

## LETTERS TO THE EDITOR

- *The British Heart Journal welcomes letters commenting on papers that it has published within the past six months.*
- *All letters must be typed with double spacing and signed by all authors.*
- *No letter should be more than 600 words.*
- *In general, no letter should contain more than six references (also typed with double spacing).*

### Non-invasive determination of cardiac output by Doppler echocardiography and electrical bioimpedance

SIR,—Dr Northridge and colleagues (1990;63:93-7) have, inadvertently I am sure, incorrectly cited the proper name of the stroke volume equation currently implemented in NCCOM3. While it is true that the general form of the equation of Sramek *et al*,<sup>1</sup> quoted under patients and methods, describes impedance derived stroke volume in a general, qualitative fashion, it is the quantitative definition of volume of electrically participating tissue (VEPT) in the equation that requires clarification.

In the work cited by Northridge and associates, the VEPT defined by Sramek *et al*<sup>1</sup> is determined in practice uniquely as a function of body height alone. However, as correctly stated by Northridge *et al*, VEPT as currently used is a constant derived from both body height and weight. NCCOM3 computes stroke volume from the Sramek equation corrected for body habitus.<sup>2,3</sup> This modified equation is now generally cited as the Sramek-Bernstein equation,<sup>4-7</sup> which is the one, apparently, used in this study.

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- 1 Sramek BB, Rose DM, Miyamoto A. Stroke volume equation with a linear base impedance model and its accuracy, as compared to thermodilution and magnetic flow meter techniques in humans and animals. Proceedings of the sixth conference on electrical bioimpedance, Zadar, Yugoslavia, 1983:38.
- 2 Bernstein DP. A new stroke volume equation for thoracic electrical bioimpedance: theory and rationale. *Crit Care Med* 1986;14:904-9.
- 3 Gotshall RW, Wood VC, Miles DS. Comparison of two impedance cardiographic techniques for measuring cardiac output in critically ill patients. *Crit Care Med* 1989;17:806-11.
- 4 Appel PL, Kram HB, MacKabee J, Fleming AW, Shoemaker WC. Comparison of measurements of cardiac output by bioimpedance and thermodilution in severely ill surgical patients. *Crit Care Med* 1986;14:933-5.
- 5 Goli VD, Teague SM, Prasad R, *et al*. Non-invasive evaluation of aortic stenosis severity utilizing Doppler ultrasound and electrical bioimpedance. *J Am Coll Cardiol* 1988;11:66-71.
- 6 Masaki DI, Greenspoon JS, Ozounian JG. Measurement of cardiac output in pregnancy by thoracic electrical bioimpedance and thermodilution. *Am J Obstet Gynecol* 1989;161:680-4.

- 7 Tibbals J. A comparative study of cardiac output in neonates supported by mechanical ventilation: measurement with thoracic electrical bioimpedance and pulsed Doppler ultrasound. *J Pediatr* 1989;114:632-5.

SIR,—We read with interest the validation of the transthoracic bioimpedance cardiac output device (BoMed NCCOM3) in acute myocardial infarction (1990;63:93-7). Northridge *et al* concluded that in most patients the transthoracic electrical bioimpedance technique was accurate and reproducible. The validity of this technique has been questioned<sup>1</sup>; we recently concluded that impedance cardiac output as implemented in the BoMed NCCOM3 was “not accurate compared with the thermodilution reference nor was it quantitative”.<sup>2</sup>

There are many pitfalls in the assessment of cardiac output and in undertaking validation studies in humans<sup>3</sup> and assessment of devices likely to be applied in critical care should be rigorous rather than enthusiastic. Validation in vitro and in vivo should be attempted, the method should be accurate compared with the reference standard, and show similar reproducibility with ability to track physiological events and the effects of pharmacodynamic interventions.<sup>4</sup> A simple rest assessment may have serious limitations and result in misleading conclusions.

