance is scaled with the Z₀ value in the calculation of cardiac index by bioimpedance, and the small value of Z₀ in these patients may be outside the range over which the assumptions used in the bioimpedance technique are valid, and cause a non-linear error.

It has been suggested that, although the values for cardiac index do not agree with the values obtained with thermodilution, in any one patient the bioimpedance can monitor trends in cardiac output [31]. The rationale for this is that each individual patient has a different relationship between cardiac index measured by thermodilution and bioimpedance, with a different gradient and offset to the regression line, and reasonably low limits of agreement. When results are pooled, as in this study, the resulting pooled limits of agreement are much worse than the individual values. For individual patients, the limits of agreement were between ±0.29 and ±0.72 litre min⁻¹ m⁻² around the bias values, the average limits of agreement were ±1.2 litre min⁻¹ m⁻². Thus on average, even in an individual patient, to be 95% certain that one value of cardiac output is significantly different from another measured by bioimpedance, the difference between the two readings has to be greater than 1.2 litre min⁻¹ m⁻². Thus, even as a monitor of changes in cardiac index in individual septic patients, the bioimpedance technique is too insensitive for clinical use. It might be of value if the patients with low limits of agreement could be identified, but this is not possible.

A significant proportion of the thoracic bioimpedance change during systole may arise because of changes in the blood volume of the lungs [1, 34]. If the change in thoracic bioimpedance that occurs in systole is caused by an increase in pulmonary blood volume by a volume equivalent to the right ventricular stroke volume, then the stroke volume might be expected to be related to the change in bioimpedance during systole, ΔZ, and not its maximum first derivative ΔZ/Δtmax. This, however, does not occur; blood also leaves the lungs during systole and so the maximum rate of change of bioimpedance, ±ΔZ/Δtmax, is used. This represents the maximum rate of increase in blood volume (i.e. flow) in the lungs and occurs in early systole when the majority of the incoming pulmonary blood flow would be expected to expand capacitance vessels and remain within the lung. By extrapolating this flow over the whole of systole, a value for stroke volume is obtained. In septic patients requiring artificial ventilation, pulmonary hypertension is an almost universal finding, and pulmonary haemodynamics are markedly altered. Thus the relationship between ΔZ/Δtmax and overall stroke volume may not remain the same, and so the extrapolations used in the thoracic bioimpedance method to calculate the cardiac index may fail.

There is also a more fundamental reason why the bioimpedance method does not measure cardiac index in the septic patient. The method relies on the oversimplified assumption that the thorax is a homogeneous conductor, shaped like a truncated cone. The change in impedance between the top and bottom of the thorax is attributed to changes in the blood content of the thorax. The impedance decreases during systole, implying that the thoracic blood volume increases during systole. This is physiologically unlikely; the change in impedance is probably caused by redistribution of blood within the thorax, which is thus not acting as a homogeneous conductor, and so the central theory of the method is suspect. Therefore, although the method works with normal subjects, if the underlying theory is unsound there is no reason why it should work in all circumstances.

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