Br Heart J 1988;59:292–8

Automated non-invasive measurement of cardiac output: comparison of electrical bioimpedance and carbon dioxide rebreathing techniques

STEPHEN A SMITH, ANDREW E RUSSELL, MALCOLM J WEST, JOHN CHALMERS

From the Department of Cardiovascular Medicine, Flinders Medical Centre, Bedford Park, South Australia

SUMMARY Two commercial automated, non-invasive systems for estimation of cardiac output were evaluated. Values of cardiac output obtained by electrical bioimpedance cardiography (BoMed NCCOM3 machine) were compared with values derived from an indirect Fick technique that uses carbon dioxide rebreathing (Gould 9000 IV system) during 103 simultaneous measurements made at rest in 19 randomly selected subjects and on exercise in 11 subjects. Cardiac output values obtained with impedance cardiography were significantly correlated with those measured by the indirect Fick method, although there was a wide scatter with over 73% of the readings lying outside the limits defined by the line of identity ±20%. This correlation was greatly reduced when stroke volume index was used instead of cardiac output. Indirect Fick results were linearly related to oxygen uptake both at rest and on exercise, while impedance cardiography results did not correlate with oxygen uptake. Impedance cardiography gave consistently lower results for cardiac output than indirect Fick at all levels of exercise. Both machines were easy to use and produced acceptable mean (SE) coefficients of variation (BoMed NCCOM3 7·7 (1·0)%, Gould 9000 IV 10·6 (1·4)%). Further validation is required before either of these machines can be recommended as an alternative to invasive monitoring in clinical practice.

An accurate and reliable non-invasive technique for measuring cardiac output would be of considerable value both in research and in clinical medicine. Over the past 60 years several potentially useful methods have been developed; the most promising of these are electrical bioimpedance cardiography[1–3] and indirect Fick techniques applied to rebreathing of carbon dioxide.[4–6] Use of these methods, however, has been limited by technical problems and uncertainties about their accuracy.[3–6] A high degree of operator skill and experience is needed to perform the tests and to interpret the results accurately.

Recently two fully automated non-invasive cardiac output measurement systems have been developed; each uses a fundamentally different technique. They both use microcomputers to guide the operator, to perform on line data validation, and to analyse the results. They are available commercially and are designed for use in intensive care and coronary care units, in exercise laboratories, and in research.

The aims of this present study were: (*a*) to compare simultaneous cardiac output results obtained both at rest and on exercise with the NCCOM3 (BoMed Medical Manufacturing, Ltd, Irvine, CA), which uses electrical bioimpedance ($\dot{Q}_{EBI}$), and the Gould 9000 IV (Gould Electronics Inc, Dayton, OH), which uses a carbon dioxide Fick method ($\dot{Q}_{Fick}$); (*b*) to compare the results from both of these machines with measured oxygen uptake; and (*c*) to determine the reproducibility, reliability, and ease of use of the machines.

Patients and methods

There were two parts to the study. Firstly, we compared simultaneously recorded supine resting cardiac output measurements obtained with the BoMed NCCOM3 and the Gould 9000 IV in subjects recruited from within the department and from medical outpatient clinics at Flinders Medical

Requests for reprints to Dr Stephen A Smith, Department of Cardiovascular Medicine, Flinders Medical Centre, Bedford Park, South Australia 5042, Australia.

Accepted for publication 15 July 1987

Centre. In the second study simultaneous measurements were made while normal untrained volunteers performed graded upright cycle exercise.

RESTING STUDY

Nineteen randomly selected subjects agreed to participate in the resting study (15 men and four women aged 18–76 years (mean (SD) 43·5 (16·8)). There were no specific exclusion criteria except unwillingness to participate. Four subjects had essential hypertension requiring drug treatment, and one had controlled cardiac failure, but none had important respiratory disease, thoracic skeletal deformity, or extreme obesity.

