Comparison of electrical velocimetry and transoesophageal Doppler echocardiography for measuring stroke volume and cardiac output

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Background. Impedance cardiography (ICG) has been used extensively to estimate stroke volume (SV) and cardiac output (CO) from changes of thoracic electrical bioimpedance (TEB). However, studies comparing ICG with reference methods have questioned the reliability of this approach. Electrical velocimetry (EV) provides a new algorithm to calculate CO from variations in TEB. As the transoesophageal Doppler echocardiographic quantification of CO (TOE–CO) has emerged as a reliable method, the purpose of this study was to determine the limits of agreement between CO estimations using EV (EV–CO) and TOE–CO.

Methods. Standard ECG electrodes were used for non-invasive EV–CO measurements. These were placed on 37 patients scheduled for coronary artery surgery necessitating transoesophageal echocardiography monitoring. Simultaneous EV–CO and TOE–CO measurements were recorded after induction of anaesthesia. EV–CO was calculated using the Bernstein–Osypka equation. TOE–CO was measured across the aortic valve using continuous-wave Doppler echocardiography and a triangular orifice model.

Results. A significant high correlation was found between the TOE–CO and the EV–CO measurements ($r^2=0.86$). Data were related linearly. The slope of the line (1.10 (± 0.07)) was not significantly different from unity, and the point at which it intersected the ordinate (0.46 (0.32) litre min$^{-1}$) was not significantly different from zero. Bland–Altman analysis revealed a bias of 0.18 litre min$^{-1}$ with narrow limits of agreement (−0.99 to 1.36 litre min$^{-1}$).

Conclusions. The agreement between EV–CO and TOE–CO is clinically acceptable, and these two techniques can be used interchangeably.

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The development of safe, simple, non-invasive and cost-effective techniques of estimating stroke volume (SV) and cardiac output (CO) is important for clinical decision-making and research in anaesthesia and critical care medicine. The uncertain risk–benefit ratio of invasive CO monitoring by pulmonary artery catheterization further highlights the importance of non-invasive alternatives. A number of non-invasive methods of assessing CO have been studied in the past, with transoesophageal Doppler echocardiography (TOE), impedance cardiography (ICG) and the carbon dioxide rebreathing method currently popular. As the availability of TOE in the operating theatre and intensive care units has recently increased, CO measurements using TOE (TOE–CO) have emerged as a valuable alternative to those measured by pulmonary artery catheter using the thermodilution technique. Research has established that TOE–CO can be measured across the aortic valve with a high degree of reproducibility and accuracy. A considerable number of studies have compared TOE–CO with other methods, and the present study aimed to compare the agreement between TOE–CO and electrical velocimetry (EV–CO).
were excluded from the study, as were patients with atrial fibrillation, pacemakers and any oesophageal or gastric pathology (contraindications to TOE). Anaesthetic management was at the discretion of the anaesthesiology team.

After induction of general anaesthesia and tracheal intubation, a multiplane TOE probe was inserted to quantify volumetric flow at the level of the aortic valve. Four disposable electrocardiographic electrodes were attached at the base of the neck and the inferior aspect of the thorax to record the changing impedance over that area of the thorax. Once haemodynamic stability was achieved, CO was measured in all patients simultaneously by the TOE technique and by EV. The EV measurements were performed according to the manufacturer’s guidelines at the same time as echocardiographic Doppler recordings were obtained by an investigator (CS) who was blinded to the impedance cardiography measurements. One pair of CO values was obtained in each individual patient. All measurements were taken at the end of anaesthetic induction prior to coronary artery surgery.

For TOE–CO measurements, standard transoesophageal two-dimensional, continuous-wave and colour-flow echocardiographic examinations were performed using a Vivid 7 ultrasound machine (GE Medical Systems, Milwaukee, WI) equipped with a multiplane TOE probe (multifrequency phased-array transducer). Recordings were stored on super-VHS videotape for later offline analysis with EchoPac™ software. Three consecutive beats were measured and averaged for each two-dimensional and Doppler parameter. SV was measured as the product of the effective systolic orifice area of the aortic valve and the velocity–time integral at that level.

