Simultaneous measurement of cardiac output by thermodilution, thoracic electrical bioimpedance and Doppler ultrasound


SUMMARY
To evaluate the accuracy of two non-invasive techniques for cardiac output (CO) measurement, we have measured CO simultaneously by thoracic electrical bioimpedance (TEB), pulsed Doppler ultrasound (DU) and standard thermodilution methods (TD) under different clinical conditions. Measurements were made in 10 patients: (I) during steady state anaesthesia with controlled IPPV ventilation (n = 131), spread over the entire ventilatory cycle; (II) during apnoea (n = 56); (III) during spontaneous breathing (n = 152) in the intensive care unit. Mean (SD) cardiac output values were: (I) CO<sub>TD</sub> 3.5 (1.0) litre min<sup>-1</sup>, CO<sub>TEB</sub> 3.4 (0.7) litre min<sup>-1</sup>, CO<sub>DU</sub> 2.8 (0.7) litre min<sup>-1</sup>; (II) CO<sub>TD</sub> 3.6 (0.6) litre min<sup>-1</sup>, CO<sub>TEB</sub> 3.5 (0.4) litre min<sup>-1</sup>, CO<sub>DU</sub> 2.9 (0.7) litre min<sup>-1</sup>; (III) CO<sub>TD</sub> 7.7 (1.5) litre min<sup>-1</sup>, CO<sub>TEB</sub> 7.6 (1.9) litre min<sup>-1</sup>, CO<sub>DU</sub> 5.2 (1.4) litre min<sup>-1</sup>. The mean percentage deviation of TEB from TD ranged from −2.2% to 1.4% and that of DU from TD was from −16% to −32%. There were no statistically significant differences between TD and TEB, but TD and DU differed significantly during IPPV, apnoea and spontaneous ventilation (P < 0.0001). (Br. J. Anaesth. 1994; 72: 133–138)

KEY WORDS
Measurement techniques: cardiac output.

Thermodilution is the most common clinical method for measurement of cardiac output. However, there are some theoretical and practical limitations to dilution techniques and small but significant associated morbidity and mortality [1, 2]. Consequently, many efforts have been made recently to develop a non-invasive method with similar accuracy and reproducibility as for thermodilution. Two of these alternative methods are thoracic electrical bioimpedance (TEB) and Doppler ultrasound (DU).

Thoracic electrical bioimpedance (TEB)
The concept of TEB waveform analysis for estimating stroke volume was introduced in 1966 by Kubicek and colleagues [3]. They assumed that the human thorax is a cylinder with a basic circumference equal to that of the thorax at the level of the xiphoid [4]. This cylinder has an electrical length (L), which is the distance between the voltage-sensing electrodes placed on the neck and the xiphoid; it is perfused homogeneously with blood of specific resistivity, ρ, (units Ω·cm) which varies with PCV and has a basic impedance, Z<sub>0</sub> (Ω).

The principle of impedance cardiography is that a constant small current (2.5 mA at 70 kHz), applied between the outer current electrodes (1 and 4) on the human thorax, produces changes in the voltage sensed with the inner electrodes (2 and 3) when the thoracic conductivity changes during systole and diastole. The first derivative of the impedance waveform, dZ/dt, is related linearly to aortic blood flow. There exist some modifications of the original assumption and similar basic analysis, such as the formula of Sramek [5], who took a truncated cone instead of a cylinder for the electrically participating tissue of the thorax and who regarded PCV as a constant. The detailed derivation of the equation of Sramek was explained in an article by Bernstein [4].

Doppler ultrasound (DU)
The Doppler effect describes the changes in sound wave frequencies when the sound and receiver are moving relative to one another. The waves are directed towards the moving blood cells and then reflected back. This results in a frequency differing from that transmitted and directly proportional to blood flow velocity. Stroke volume can be calculated when the area under the velocity curve and the cross-sectional area (CSA) of the aorta are known. A newer pulsed Doppler obviates the need for measuring CSA separately by insonating the ascending aorta with a two-element, pulsed, 2-MHz ultrasound beam from the suprasternal notch. The ultrasound beam comprises a wide beam, which insonates the total lumen of the ascending aorta and...
Normally, a measuring time of 15—30 s was necessary to obtain one averaged CO, DU, the mean taken for comparison. Thereafter, the four to six values, depending on the heart rate, and values were derived by beat-to-beat mode, normally during injection of the ice-glucose until the pre-tories. Measurement procedure was as follows:

- Minimally variability. Deadspace correction was made 30% of its peak, because this point is related to angle increases, the velocity increases and the lumen area decreases proportionally. This independence, which is new compared with other Doppler measurements of CO, is important for the practical use of this method.

