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Electrical velocimetry for measuring cardiac output in children with congenital heart disease

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Background. The purpose of this study was to evaluate the agreement of cardiac output measurements obtained by electrical velocimetry (CO_{EV}) and those that derived from the direct Fick-oxygen principle (CO_F) in infants and children with congenital heart defects.

Methods. Simultaneous measurements of CO_{EV} and CO_F were compared in 32 paediatric patients, aged 11 days to 17.8 yr, undergoing diagnostic right and left heart catheterization. For non-invasive measurements of cardiac output by electrical velocimetry, which is a variation of impedance cardiography, standard surface electrodes were applied to the left side of the neck and the left side of the thorax at the level of the xiphoid process. Cardiac output determined using direct Fick-oxygen principle was calculated by direct measurement of oxygen consumption (VO_2) and invasive determination of the arterio-venous oxygen content difference.

Results. An excellent correlation (r=0.97) was found between CO_{EV} and CO_F ($P<0.001$). The slope of the regression equation [0.96 (SD 0.04)] was not significantly different from the line of identity. The bias between the two methods ($CO_{EV}-CO_F$) was 0.01 litre min^{-1} and the limits of agreement, defined as the bias (2 SD), were -0.47 and +0.45 litre min^{-1}.

Conclusions. CO_{EV} demonstrates acceptable agreement with data derived from CO_F in infants and children with congenital heart disease. The new technique is simple, completely non-invasive, and provides beat-to-beat estimation of CO.

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Comprehensive evaluation of a patient's haemodynamic status should include appraisal of cardiac output. Continuous assessment of cardiac output is useful in the intensive care unit for monitoring patients with heart failure or shock and for the titration of cardiovascular drugs and fluids.[1]

Most currently available techniques for measuring cardiac output, such as dye dilution, thermodilution, and methods based on the Fick principle, are invasive and require strict adherence to rigid protocols for accurate and reproducible results.[2–5] Doppler-echocardiography and carbon dioxide re-breathing are commonly used non-invasive techniques in adults, but require an experienced operator.[6 7] There have been few studies of cardiac output measurement in infants and children with congenital heart defects.[7] With the exception for pulse contour analysis,[8] which is invasive, there is no single technique available for measuring cardiac output continuously and accurately in children with congenital heart defects.

Impedance cardiography is a non-invasive method of obtaining continuous measurements of stroke volume and cardiac output.[9] Impedance cardiography technology was developed for NASA by Kubicek and colleagues[10] in the 1960s and is based upon the assumption that the human thorax is electrically a non-homogeneous bulk conductor and behaviourally conforms to parallel conduction theory when exposed to a field of alternating current.[11] In contrast to the original Kubicek equation[10] and its modification by Bernstein in the 1980s,[12] the formula incorporated into the new impedance cardiometry monitor AESCULON®

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relates the maximum rate of change of impedance to peak aortic blood acceleration, and derives the mean aortic blood velocity using a transformation.[13] The monitor is based on the premise that the orientation of the erythrocytes in the aorta changes quickly from random to alignment in the direction of blood flow upon opening of the aortic valve. The alignment of erythrocytes during early systole and the following increasingly random orientation produces a pulsatile change in electrical conductivity which is reflected in a decrease in thoracic electrical bioimpedance (TEB) during early systole and an increase later. In contrast to former approaches, a recently reported new method, referred to as electrical velocimetry,[13] focuses on the changes in the compartment with the greatest conductivity and the major contributing factor to conductivity changes, the blood in the aorta.

In the current study, conducted in children with congenital heart defects, we compared cardiac output measurements obtained by electrical velocimetry (CO_{EV}) with cardiac output determined by the 'gold-standard' direct Fick-oxygen method (CO_F).

Methods

Study population

From 1 July 2005 to 31 January 2006, 32 infants, children, and adolescents undergoing haemodynamic evaluation or for an intervention in the cardiac catheter laboratory and requiring general anaesthesia were considered for inclusion. Twelve female and 20 male patients were studied with a mean age of 3.4 yr (range: 12 days to 17.8 yr; median 0.7 yr) and mean weight of 13.8 kg (range: 2.7–54 kg; median 7.1 kg). The study was approved by the institutional ethics committee and written consent was obtained from the patient's guardian, and, depending on age, the patient as well.