Subjects rested for 10 minutes before cardiac output was simultaneously measured by both methods. Three to eight pairs of measurements were taken every five minutes. Great care was taken to ensure that all measurements were taken in strict accordance with the manufacturers' detailed instructions. $\dot{Q}_{Fick}$ was measured by the Gould 9000 IV. Its components are a paramagnetic oxygen analyser, an infrared absorption carbon dioxide analyser, a dry rolling seal spirometer, a microcomputer with a monitor, and a report printer. The analysers have resolutions of 0·01% and accuracies of ±0·10% over the range zero to 25% for oxygen and zero to 10% for carbon dioxide. The spirometer measures expired minute ventilation with a resolution and an accuracy of 0·01 l/min and ±0·025 l/min respectively. The accuracy of these systems has been independently validated.[7] The analysers were calibrated before each study with room air and calibration gas containing 5·17% carbon dioxide in nitrogen. The subject was required to breathe into a one way respiratory valve (Hans Rudolph) attached to a light headframe and connected to the machine via a flexible hose. $\dot{Q}_{Fick}$ was calculated from the Fick equation as follows:

$$\dot{Q}_{Fick} = \frac{\dot{V}CO_2}{C_{\bar{v}}CO_2 - C_{\bar{a}}CO_2}$$

where $\dot{V}CO_2$ is the rate of carbon dioxide production and $C_{\bar{v}}$ and $C_{\bar{a}}CO_2$ are mixed venous and arterial carbon dioxide concentrations. Carbon dioxide production was calculated by continuous analysis of the carbon dioxide concentration and the volume of expired air. Oxygen uptake was similarly calculated. $C_{\bar{a}}CO_2$ was calculated by the computer from the end tidal partial pressure of carbon dioxide from standard dissociation curves. $C_{\bar{v}}CO_2$ was calculated in a similar manner from the partial pressure of carbon dioxide determined by a rebreathing method as described by Collier.[8] This assumes that during rebreathing of a mixture of carbon dioxide in oxygen the concentration of carbon dioxide in the bag, alveoli, and pulmonary capillaries will reach an equilibrium at which time there will be no net exchange across the alveolar capillary membrane. The concentration of carbon dioxide at that point will be equal to that of mixed venous blood. Subjects were required to rebreathe 1·5 times their tidal volume of a mixture of 10% carbon dioxide in oxygen for approximately 15 seconds. The plateau phase which indicated equilibrium was determined by the computer which also performed all calculations and made corrections for temperature and barometric pressure. During rebreathing the output of the carbon dioxide analyser was continuously displayed on a television screen, enabling the operator to confirm that an adequate plateau was achieved.

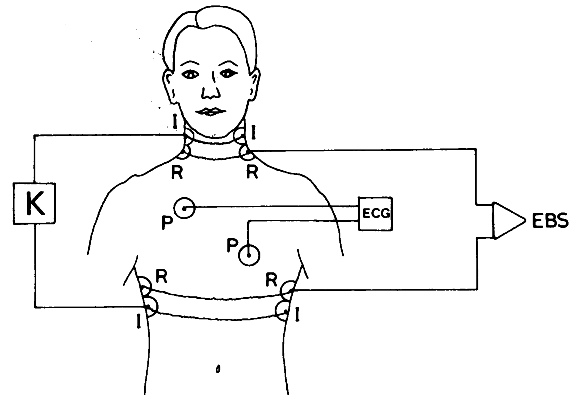

Fig 1 *Electrode positions for measuring the electrical bioimpedance signal (EBS). Pairs of recording electrodes (R) were placed at the root of the neck and at the level of the xiphisternum. The constant current sinusoidal field generator (K) was connected to the injecting electrodes (I) placed 5 cm above and below the recording electrodes. The electrocardiogram (ECG) was recorded using precordial electrodes (P).*

$\dot{Q}_{EBI}$ was measured by the BoMed NCCOM3. The technique depends upon the conversion of changes in thoracic impedance during each cardiac cycle into information about blood flow. Ten, low contact impedance, self adhesive electrodes were positioned for recording the electrocardiogram and bioimpedance signals as shown in fig 1. The machine generated a constant current, high frequency, sinusoidal field across the thorax through the outer pairs of electrodes. An impedance signal was recorded from the inner pairs. Stroke volume (SV) was calculated in ml according to an empirical formula described by Sramek *et al*[9]:

$$SV = VEPT \times T \times \frac{(dz/dt)max}{Zo}$$

where VEPT is the volume of electrically participating tissue (ml), T is the ventricular ejection time (s), Zo is the thoracic base impedance (Ω) and (dz/dt)max is the maximum rate of change of impedance during the systolic upstroke (Ω/s). The VEPT was calculated from the subject's age, sex, and height by a nomogram.[10] Analysis of the impedance signal and calculations were performed on line by the machine, which can give beat by beat or period mean values for $\dot{Q}_{EBI}$, heart rate, and stroke volume.