The aortic valve was located by advancing the TOE probe into the mid-oesophagus, approximately 30 cm from the teeth, until the superior portion of the left atrium was seen in the near field of the image sector. The exact position of the probe was determined by carefully flexing, turning, advancing, withdrawing and rotating as needed until the aortic valve was in the centre of the display. The multiplane angle was increased from 0° to ~30–60° until a symmetrical image of the three cusps of the aortic valve came into view. During systole, the area of the aortic valve is constantly changing in size and in shape. Therefore the effective orifice area of the aortic valve has to be approximated by a geometrical model. The triangular model proposed by Darmon and colleagues assumes that the area of the aortic valve is best represented as the triangular orifice occurring during end-systole (Fig. 1A). Using the TOE frame in which each aortic valve cusp appeared precisely as a straight line forming one side of the triangle, the length of all cusps was measured, and the average value was substituted in the following equation:

\[
\text{AVOA} = 0.5 \times \cos 30° \times L^2 = 0.433 \times L^2 \ (\text{cm}^2)
\]

where AVOA is the effective systolic orifice area of the aortic valve and L is the average length (cm) of the three cusps of the aortic valve.

Methods

Approval to conduct this study was obtained from the institutional review board and written informed consent was obtained from each patient enrolled in the study. Between February and April 2003, 37 patients scheduled for coronary artery surgery and requiring TOE monitoring were considered for inclusion. Patients with significant valvular disease were excluded from the study, as were patients with atrial
For measurements of the velocity–time integral across the aortic valve (VTI), the Doppler recordings of instantaneous flow velocities at the level of the aortic valve were obtained from a modification of the classical transgastric view, visualizing the long axis of the heart from an apical aspect. The view is anatomically referred to as the deep transgastric long-axis view of the left ventricle (deep TG LAX). In order to develop this view, the TOE probe was advanced deep into the stomach. The tip of the probe was fully moved anteriorly and to the left. Careful withdrawal of the flexed probe then resulted in the tip being positioned close to the apex of the left ventricle with the multiplane angle at 0°. The imaging plane was directed superiorly toward the base of the heart until the left ventricle, the left ventricular outflow tract, the aortic valve and the ascending aorta were aligned in an almost vertical direction (Fig. 1B). Doppler quantification of outflow velocities through the aortic valve was performed by directing the continuous-wave Doppler beam exactly through the middle of the aortic valve as parallel to the direction of blood flow as possible. Care was taken to maximize the velocity signal with a distinct closing signal on spectral display and to reduce the wall filter so that signals were complete and outlined to the baseline. Recordings of 5–10 cardiac cycles were made at a sweep speed of 100 mm s⁻¹. For off-line analysis of Doppler registrations three consecutive high-quality Doppler spectra were analysed by manually enveloping along the brightest border of the flow velocity profile to sum the instantaneous blood flow velocities (Fig. 1C). The VTI is the calculated area under the Doppler curve. It was measured using the analysis package of Vivid 7 (GE Medical Systems). No correction was applied to adjust for the angle of incidence between the ultrasound beam and aortic blood flow, because this angle was <10° in all patients.

The average VTI was used to derive CO from the product of VTI, AVOA and heart rate. CO was calculated as follows:

\[
CO = \frac{\text{VTI} \times \text{AVOA} \times \text{HR}}{1000 \text{ litre min}^{-1}}
\]
where CO is the cardiac output, VTI is the velocity–time integral (cm), AVOA is the effective systolic aortic valve orifice area (cm²) and HR is the heart rate (beats min⁻¹).

To test the inter-observer variability, the two-dimensional and Doppler measurements were repeated by a second observer who was unaware of the results of the first examination. Variability was calculated as the mean percentage error, calculated as the difference between the two sets of measurements divided by the mean of the observations.