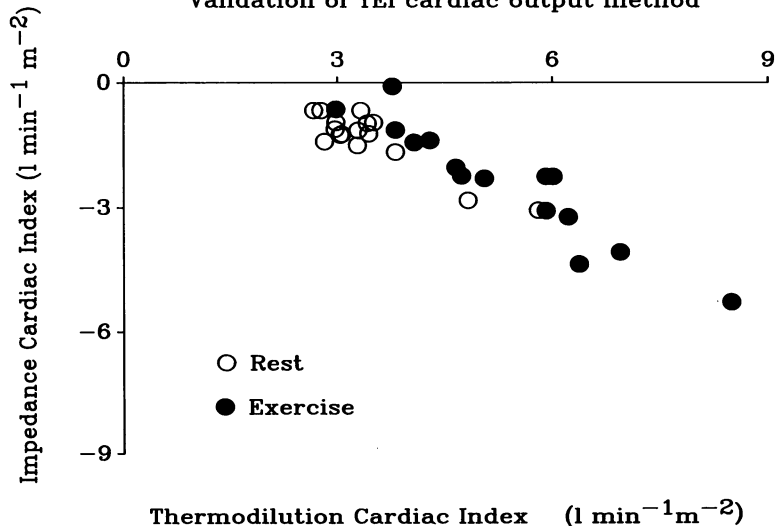
Several crucial points in the Northridge paper may have contributed to the outcome. It is unclear whether investigators were blind to each other—this should be mandatory to avoid unconscious bias. Ten averaged estimates of impedance cardiac output were compared with three averaged thermodilution estimates: this is not reasonable. After the establishment of control haemodynamic stability, measurements should be paired, simultaneous, and consecutive; discarding of data (“outliers”) and averaging generates spurious accuracy. The reference thermodilution system is at best under conditions of physiological stability.<sup>5</sup> Perusal of the data on control cardiac output (3.95 l/min) indicates that this lies outside the 95% confidence limits for acute heart failure (mean 4.31 (95% confidence interval +0.16) based on 32

studies of acute heart failure<sup>6</sup>); this suggests haemodynamic compromise, with subjects unlikely to be haemodynamically stable. Validation studies should cover as wide a range of comparison points to ensure the method has no systematic bias; clearly this was not achieved because of the patient population selected. In three of the patients there were considerable discrepancies between the methods—were these with higher cardiac outputs?

Our assessment of the BoMed impedance device in 16 patients with stable coronary disease was as follows.<sup>7</sup> Ten consecutive cardiac output measurements were compared with 10 impedance estimations over a 15 minute period. Subjects were studied fasting without premedication after a period of sub-maximal exercise to minimise haemodynamic variability. Observers were blind to each other; the thermodilution method had previously been validated in vitro and in vivo with accuracy and reproducibility determined.<sup>8</sup> Data were not averaged and all data were included to obviate observer bias. The data (figure) clearly suggested large discrepancies between the impedance estimate of cardiac output and the thermodilution reference (average difference 1.33 l min<sup>-1</sup> m<sup>-2</sup>; 95% limits of agreement 0.13 to 2.79 l min<sup>-1</sup> m<sup>-2</sup>). During 4 minutes supine bicycle exercise, with techniques to minimise chest movement, these differences increased (average difference 2.36 l min<sup>-1</sup> m<sup>-2</sup>; 95% limits of agreement -0.56 to 5.28 l min<sup>-1</sup> m<sup>-2</sup>). We concluded that the BoMed impedance method as currently implemented in the NCCOM3 device produced uniformly low values compared with thermodilution estimates, suggesting that the incorporated algorithms were not appropriate to the ischaemic population. Our observations suggested that the method at present is unacceptable for scientific or clinical applications.

Devices which rely on empirically determined formulas (impedance changes in transthoracic impedance have been correlated with cardiac stroke output in volunteers) depend absolutely on the reliability of these relations; it may be oversimplistic to expect similar volume conduc-

### Validation of TEI cardiac output method



Validation of transthoracic bioimpedance (TEI) method.

tance characteristics in normal volunteers and patients with coronary disease (many with concomitant respiratory disease). Though the bioimpedance technique has undoubted potential for non-invasive cardiac output determination in humans, the NCCOM3 technique is not a satisfactory implementation of this method.