Measurements

Anaesthetic management, including the use of cuffed and uncuffed endotracheal tubes, was at the discretion of the paediatric anaesthesiology team. Because oxygen consumption (VO_2) was being measured and for patient safety, the tube size chosen had to fulfil the requirement of easy insertion through the cricoid cartilage. Uncuffed tubes were required to seal at up to 20 cm H_2O with a subsequent air leak at a peak inspiratory airway pressure of 25 cm H_2O. This was assessed by means of placing a stethoscope over the patient's mouth. After induction of general anaesthesia and tracheal intubation, a spirometry system (Vmax Encore®, Viasis Healthcare, Hoechberg, Germany) was connected to the anaesthetic circuit (Cato®, Draeger, Lubeck, Germany) to measure oxygen consumption (VO_2). Electrical velocimetry was applied before insertion of a catheter introducer sheath into the femoral vein. Haemodynamic measurements were performed approximately 20–40 min after induction of anaesthesia when the patient was haemodynamically stable and before the first angiography.

Non-invasive cardiac output measurement by electrical velocimetry (CO_{EV})

Cardiac output measurement using the AESCULON® monitor (Osypka Medical, Berlin, Germany and San Diego, CA, USA) requires placement of four disposable standard surface ECG electrodes connected to the monitor by a cable. The monitor emits a high-frequency (50 kHz) AC current of a constant magnitude (2 mA, rms) through a pair of electrodes, inducing a current field.[14] By means of voltage-sensing electrodes placed within the current field, the quasi-static basal transthoracic impedance Z_0 (ohms) and the impedance change $\Delta Z(t)$ are calculated by Ohm's Law ($Z=U/I$) from the demodulated basal transthoracic voltage U (volts) and cardiac-synchronous voltage change $\Delta U(t)$, respectively. By electronic differentiation of $\Delta Z(t)$ [$dZ(t)$ in Fig. 1], the first time-derivative is obtained $dZ(t)/dt$, from which its peak magnitude, $dZ(t)/dt_{min}$, and left ventricular ejection time (flow time) are measured and entered into the Bernstein–Osypka SV equation[13 15] to compute CO_{EV}. The Bernstein–Osypka SV equation is given in its general form as follows:

$$SV_{B-O} = V_{EPT} \cdot \sqrt{\left(\frac{|dZ(t)/dt_{min}|}{Z_0}\right)} \cdot T_{LVE}$$

where SV_{B-O} is the stroke volume from the Bernstein–Osypka equation (ml); V_{EPT} the volume of electrically participating thoracic tissue in ml (V_{ITBV}/ζ^n); V_{ITBV} (ml) intrathoracic blood volume obtained from body weight (W, kg) by the relationship aW^b, where the coefficient 'a' is $\approx$0.25 of patient indexed blood volume in ml kg^{-1} and exponent 'b'$\approx$1; ζ the index of transthoracic aberrant conduction (dimensionless) and 'n' is an exponent between 1 and 2; $dZ(t)/dt_{min}$ the ohmic mean acceleration ($\Omega\ s^{-2}$); Z_0 the quasi-static transthoracic base impedance (Ω); $\sqrt{(|dZ(t)dt_{min}|/Z_0)}$ the square root acceleration step-down transformation, ohmic mean velocity ($1\ s^{-1}$); T_{LVE} the left ventricular ejection time (flow time) (s); CO_{EV} (litre min^{-1}) was calculated as follows: $CO_{EV} = [SV_{B-O} \times$ heart rate (beats min^{-1})]/1000.

Upon satisfactory initialization of AESCULON®, CO_{EV} was continuously displayed and recorded as an average value over 10 valid cardiac cycles. Averaged CO_{EV} data were stored on disc by AESCULON® over the period in which VO_2 and invasively derived arterio-venous oxygen content measurements were obtained.

Invasive cardiac output by the direct Fick-oxygen method (CO_F)

To determine CO_F, blood samples were obtained from the caval veins, right atrium, or pulmonary trunk for mixed