For EV–CO measurements, the bioimpedance method of CO determination measured changes in transthoracic impedance during cardiac ejection to calculate SV. Impedance measurements were obtained with a new comprehensive cardiovascular monitor (Aesculon Electrical Velocimetry, Osypka Medical GmbH, Berlin, Germany). The Aesculon device emitted a high frequency (50 kHz) and low-amperage (2 mA) alternating electrical current of constant amplitude via a pair of surface electrodes across the left side of the thorax. The voltage drop due to the current application was registered together with the ECG via a second pair of sensing electrodes which were located at the left side of the neck and the left side of the thorax at the level of the xiphoid process, inside the current electrodes (Fig. 2A). Verification of the correct signal quality was accomplished by visualization of the ECG, the impedance waveform and its first derivative (Fig. 2B). The maximum rate of change of TEB over that area of the thorax was interpreted as the ohmic equivalent of mean blood flow velocity in the ascending aorta, and CO was calculated using the following equation:

\[
CO = \frac{(V_{EPT} \times LVET \times FTN \times HR)}{1000 \text{ litre min}^{-1}}
\]

where CO is the cardiac output, \(V_{EPT}\) (ml) is the volume of electrically participating tissue derived from body mass and height, \(\text{LVET}\) (s⁻¹) is the ohmic equivalent of mean aortic blood velocity during left ventricular ejection, \(\text{FTN}\) (s) is the normalized flow time derived from left ventricular ejection time (s), and \(HR\) (beats min⁻¹) is the heart rate.

This equation requires an ohmic equivalent of mean aortic blood velocity during left ventricular ejection to determine SV (\(SV = V_{EPT} \times \text{LVET} \times \text{FTN}\)). Therefore, the Aesculon monitor incorporates an algorithm which transforms the ohmic equivalent of mean aortic blood flow acceleration into an equivalent of mean aortic blood flow velocity:

\[
\nu_{\text{LVET}} = \left[\frac{(dZ(t)/d\text{t})_{\text{min}}}{Z_0}\right]^n
\]

where \((dZ(t)/d\text{t})_{\text{min}}\) is the maximum rate of change of TEB during systole, \(Z_0\) is the base impedance
(average value over 10 cardiac cycles) and $n$ is an exponent which is $<1$.

Unlike the traditional approach of ICG, which interprets the maximum rate of change of TEB as the ohmic equivalent of the systolic dilation of the aorta and its major tributaries, this new method is based on the properties of pulsatile blood flow and the alignment of erythrocytes from a random orientation prior to aortic valve opening (Fig. 2n, fiducial point B) towards an orientation with their disk-shaped bodies parallel to the axial blood flow $~60$ ms after opening of the aortic valve (Fig. 2n, fiducial point C). The parallel alignment of erythrocytes produces a change in the resistivity of blood in the aorta, which is equivalent to mean aortic blood flow acceleration.24

EV–CO was recorded continuously online, and data were saved to a computer. At the beginning of Doppler registration of flow velocity profiles, an event mark was set into the impedance recording for later output of the corresponding EV–CO values. A period of 30 s around the time of Doppler registration was used for calculating the mean value of the impedance-derived CO. The EV–CO was defined as the mean of 10 successive CO values. Body weight, body height and age were used for SV correction by the Aesculon software.