- When compared with standard invasive methods, the results of TEB and Doppler methods range from poor correlation [6-10] to good agreement [11-16].

The purpose of this study was to evaluate the accuracy of CO measurements obtained simultaneously by TEB and DU in comparison with the standard TD method in different clinical conditions.

**MATERIAL AND METHODS**

The study was approved by the local Ethics Committee and the patients gave written, informed consent. We studied 10 patients (four male), ASA III and IV, aged 35—65 yr, who had a Swan—Ganz catheter (93A-131-7F, Baxter Edwards Laboratories, Irvine, CA) inserted during neurosurgical removal of intracranial tumour or aneurysm. The catheter was inserted via the right internal jugular incision of the dura mater at steady-state conditions of arterial pressure and heart rate. TEB and TD measurements (Cardiac Output Computer 9520A, Baxter Edwards Laboratories, Irvine, CA with a closed injectate system) were made simultaneously. Ice-cold 5% glucose 10 ml was injected via a closed system for TD measurements. Measurement of CO was performed by a time—temperature integration curve of the indicator—blood mixture. As it is the standard method used by Baxter, integration was terminated automatically when the curve returned to 30% of its peak, because this point is related to minimal variability. Deadspace correction was made according to instructions given by Edwards Laboratories. Measurement procedure was as follows: during injection of the ice-glucose until the presentation of the result by the TD computer, CO values were derived by beat-to-beat mode, normally four to six values, depending on the heart rate, and the mean taken for comparison. Thereafter, the Doppler transducer (Quanzoscope—Vital Science, Denver, CO) was placed at the suprasternal notch. Normally, a measuring time of 15—30 s was necessary to obtain one averaged CO value, depending on the signal quality, which was then taken for comparison with the two other methods. One single TD measurement was compared with the averaged TEB and DU values.

Simultaneous measurement of TEB and DU leads to prolonged disturbance of the impedance signal. The metallic Doppler transducer absorbs a large portion of the current between the two inner sensing electrodes of the impedance cardiograph; this reduces the dZ/dmax signal and thus calculation of the TEB cardiac output results in decreased CO values. The investigator using the Doppler signal was unaware of any of the TD and TEB measurements. CO measurements took place during the entire ventilatory cycle (I) and during end-expiratory apnoea (II). Mechanical ventilation was set at a ventilatory frequency of 12 b.p.m. and a minute volume of 100 ml kg⁻¹. Measurement of TD, TEB and DU was repeated on the next day in the intensive care unit during spontaneous breathing (III) after tracheal extubation.

Data are presented as mean (sd) and as mean differences with sd of the differences (sd). They were analysed for statistical significance using the Wilcoxon matched pairs signed rank test for non-parametric data. Statistically significant differences between TD and TEB and between TD and DU were assigned at P < 0.05.

A bias analysis was performed for cardiac outputs obtained using TD and TEB and using TD and DU. According to the statistical method of Bland and Altman [17], we plotted the mean of TD and TEB and the mean of TD and DU against the percentage deviation of TEB from TD and of DU from TD. As confidence and bias are the same when expressed as percentages, we modified the Bland—Altman method using percentage deviations instead of absolute values. Two sd was chosen as confidence interval. In this manner, the limits of agreement of each non-invasive method compared with TD can be taken as bias ± 2sd.

**RESULTS**

During IPPV, 131 simultaneous measurements of TD, TEB and DU were analysed in 10 patients. The mean of all TD CO measurements was 3.5 (sd 1.0) litre min⁻¹, that of TEB 3.4 (0.7) litre min⁻¹ and that of DU 2.8 (0.7) litre min⁻¹. During IPPV, the respective mean percentage deviation of TEB from TD was 1.4 (sd 16.2)% and that of DU from TD −16 (21)% (fig. 1).

During apnoea, the mean of all TD measurements was 3.6 (0.6) litre min⁻¹, that for TEB 3.5 (0.4) litre min⁻¹ and that for DU 2.9 (0.7) litre min⁻¹. The mean percentage deviation of TEB from TD was −2.2 (11.2)% and that of DU from TD −18.7 (16.3)% (fig. 2).