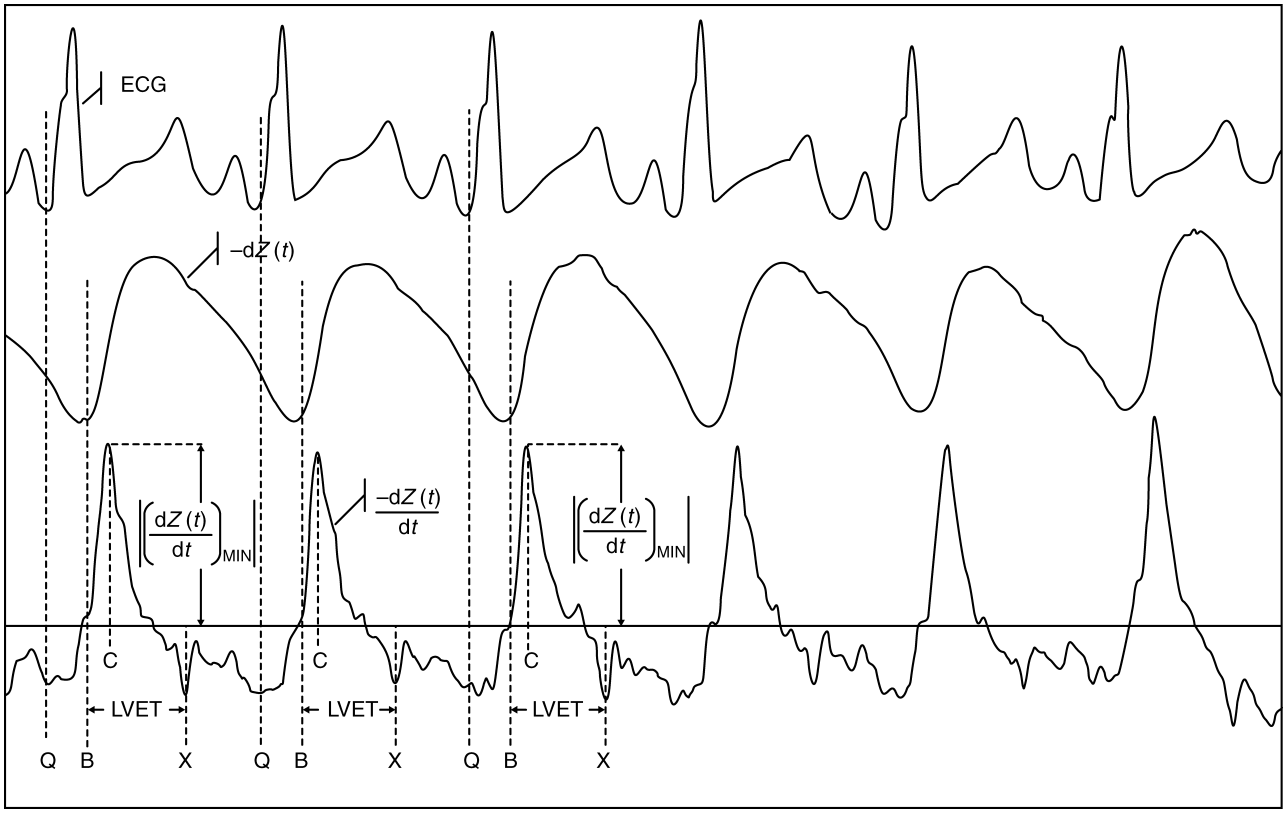

Fig 1 Surface ECG, impedance waveform [$-\mathrm{d}Z(t)$, also known as $\Delta Z(t)$], and the electronically differentiated first time-derivative of $-\mathrm{d}Z(t)$, $-\mathrm{d}Z(t)/\mathrm{d}t$, obtained from a 25-day-old male (HR=142 beats min^{-1}, SV=3.3 ml, CO=0.47 litre min^{-1}). Note that the impedance change $-\mathrm{d}Z(t)$ and its rate of change, $-\mathrm{d}Z(t)/\mathrm{d}t$ are given in their inverted form, which is the traditional presentation because the shape of the $-\mathrm{d}Z(t)$ waveform exhibits some adherence to an aortic pressure tracing. The marker labelled 'Q' on the ECG marks the beginning of ventricular depolarization and thus the onset of electro-mechanical systole. Shortly after aortic valve opening, which is indicated by the marker labelled 'B', the $-\mathrm{d}Z(t)$ waveform exhibits a significant upslope and, consequently, its time-derivative $-\mathrm{d}Z(t)/\mathrm{d}t$, a nadir which is indicated by the marker labelled 'C'. The amplitude at the point which in the traditional presentation is depicted as a positive deflection is the maximum slope or peak rate of change of the transthoracic electrical impedance during a particular cardiac cycle, and measured beat-to-beat. The time-to-peak (rise time) of $-\mathrm{d}Z(t)/\mathrm{d}t$ is concordant with the time to peak of $-\mathrm{d}v(t)/\mathrm{d}t$ of the aortic blood velocity waveform. The magnitude at the peak of $-\mathrm{d}Z(t)/\mathrm{d}t$, that is $|(\mathrm{d}Z(t)/\mathrm{d}t)_{\mathrm{MIN}}|$, is analogous to the magnitude $|\mathrm{d}v(t)/\mathrm{d}t)_{\mathrm{MIN}}|$ of this waveform. The first-time derivative of the impedance waveform, $-\mathrm{d}Z(t)/\mathrm{d}t$, exhibits a deflection at the time of aortic valve closure, which is indicated by the label 'X'. The temporal interval between points B and X is defined as the left ventricular ejection time.