Statistical analysis

All results were analysed using GraphPad Prism 4 software (GraphPad Software Inc., San Diego, CA) on an Apple Macintosh computer. All results are expressed as mean (SD). Agreement between TOE–CO and EV–CO was evaluated in three ways. First, the differences between the paired CO values were plotted against the average CO values of both measurements. This statistical method was recommended by Bland and Altman27 for evaluation studies. Bias was calculated as the mean difference between TOE–CO and EV–CO. The upper and the lower limits of agreement were calculated as bias±2SD, and defined the range in which 95% of the differences between the methods were expected to lie. The percentage error between the two measurements was calculated as twice the standard deviation of the bias divided by the mean CO.28 Secondly, the mean CO values of Doppler echocardiography and EV were compared using a paired Student $t$-test. Thirdly, correlation between these values was evaluated by calculating the Pearson correlation coefficient $r$ and applying a linear regression model of the EV–CO on TOE–CO. The spread of the slope and the ordinate of this relationship is expressed as their standard errors. The correlation coefficient was calculated to allow comparison of the results presented here with other studies. A $P$-value $<0.05$ was considered statistically significant.

Results

Thirty-seven patients were enrolled in the study. No patient was omitted from analysis because of inability to obtain TOE–CO or EV–CO. No serious complications occurred during the study. The final analysis included 10 women and 27 men. The mean age was 65.8 (43–81) years, and the mean height and body weight were 172 (10) cm and 82 (13) kg, respectively (Table 1). Eight of the 37 patients had two-vessel disease and 29 had three-vessel disease, 19 had prior myocardial infarction, 10 had prior coronary angioplasty and seven had prior coronary bypass surgery. All patients had an uneventful course during induction of anaesthesia and subsequent coronary artery surgery.

Figure 3A shows a scatterplot of the data from 37 matched TOE–CO and EV–CO measurements. There was no significant difference between the means as evaluated by the paired Student’s $t$-test, with a mean CO of 4.11 (1.36) litre min$^{-1}$ and 3.93 (1.57) litre min$^{-1}$ for TOE–CO and EV–CO, respectively ($P=0.073$). The ranges of CO values were 2.59–7.93 litre min$^{-1}$ (TOE–CO) and 1.78–8.06 litre min$^{-1}$ (EV–CO). A significant high correlation was found between the TOE–CO and the EV–CO measurements ($P<0.001$). Pearson’s correlation coefficient $r$ was 0.93 ($r^2=0.86$). EV–CO was linearly related to TOE–CO. The slope of the line (1.10 (SE 0.07)) was not significantly different from unity, and the point at which it intersected the ordinate (0.46 (SE 0.32) litre min$^{-1}$) was not significantly different from zero.

The results of the analysis of agreement and the distribution of the observed differences are shown in Fig. 3n. The mean difference (bias) between TOE–CO and EV–CO was 0.18 litre min$^{-1}$ with a standard deviation (precision) of 0.59 litre min$^{-1}$. The limits of agreement are defined as the mean difference (±2SD), and the lower and upper limits for this study were −0.99 litre min$^{-1}$ and 1.36 litre min$^{-1}$, respectively. The percentage error between the methods was 29%. The scatter of differences was evenly distributed along the abscissa.

Both AVOA and VTI measurements showed little variation between their first and second determinations. The mean

| Table 1 Patient characteristics and haemodynamic measurements (n=37). |
|-----------------------------|-----------------------------|
| Age (yr)                    | 65.8 (43–81)                |
| Height (cm)                 | 172 (10)                    |
| Weight (kg)                 | 82 (13)                     |
| Diuretic use                | 4 (11%)                     |
| Calcium entry blocker use   | 8 (22%)                     |
| Long-acting nitrate use      | 21 (57%)                    |
| Angiotensin-converting enzyme inhibitor use | 12 (32%) |
| β-adrenergic receptor blocker use | 33 (89%) |
| Left ventricular ejection fraction (%) | 55.1 (11.3) |
| Mean arterial pressure (mm Hg) | 79 (12)                |
| Central venous pressure (mm Hg) | 10 (5)                  |
| Heart rate (beats min$^{-1}$) | 63 (16)                    |
| Velocity–time integral (cm) | 24.0 (7.6)                  |
| Effective aortic valve orifice area (cm$^2$) | 2.86 (0.48) |
| TOE–CO (litre min$^{-1}$)   | 4.11 (1.36)                 |
| EV–CO (litre min$^{-1}$)    | 3.93 (1.57)                 |
percentage errors (sd)\(^{6}\) for inter-observer variability of AVOA and VTI were 1.4 (1.1)% and 1.7 (1.4)%, respectively. Inter-observer variability was calculated from the results of an offline analysis of video recordings.