In the intensive care unit, during spontaneous ventilation, the mean of TD measurements was 7.7 (1.5) litre min⁻¹, that for TEB 7.6 (1.9) litre min⁻¹ and that for DU 5.2 (1.4) litre min⁻¹. The mean percentage deviation of TEB from TD was −2.1 (11.0)% and of DU from TD −32.4 (12.4)% (fig. 3).

There was no statistically significant difference...
between TD and TEB during the different conditions of measuring, but there was between TD and DU and TEB and DU during IPPV, apnoea and spontaneous ventilation ($P < 0.0001$).

We chose the method of Bland and Altman to average the respective values of TD and TEB and of TD and DU in order to minimize the inaccuracies in the assumption that TD may not be a "gold standard" of measuring CO [18]. As shown in figure 1, agreement between $CO_{TEB}$ and $CO_{TD}$ was best during IPPV; it was reduced slightly during apnoea and spontaneous breathing. For $CO_{DU}$ also, the best agreement was during IPPV, with the largest bias during spontaneous breathing.

During IPPV, apnoea and spontaneous breathing, TEB overestimated CO compared with TD at
smaller values of CO, whereas there was an underestimation at greater CO compared with TD during spontaneous breathing.

DU seemed to underestimate CO continuously compared with TD during all conditions.

**DISCUSSION**

According to Bland and Altman, bias analysis (the mean difference between two methods) is more appropriate than correlation and regression analysis for comparing two methods that measure the same variable. The bias represents the systematic error between two measurement techniques, whereas SD of the bias represents the random error of variability between the two different techniques. Variability in CO_{TEB}, CO_{DU}, or CO_{TD} measurements can affect the differences between the methods. (For within-technique variabilities, see the work of Wong and colleagues [19].) This variability may be caused by systematic and random errors based on the different principles for determination of CO. TEB and DU measure CO of the left heart, whereas a thermodilution catheter is placed in the right heart. Left and right ventricular stroke volume are not necessarily equal [20, 21]. There is a greater constancy on the left side [22, 23], as the influence of ventilation, above all during artificial ventilation, is less on the left ventricle. Right ventricular stroke volume changes significantly during inspiration and expiration as a result of decreased venous return and changing intrathoracic pressure [24, 25]. These non-continuous flow render the TD method and all dilution methods more inaccurate compared with continuous flow models [26, 27] because the Stewart-Hamilton equation is not correct for varying flow conditions.

Mackenzie and co-workers [28] assessed the accuracy and reproducibility of thermodilution in an artificial circulation during continuous or pulsatile flow at several flow rates, using three different cardiac output computers: Instrumentation Laboratories IL 701, Edwards 9520A and Gold SP 1435. Pulsatile instead of continuous flow produced a pronounced and similar increase in the variability of measurement of all three devices, with the SD of the prediction being approximately double that with continuous flow. The accuracy of the measurements was reduced, with flow rates being overestimated. With pulsatile flow, injectate at ice temperature and a 10-ml injectate, the Edwards 9520A computer gave least variability.

According to Stetz and colleagues [18], who reviewed the published literature and evaluated the reproducibility and accuracy of the TD method, it is difficult to determine the accuracy of this technique, especially for clinical CO determination. Both the Fick and the dye dilution methods are dilution techniques with the same theoretical errors. With a single TD measurement, a difference of about 22% is needed, particularly in the intensive care setting, to demonstrate significant trends in CO. As a result, TD measurements in determining CO of 3.5 and 4.5 litre min⁻¹ during therapeutic intervention may represent only reproducibility error, rather than therapeutic success. Even with triplicate measurements, changes of 15% in CO may not be significant. Stetz's group used the standard error of the mean (SEM %) (SEM/average CO) for examination of the reproducibility of the TD technique. It varied from 2.0% to 5.0% for three measurements per determination and from 3.5% to 8.7% for single measurements. The SEM% values predict that the TD method may need to differ by 6.0-15.0% (3 x SEM%) for triplicate measurements and by 9.5-26.1% for single measurements, in order to establish a significant change.

Other problems with TD are injectate volume and temperature, injection velocity (that may itself produce accelerations of flow in the pulmonary artery system [29]), heat loss in the catheter system and in the vessel wall, and placement of the thermistor in the pulmonary artery. As a consequence, thermodilution cannot be regarded as the gold standard.