EXERCISE STUDY

Eleven (nine men, two women; aged 18–39, mean (SD) 28 (4)) of the subjects who took part in the resting study went on to complete the exercise study. None had important cardiovascular or pulmonary disease, thoracic skeletal deformity, or extreme obesity. None of them engaged in regular physical training.

Submaximal upright exercise was performed on a cycle ergometer. For the men, simultaneous measurements of $\dot{Q}_{EBI}$ and $\dot{Q}_{Fick}$ were made at rest while they were seated on the bicycle, after 5 and 10 minutes of exercise at 65 W (400 kpm/min) and after 5 minutes at 130 W (800 kpm/min). Measurements were made at similar times in women but workloads were reduced by 25%.

CALCULATIONS AND STATISTICAL ANALYSIS

Stroke volume index (SVI) was calculated according to the formula:

$$SVI = \frac{\text{Cardiac output}}{\text{Heart rate} \times \text{Body surface area}} (\text{ml/beat/m}^2)$$

Correlation between paired data sets was determined by linear regression analysis. Statistical significance of differences between groups was calculated by standard methods of analysis of variance. Results were expressed as mean (SE). Statistical significance was assumed when $p<0.05$.

Results

Figure 2 is a scattergram which shows a total of 103 pairs of simultaneous measurements obtained during both the resting and the exercise studies. Although there was a significant correlation ($r = 0.56$, $p < 0.001$), there was a wide scatter with over 73% of the readings lying outside limits defined by the line of identity ±20%. Statistical significance was greatly reduced ($r = 0.24$, $p < 0.05$) when stroke volume index was used instead of cardiac output (fig 3). $\dot{Q}_{EBI}$ was consistently lower than $\dot{Q}_{Fick}$ during all stages of exercise (fig. 4).

Figure 5 shows the relation between cardiac output

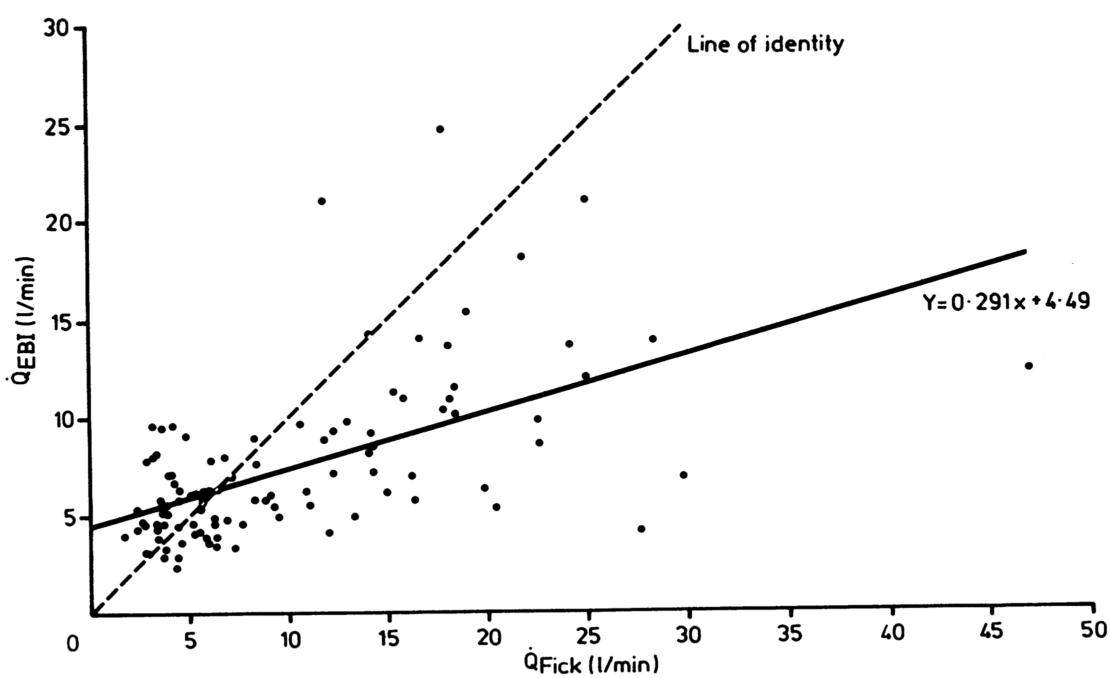

Fig 2 *Scattergram showing 103 paired measurements of cardiac output made at rest and on exercise by electrical bioimpedance ($\dot{Q}_{EBI}$) and carbon dioxide rebreathing indirect Fick ($\dot{Q}_{Fick}$) techniques.*