Discussion

To the best of our knowledge, this report is the first study comparing CO measurements derived from thoracic electrical bioimpedance and transoesophageal Doppler echocardiography. EV–CO and TOE–CO, as measured after induction of anaesthesia in surgical patients with coronary heart disease, correlated significantly (\(r^2=0.86\)). The bias between the two measurements was small (0.18 litre min\(^{-1}\)), the upper and lower limits of agreement were −0.99 litre min\(^{-1}\) and +1.36 litre min\(^{-1}\), respectively.

In a meta-analysis of studies using bias and precision statistics to compare CO measurement techniques, Critchley and colleagues\(^{28}\) reported an overall mean CO of 4.8 litre min\(^{-1}\) from the 23 bioimpedance studies which were included. The bioimpedance method was compared with thermodilution, dye dilution or the Fick method which was used mainly in children. The overall bias from these studies was 0.6 litre min\(^{-1}\), and the overall limits of agreement were ±1.7 litre min\(^{-1}\). The percentage error for studies using the bioimpedance method was 37%. The authors provided criteria which allowed quantification of acceptable limits of agreement between two CO measurement techniques. They assumed an inherent error of ±20% for measurement of physiological variables such as CO. For example, the error in the thermodilution technique was proved to be 22% for single measurements.\(^{29,30}\) By combining the errors of both the test and the reference method using an errorgram, Critchley and colleagues demonstrated that a mean percentage error of ~30% between two different methods is clinically acceptable if the inherent errors in both techniques are similar to the expected error in thermodilution CO measurements. Thus, according to objective criteria, the agreement between EV–CO and TOE–CO, which was assessed in the current study, can be judged as acceptable, and these two techniques can be used interchangeably.

Measurement of CO can be extremely useful when assessing circulatory function, and a simple and reliable method of measuring CO is frequently required both clinically and for research purposes. However, the thermodilution technique using a pulmonary artery catheter is highly invasive, and recently the use of pulmonary artery catheters for invasive haemodynamic monitoring has been increasingly criticized because of its uncertain risk–benefit ratio and cost.\(^{2}\) As a result, there is a continuing search for a method of CO measurement that is less invasive than its predecessors. In this respect ICG, which calculates SV and CO from changes in the instantaneous impedance of a small electrical current transferred through the body, has received much attention in the last four decades as it is non-invasive, easy to use, cost-effective and adapted for continuous monitoring of CO and related parameters. In order to investigate the validity of ICG, numerous studies have compared the results obtained from ICG with values obtained from reference methods in
different research settings. These studies have reported both very good\textsuperscript{12} and very bad correlations.\textsuperscript{13} In a comprehensive meta-analysis of the literature Raaijmakers and colleagues\textsuperscript{14} explained the variations in the reported results as being caused by differences in study design, subject characteristics, reference method and ICG methodology. They pooled a total of 164 correlation coefficients of 112 studies which yielded an overall $r^2$ of 0.67. Only 31 studies satisfied the criteria for single-measurement design. In the data for single-measurement design, the correlation coefficient was significantly lower ($r^2=0.53$) than for repeated-measurement design, because the between-subject variability of measurement results is usually much larger than the within-subject variability. The performance of ICG was similar in various groups of patients, with the exception of cardiac patients where the correlation was decreased ($r^2=0.44$ for the single-measurement design studies).