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- 1 Keim HJ, Wallace JM, Thurston H, Case DB, Drayer JIM, Laragh JH. Impedance cardiography for determination of stroke index. *J Appl Physiol* 1976;41:797-800.
- 2 Silke B, Permenkil R, Maitra S, Verma SP, Taylor SH. A new transthoracic bioimpedance (TEI) method of cardiac output determination. *Br J Clin Pharmacol* 1989;28:738P.
- 3 Taylor SH, Silke B. Is the measurement of cardiac output useful in clinical practice? *Br J Anaesth* 1988;60:90S-8S.
- 4 Silke B, Zezulka AV, Verma SP, Taylor SH. Hemodynamic assessment of nicardipine alone and with atenolol in coronary artery disease using a modified echo-doppler device. *Am J Cardiol* 1989;64:28H-34H.
- 5 Nelson GIC, Silke B. Management of acute heart failure following myocardial infarction. *Curr Concepts in Hypertens and Cardiovasc Dis* 1983;5:12-6.

These letters were shown to the authors, who reply as follows:

SIR,—We are grateful for the opportunity to reply to the points raised in these two letters.

We agree entirely with Dr Shoemaker's comments. The bioimpedance stroke volume equation used in the BoMed NCCOM3 was

first described by Dr Sramek. The contribution of Dr Bernstein, which we would not wish to underestimate, was an improved method for calculating VEPT (one variable in the Sramek equation) rather than a modification of the equation itself. As stated in our paper, VEPT was determined from both body height and weight—the Bernstein method.

We take issue with many of the points raised by Dr Silke. The thermodilution results were taken simultaneously with electrical bioimpedance by two blinded observers. As we stated, the bioimpedance estimate was taken as an average of 120 heart beats, not 10. This was compared with three averaged thermodilution estimates because these require a similar length of time. Each thermodilution estimate is in itself an average over a number of cardiac beats. We disagree with Dr Silke's assertion that averaging generates spurious accuracy. In fact we deliberately made only one estimate of cardiac output with each method per patient to avoid the spurious correlations that can be generated when multiple measurements are made in the same patient.

We do not follow Dr Silke's reasoning regarding the haemodynamic status of our patients. They were not chosen for their haemodynamic stability—unlike the patients included in the drug studies cited. Since we made the thermodilution and bioimpedance measurements simultaneously, any haemodynamic instability would not bias our results.

Dr Silke suggests that we did not study a wide enough range of cardiac outputs. In fact the thermodilution results ranged from 2 l/min to over 6 l/min which covers most values commonly encountered in clinical practice. He also suggests that the three patients in whom there was considerable disagreement

between electrical bioimpedance and thermodilution might have been those with the highest cardiac outputs. Inspection of figure 3 of our original paper clearly shows that this was not the case. There was no relation between the size of the errors and the mean of the two estimates of cardiac output.

There are several possible reasons to explain the poorer results obtained by Dr Silke with electrical bioimpedance. However, it is difficult to compare our methods because his study has not been published in full. The most obvious difference between the studies is that our measurements were not made during exercise. A previous report concluded that the BoMed NCCOM3 was inaccurate during exercise.<sup>1</sup> Another problem with Dr Silke's study is that electrical bioimpedance is compared with thermodilution—a technique that may be unreliable during exercise because of the development of tricuspid incompetence.<sup>2</sup> Therefore the lack of agreement between bioimpedance and thermodilution during exercise should not discourage physicians from using this device in patients at rest, especially to monitor changes in cardiac output.

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- 1 Smith SA, Russell AE, West MJ, Chalmers J. Automated non-invasive measurement of cardiac output: comparison of electrical bioimpedance and carbon dioxide rebreathing techniques. *Br Heart J* 1988;59:292-8.
- 2 Lipkin DP, Poole-Wilson PA. Measurement of cardiac output during exercise by the thermodilution and direct Fick techniques in patients with chronic congestive heart failure. *Am J Cardiol* 1985;56:321-4.