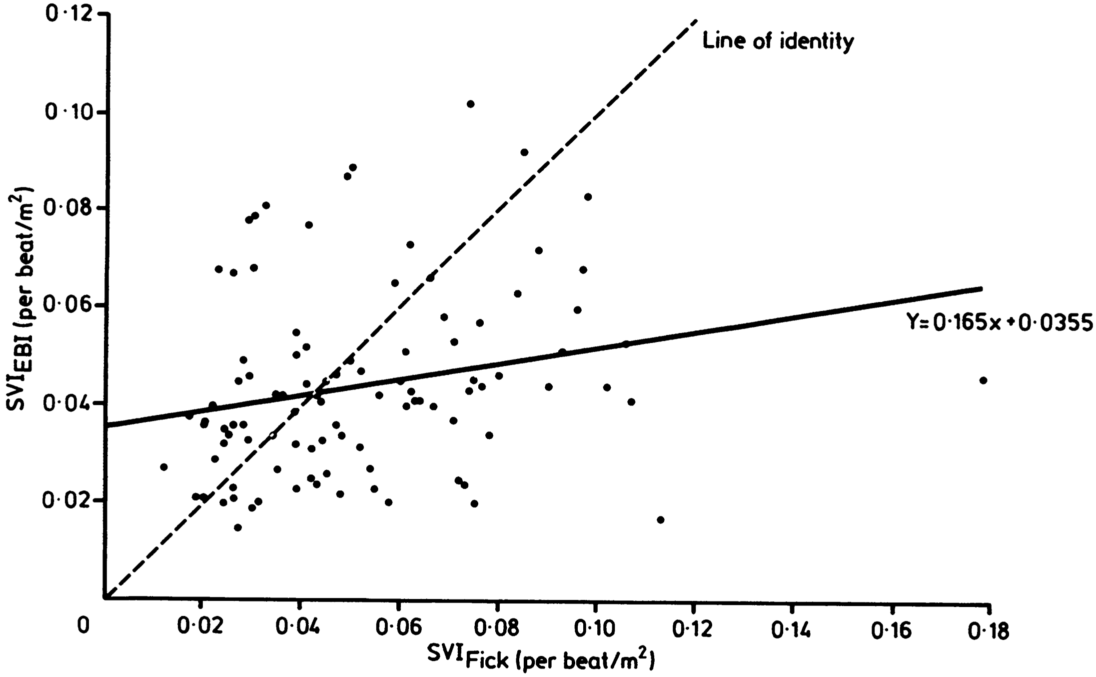

Fig 3 *Scattergram showing comparison between stroke volume index measured by electrical bioimpedance (SVI_{EBI}) and carbon dioxide rebreathing indirect Fick (SVI_{Fick}) techniques. These data were calculated from the points used in fig 2.*

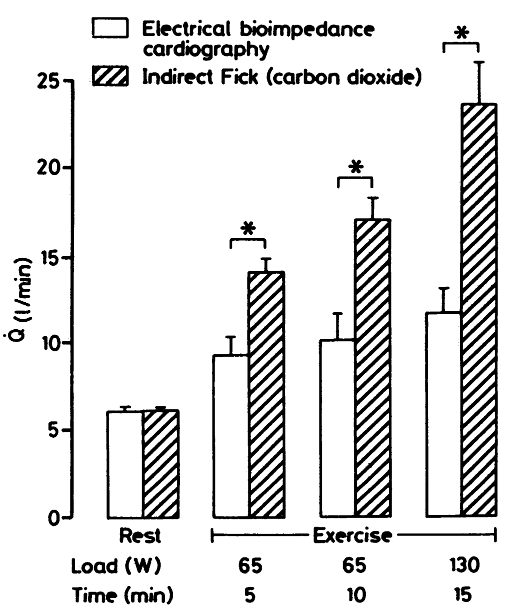

Fig 4 *Cardiac output ($\dot{Q}$) measurments obtained by each machine during graded bycycle exercise in 11 normal volunteers.* * = $p < 0.005$.