Considering that ICG performed so poorly in cardiac patients, it is important to note that correlation and agreement in the current study were much higher. This finding might be explained by the fact that transoesophageal Doppler echocardiography was used as the reference method in our study, whereas the studies summarized in the meta-analysis by Raaijmakers and coworkers\textsuperscript{14} almost exclusively used thermodilution as the reference. Hence the thermodilution technique may have contributed to the value of the correlation coefficient, as was suggested by Jensen and coworkers.\textsuperscript{13} The potential hazard of using thermodilution as the only reference standard for CO measurement has recently been demonstrated by Yung and colleagues.\textsuperscript{31} In their study of spontaneously breathing non-intubated pulmonary hypertension patients, ICG had greater bias and less precision and correlation when compared with thermodilution than when compared with the direct Fick method. This result is duplicated in another three-way comparison in heart failure patients, where the level of agreement between ICG and thermodilution was similar to that between thermodilution and the direct Fick method.\textsuperscript{32} As it seems highly unlikely that the performance of any ICG measurement is influenced by the reference method used, these results might mirror the inaccuracy of the reference methods themselves. However, by using the reference method as the 'gold standard', the inaccuracies are erroneously attributed to ICG exclusively, rather than taking into account the well-known limitations of the thermodilution technique, of which some are operator dependent and some are related to limitations of the technique, especially when CO is low or high.\textsuperscript{16,17,29,30}

The methodology used to calculate stroke volume and CO from changes in the electrical impedance of the thoracic cavity that occur with the ejection of blood during cardiac systole has evolved significantly in the last two decades, so that better and more reliable CO determination has been achieved in recent years.\textsuperscript{5} Originally, the Kubicek equation was used.\textsuperscript{19} This technique, with automated and continuous measurements, is non-invasive and simple to perform. The original Kubicek equation for calculating stroke volume was modified by Bernstein.\textsuperscript{21} Different devices operating on the basis of these formulae have been tested against reference methods with contradictory results. The classical equations of ICG use two components: the basal thoracic impedance $Z_0$, which represents the variations in the steady-state mean thoracic impedance, and the pulsatile variation in impedance $\Delta Z$, which is mainly a function of variations in the blood volume of the thoracic aorta.\textsuperscript{22} $Z_0$ depends on multiple factors such as thorax morphology, homogeneity of thorax perfusion and fluid and gas content. By comparing bioimpedance recordings with a specially designed ballistocardiogram, Tischenko\textsuperscript{39} hypothesized that the origin of $\Delta Z$ is to be found in the systolic dilation of the aorta and its major branches. In the study presented here, a new impedance cardiometry device, the Aesculon Electrical Velocimetry Comprehensive Cardiovascular Monitor (Osypka Medical GmbH, Berlin, Germany), was tested. The basic equation for calculating SV and CO has been modified profoundly. In contrast with the classical approach, the formula incorporated into the Aesculon monitor relates the maximum rate of change of impedance to peak aortic blood acceleration, and derives the mean aortic blood velocity using a transformation.\textsuperscript{24} According to the theory, the orientation of disk-shaped erythrocytes in the aorta changes quickly from random to alignment in the direction of blood flow upon opening the aortic valve. The pulsatile alignment of the erythrocytes during early systole and the increasingly random orientation during the course of diastole correspond to a pulsatile increase and decrease, respectively, in electrical conductivity which is reflected in a decrease in TEB during early systole and an increase later. Thus, in contrast with former approaches, this newly introduced equation focuses on the changes in the compartment with the greatest conductivity, the blood in the aorta. The aorta is also the major contributing factor to conductivity changes. Minor changes in high-resistance low-conductivity compartments, such as lung, gas and surrounding tissues, are neglected. Therefore this approach is likely to provide more accurate information on CO, independent of the volume of the surrounding tissue which is highly variable and might interfere with the results of traditional ICG.

To summarize, it has been demonstrated that electrical velocimetry, a new ICG algorithm, can provide CO evaluations with clinically acceptable accuracy. The method does not require an experienced operator, is simple and involves only the application of standard ECG electrodes. It is non-invasive and provides a continuous beat-to-beat estimation of CO over an arbitrarily long period.

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