Compared with TD, TEB slightly overestimates cardiac output in the normal range during spontaneous ventilation and IPPV. In increased cardiac output states there is a tendency to overestimation during spontaneous ventilation, whereas during IPPV, TEB seems to underestimate cardiac output.

There are two major problems of the TEB method: the correct signal processing of the critical parameters $Z_o$, LVET and dZ/dmax [30] and the empirically derived equation. The assumption by Sramek [5] that the volume of the thorax, as electrically participating tissue, is calculated as a truncated cone instead of as Kubicek’s cylinder, may improve the accuracy [4] or not [31], but does not correct overestimation of stroke volume produced by the TEB method in spontaneous breathing patients. One of the reasons for this overestimation is the assumption that the ejection velocity during systole is constant during the entire left ventricular ejection time in the equations of Kubicek and colleagues [3] and Sramek [5], whereas in reality the ejection velocity decreases to zero after reaching its peak, represented as the ohmic counterpart dZ/dmax in the impedance-stroke volume calculations. This is supported by the findings of Coloucosis, Huntsman and Curreri [32], in animal experiments measuring CO by continuous-wave Doppler technique, that at small stroke volumes the ejection period is abbreviated and the velocity record is symmetrical, while at large values of SV there is a prolongation of ejection and loss of symmetry. Other investigators [33, 34] observed changes in ejection shape and duration in response to altered haemodynamic conditions or heart rate. During mechanical ventilation, this velocity profile is altered, as TEB overestimates CO compared with TD in low flow conditions and underestimates CO during sepsis [35]. Alteration of $Z_o$, as basic impedance which represents the basic fluid volume of the thorax may be excluded, as our own investigations [13] and those of Edmunds, Godfrey and Tooley [36] demonstrated no loss of accuracy during different lung volumes. The limitations for TEB are aortic regurgitation, tachyarrhythmias, open heart surgery and extreme obesity. Compared with TD, DU underestimates CO con-
sistantly, above all in increased cardiac output states during spontaneous ventilation, as described also for transtracheal Doppler [9]. Technical problems arose from the fact that our Doppler device averaged CO over a 12-s interval, which implies more than one ventilatory cycle. Moreover, DU measurements took place after termination of the TD and TEB measurements.

Methodological problems in the Doppler method include the assumption that the aorta is circular and that there is no diameter change during systole [37]. As the cross-sectional area is a quadratic function of the radius, small errors in measurement of diameter may produce large errors in CO values [38]. Pulsations of the non-rigid aorta during systole produce 5–17% changes in CSA from its diastolic to systolic pressure extremes [39]. In the presence of turbulence which may occur with anaemia, tachycardia, etc., the mean velocity measured by the Doppler beam is unrepresentative of the forward flow that represents CO [14]. Another phenomenon, known as aliasing, occurs with the pulsed Doppler in high flow states and makes accurate measurement of blood velocity impossible [6]. Doppler frequency shift can be measured accurately only if it is less than 50% of the sampling frequency.

Practical considerations

The DU method is user-dependent and requires a long period of training [40]. It often takes a long time to obtain a satisfactory signal. The recorded Doppler signals selected for calculation of cardiac output should be of optimal quality. With bad positioning of the probe, the large beam does not cover the whole lumen of the aorta and it may be impossible to obtain an adequate signal in some patients [12]. Other sources of error are a bad ultrasound contact through the skin or the electric activity of surgical cautery.

Continuous monitoring is not possible, so it is impossible to detect sudden changes in CO.

Our results on the accuracy of DU compared with TD relate only to the dual beam Doppler.

In contrast, the TEB method is easy to perform. The advantage of using normal ECG electrodes instead of aluminium strips makes it comfortable for the patient and it can be performed by nursing staff after a short period of instruction.

Sources of errors in the TEB method include incorrect electrode placement. Small alterations in the position of the sensing inner electrodes 2 and 3 produce changes in CO of 5–10%; decreased distance leads to overestimation, whereas increasing distance produces underestimation of CO. Incorrect input of height and weight of the patient in the computerized system has similar effects. Normally, 2–3 cm errors in the adult range of the length L of the human thorax (25–32 cm), which is implicated in the Sramek equation [5] in the third power, would produce errors of 20–30% in stroke volume calculation. As L is standardized as a percentage of the patient's height H (0.17 H)³ in the Sramek equation, the actual distance between the inner electrodes is less important; the actual error in calculation is reduced to about 10%. Both lead to a constant error in COₜₑᵇ.