and oxygen uptake at rest and during exercise. $\dot{Q}_{EBI}$ was not significantly correlated with oxygen uptake at rest, and only weakly correlated on exercise. $\dot{Q}_{Fick}$ correlated well with oxygen uptake both at rest and on exercise; however, the regression slopes were steeper than previously reported.[11-13]

Coefficients of variation were calculated for the resting data to access random error. The mean (SE) coefficient of variation for $\dot{Q}_{EBI}$ was 7·7 (1·0%) (range of 0–18·2%). Corresponding figures for $\dot{Q}_{Fick}$ were 10·6 (1·4%) (0–21·7%). We found both machines reasonably easy to use. The Bomed NCCOM3 was simply plugged into a power source, switched on, and connected to correctly positioned electrodes. A value related to the volume of electrically participating tissue, determined from a nomogram and the patient's sex, height, and weight, was entered on a keyboard. The machine then produced consecutive real time readings displayed either as beat by beat values or period means.

The Gould 9000 IV was more difficult to operate. The machine had to be switched on for at least an hour to allow temperature stabilisation and had to be calibrated before each study. The operator was required to prompt the computer and to switch in the

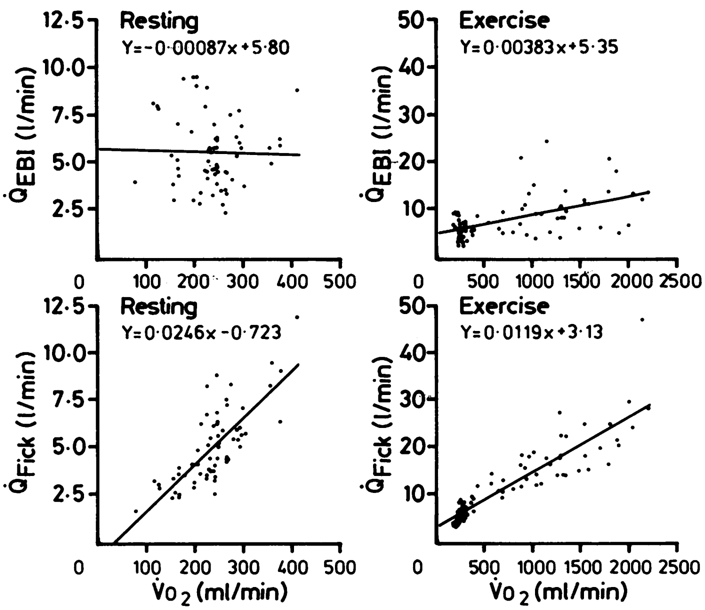

Fig 5 *Scattergrams showing the relation between cardiac output measured by electrical bioimpedance ($\dot{Q}_{EBI}$) and carbon dioxide rebreathing indirect Fick ($\dot{Q}_{Fick}$) techniques and oxygen uptake ($\dot{V}O_2$) both at rest and on exercise.*

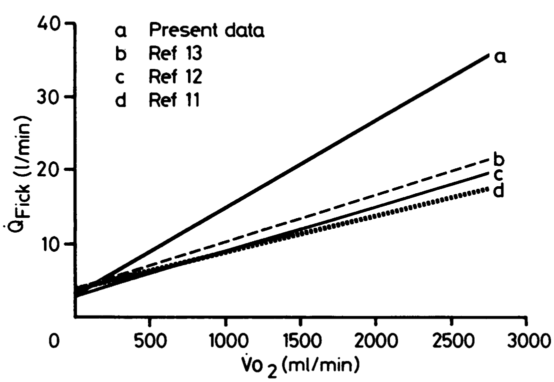

Fig 6 *The regression slope relating cardiac output ($\dot{Q}_{Fick}$) determined by the carbon dioxide rebreathing indirect Fick technique to oxygen intake ($\dot{V}O_2$) in this study (a) was steeper than described by others who used invasive techniques.*

rebreathing mixture in order to obtain individual measurements. None the less, the computer software guides the operator through the calibration and rebreathing procedures. New operators needed about four hours training to use the machine correctly. The technique could only be used in spontaneously breathing subjects.

Discussion

Scientific evaluation of techniques for measuring cardiac output is difficult because there are no gold standards. All available methods, including direct Fick, indicator dilution, radiopharmaceutical, echocardiographic, and Doppler techniques, produce errors of at least ± 10%.[14 15] We chose to use measured oxygen uptake as the standard by which to determine accuracy because many workers have demonstrated that cardiac output is linearly and predictably related to oxygen uptake in normal subjects.[11-13] Many previous studies have evaluated these non-invasive methods. Indirect carbon dioxide Fick methods have been compared with direct oxygen Fick[16] and with indicator dilution[17] techniques, both at rest[18] and on exercise.[17] Studies have been performed in controls[16] and in patients with heart failure[19] and respiratory disease.[20] Most of these studies found that the technique was accurate and reproducible. There have been more than 50 studies to compare electrical bioimpedance cardiography with other methods; most of these have shown good correlations[21-23] though some have found it inaccurate.[24 25]

Published information about the BoMed NCCOM3 and the Gould 9000 IV is scanty, however, despite the fact that they are available commercially. We are not aware of any previous reports validating cardiac output assessment by the Gould 9000 IV and there have been only two papers describing use of the BoMed NCCOM3 in man.[26 27] These groups both found a reasonably good correlation with thermodilution methods in critically ill patients. In one study the analogue first derivative impedance signal was recorded and examined to ensure adequate quality before results were included.[26] This facility is not routinely available with the commercially produced machine. Neither study was able to examine the accuracy of the BoMed NCCOM3 on exercise. This lack of information is particularly disturbing because this machine uses a new and relatively untested stroke volume formula.

$\dot{Q}_{Fick}$ was linearly related to oxygen uptake. The regression slope was steeper than that described before with invasive methods,[11-13] suggesting that the Gould machine may overestimate cardiac output during moderate exercise. An alternative explanation could be that our subjects were untrained and many were older than those who took part in previous studies: these factors may alter the relation between cardiac output and oxygen uptake.[11] In contrast, there was no significant relation between $\dot{Q}_{EBI}$ and oxygen uptake. These data suggest that the carbon dioxide Fick method produced results that were, at least, related to cardiac output, while results derived from electrical bioimpedance cardiography were likely to be wrong. We realise that carbon dioxide production, which was used in the Fick equation, and oxygen uptake were not completely independent variables as they were both calculated from the same minute volume which was measured by the Gould 9000 IV. None the less, oxygen and carbon dioxide were measured by completely independent analysers. Any errors in the measurement of minute volume would equally affect both $\dot{Q}_{Fick}$ and oxygen uptake.

We found a statistically significant correlation between simultaneous measurements of $\dot{Q}_{EBI}$ and $\dot{Q}_{Fick}$, although there was poor agreement for individual measurements. This correlation was greatly attenuated when stroke volume index results from each of the machines were compared. This accords with a previous study that examined electrical impedance cardiography and found that it "did not determine reliably absolute values of stroke index and is not suitable to evaluate changes in stroke index".[3] Other workers found that impedance estimates of an angiographically determined left ventricular stroke volume of 100 ml ranged from 40 to 150 ml.[28] Most reports of the evaluation of electrical bioimpedance cardiography have concentrated on cardiac output rather than stroke volume index. These workers may have produced fortuitous correlations that were not necessarily related to putative electrical impedance changes in the thorax. The empirical formulas used in electrical bioimpedance cardiography were designed to determine stroke volume. Cardiac output is, of course, the product of stroke volume and heart rate, with heart rate being the most important of these determinants, particularly on exercise.[29] Multiplication of electrical bioimpedance-derived stroke volume by independently measured heart rate will be likely to produce correlation when the result is compared with some other measure of cardiac output. In addition, stroke volume is related to the body size. Both the earlier Kubicek formula[1] and the Sramek formula[9] used in the BoMed NCCOM3 use a measure related to body size in the numerator and the thoracic base impedance, which is inversely related to body size,[30] in the denominator. These factors may be in the first or second power depending upon the formula used: both combine to produce stroke volume results that are positively related to body size. Any critical analysis of electrical bioimpedance cardiography should remove the effects of heart rate and body size by examining stroke volume index.

In a neglected paper Hill *et al* examined the principles of electrical bioimpedance in a series of careful in vitro experiments.[31] They found that as a function of blood flow true impedance signals were so small as to be unmeasurable and that impedance cardiographs produced "totally uncalibratable strain gauge type signals". They concluded that "electrical impedance cardiography, as it is currently used and interpreted, appears to be in error". We have found no evidence in published reports or in our data to contradict this statement.

The impedance equipment (BoMed NCCOM3) did not accurately assess cardiac output during exercise although it is recommended for use during diagnostic exercise testing by the manufacturers. Previous studies have shown electrical bioimpedance cardiography to be applicable during exercise.[32,33] We assume that the impedance signals became distorted during exercise, making measurement of the thoracic base impedance, the maximum rate of change of impedance during the systolic upstroke, and the ventricular ejection time inaccurate. Nevertheless, the machine produced readings throughout the test in all subjects. We were unable to find any independent published data on the accuracy and resolution of measurement of these variables by this machine.

We conclude that the Gould 9000 IV carbon dioxide Fick system was reasonably easy to use, produced acceptably reproducible results and was accurate, when compared with measured oxygen uptake, both at rest and on exercise. Further work is required to compare this machine with invasive measurements of cardiac output before it can be recommended for clinical use. The BoMed NCCOM3 electrical bioimpedance cardiograph was very simple to use and gave remarkably reproducible results. Its accuracy compared with oxygen uptake was poor even at rest. The machine was of no value during upright bicycle exercise and of limited value in resting patients. It should not be used in clinical practice as an alternative to invasive monitoring.

SAS holds a British Heart Foundation/Australian National Heart Foundation Reciprocal Travelling Fellowship. AER is a Lions Heart Research Scholar. We thank Mrs S Taylor for help with the statistical analyses and with preparation of the manuscript.

References

1 Kubicek WG, Karnegis JN, Patterson RP, Wittsoe DA, Mattson RH. Development and evaluation of an impedance cardiac output system. *Aerospace Med* 1966;**37**:1208–12.

2 Harley A, Greenfield JC. Determination of cardiac output in man by means of impedance plethysmography. *Aerospace Med* 1968;**39**:248–54.

3 Keim HJ, Wallace JM, Thurston H, Case DB, Drayer JIM, Laragh JH. Impedance cardiography for determination of stroke volume index. *J Appl Physiol* 1976;**41**:797–800.

4 Defares JG. Determination of $PvCO_2$ from the exponential CO_2 rise during rebreathing. *J Appl Physiol* 1968;**13**:159–64.

5 Bock AV, Dill DB, Talbot JH. Studies in muscular activity. I. Determination of the rate of circulation of blood in man at work. *J Physiol (Lond)* 1928;**66**: 120–32.

6 Clausen JP, Larsen OA, Trap-Jensen J. Cardiac output in middle aged patients determined with a CO_2 rebreathing method. *J Appl Physiol* 1970:**28**:337–47.

7 Eccles RC, Swinamer DL, Jones RL, Garner King E. Validation of a compact system for measuring gas exchange. *Crit Care Med* 1986;**64**:807–11.

8 Collier CR. Determination of mixed venous CO_2 concentrations by rebreathing. *J Appl Physiol* 1956;**9**: 25–9.

9 Sramek BB, Rose DM, Miyamoto A. Stroke volume equation with a linear base impedance and its accuracy, as compared to thermodilution and electromagnetic flow meter techniques in animals and humans. Proceedings of the Sixth International Conference on Electrical Bioimpedance. Zadar, Yugoslavia, 1983, p 38.

10 Bernstein DP. A new stroke volume equation for thoracic electrical bioimpedance: theory and rationale. *Crit Care Med* 1986;**14**:904–9.

11 Saltin B, Blomqvist G, Mitchell JH, Johnson RL, Wildenthal K, Chapman CB. Response to exercise after bed rest and after training. A longitudininal study in adaptive changes in oxygen transport and body composition. *Circulation* 1968;**38**(suppl 7):1–78.

12 Astrand PO, Cuddy TE, Saltin B, Stenberg J. Cardiac output during submaximal and maximal work. *J Appl Physiol* 1964;**19**:268–74.

13 Saltin B. Circulatory response to submaximal and maximal exercise after thermal dehydration. *J Appl Physiol* 1964;**19**:1125–32.

14 Haites NE, Mowat DHR, McLennan FM, *et al*. How far is the cardiac output. *Lancet* 1984;**ii**:1025–7.

15 Levett JM, Replogle RL. Thermodilution cardiac output: a critical analysis and review of the literature. *J Surg Res* 1979;**27**:392–401.

16 Luft UC. Specialised physiological studies in support of manned space flight. Part A. Evaluation of the single breath method for determining cardiac output. Houston, TX: Manned Spacecraft Centre, Res Rep Contract NAS9-12572. 1973.

17 Gilbert B, Auchincloss JH. Comparison of single breath and indicator dilution measurement of cardiac output. *J Appl Physiol* 1970;**29**:119–22.

18 Chen H, Silverton NP, Hainsworth R. Evaluation of a method for estimating cardiac output from a single breath in humans. *J Appl Physiol* 1982;**53**:1034–8.

19 Franciosa JA, Ragan DO, Rubenstone SJ. Validation of the CO_2 rebreathing method for measuring cardiac output in patients with heart failure or hypertension. *J Lab Clin Med* 1976;**88**:672–82.

20 McEvoy S, Jones NL, Campbell E. Alveolar-arterial pCO_2 difference during rebreathing in patients with chronic hypercapnia. *J Appl Physiol* 1973;**35**:542–9.

21 Smith JJ, Bush JE, Wiedmeier VT, Tristani FE. Application of impedance cardiography in the study of postural stress. *J Appl Physiol* 1970;**29**:133–7.

22 Lababidi Z, Ehmke DA, Durnin RE, Leaverton PE, Laver RM. Evaluation of impedance cardiac output in children. *Pediatrics* 1971;**47**:870–8.

23 Judy WV, Langley FM, McCowan KD, Stinnett DM, Baker LE, Johnson PE. Comparative evaluation of the thoracic impedance and isotope dilution methods for measuring cardiac output. *Aerospace Med* 1969;**40**:532–7.

24 Harley A, Greenfield JC. Determination of cardiac output in man by means of impedance plethysmography. *Aerospace Med* 1968;**39**:428–34.

25 Bache RJ, Harley A, Greenfield JC. Evaluation of thoracic impedance cardiography as an indicator of stroke volume in man. *Am J Med Sci* 1969;**258**:100–4.

26 Appel PL, Kram HB, Mackabee J, Flemming AW, Shoemaker NC. Comparison of measurements of cardiac output by bioimpedance and thermodilution in severely ill surgical patients. *Crit Care Med* 1986;**14**:933–5.

27 Bernstein DP. Continuous noninvasive real time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. *Crit Care Med* 1986;**14**:898–901.

28 Ebert TJ, Eckberg DL, Vetrovec GM, Cowley MJ. Impedance cardiograms reliably estimate beat by beat changes of left ventricular stroke volume in humans. *Cardiovasc Res* 1984;**18**:354–60.

29 Higginbotham MB, Morris KG, Williams S, McHale PA, Coleman RE, Cobb FR. Regulation of stroke volume during submaximal and maximal upright exercise in normal man. *Circ Res* 1986;**58**:281–91.

30 McKinney ME, Buell JC, Eliot RS. Sex differences in thoracic impedance: evaluation of effects on calculated stroke volume index. *Aviat Space Environ Med* 1984;**55**:893–5.

31 Hill RV, Jansen JC, Fling JL. Electrical impedance plethysmography: a critical analysis. *J Appl Physiol* 1967;**22**:161–8.

32 Miles DS, Sawka MN, Wilde SW, Doerr BM, Bassett Frey MA, Glaser RM. Estimation of cardiac output by electrical impedance during arm exercise in women. *J Appl Physiol* 1981;**51**:1488–92.

33 Teo K-K, Hetherington MD, Haennel RG, Greenwood PV, Rossall RE, Kappagoda T. Cardiac output measured by impedance cardiography during maximal exercise tests. *Cardiovasc Res* 1985;**19**:737–43.