venous oxygen saturation ($S\mathrm{v}_{\mathrm{O}_2}$) and from the aorta or femoral artery for systemic arterial oxygen saturation ($S\mathrm{a}_{\mathrm{O}_2}$). Samples were collected during the time interval over which $\mathrm{CO}_{\mathrm{EV}}$ was calculated and recorded by AESCULON®, and were analysed by a blood gas analyser (Hemoximeter OSM 3, Radiometer, Copenhagen, Denmark). The Fick principle for measuring CO was determined by dividing the VO_2 by the arterio-venous oxygen content difference via the following equation:

$$\mathrm{CO_F\,(litre\ min^{-1})} = \frac{\mathrm{VO_2(ml\ min^{-1})}}{\mathrm{Hb\,(g\%)} \times 1.34\,\mathrm{(ml\,g^{-1})} \times 10 \times [S\mathrm{a_{o_2}(\%)} - S\mathrm{v_{o_2}(\%)}]}$$

Haemoglobin concentration (Hb) was obtained from the first blood sample, which was taken during heart catheterization. VO_2 was determined by spirometry. We used the Vmax Encore Spirometry System according to the manufacturer's guidelines, measuring VO_2 continuously during a period of ~20 min, thus encompassing the time blood samples were taken. We used the mean VO_2 from all measurements during the period of blood sampling for calculation of CO_{F}. At the beginning and end of blood samples for CO_{F} measurement, an event mark was set into the impedance recording to define the corresponding $\mathrm{CO}_{\mathrm{EV}}$. At the completion of the catheterization procedure, mean CO_{F} was compared with the corresponding mean $\mathrm{CO}_{\mathrm{EV}}$.

Statistical analysis

All results were analysed using GraphPad Prism 4 software (GraphPad Software, Inc., San Diego, CA, USA) on a Windows computer. All results are expressed as mean (SD). Interchangeability or equivalence between $\mathrm{CO}_{\mathrm{EV}}$ and CO_{F} was evaluated using two different methods. First, the closeness of association, or correlation, between the two

methods, was computed using the Pearson correlation coefficient r^2 and applying a linear regression model. The spread of the slope and the ordinate of this relationship were expressed as their standard errors. A P-value of <0.05 was considered statistically significant. Secondly, to assess agreement between CO_{EV} and CO_F, the method of Bland and Altman[16] was employed, by computing bias, precision, and limits of agreement.

Results

The details of the patients, VO_2 index (ml kg^{-1} m^{-2}), haemoglobin (g dl^{-1}), Sa_{O_2} (%), and CHD diagnosis are given in Table 1. In all cases with a VSD, the left-to-right shunt was significant with pulmonary blood flow (Qp) substantially greater than systemic blood flow (Qs), Qp/Qs>2.3.

Figure 2 shows a scatter-plot of the data from 32 simultaneously obtained measurements of CO_{EV} and CO_F. An excellent correlation (r^2=0.94, $P<0.0001$) was found between the two techniques. The slope of the regression equation [m=0.96 (SD 0.04)] was not significantly different from unity with $b\approx0$. For the subgroup of nine infants with cyanotic heart defects ($Sa_{O_2}<94\%$), the correlation between CO_{EV} and CO_F was very good (r^2=0.80, P=0.007). The lower correlation coefficient of r^2=0.80 in this subgroup compared with that in all patients (r^2=0.94) is predominantly a statistic effect due to the small number of patients.

The results of the Bland and Altman analysis for all patients are shown in Figure 3. The mean difference (bias) between CO_{EV} and CO_F was 0.01 litre min^{-1} with standard deviation (precision) of 0.23 litre min^{-1}. The upper and lower limits of agreement (±2 SD) were 0.47 and 0.45 litre min^{-1}, respectively.

There were no significant correlations between the accuracy of the two CO methods and body weight (r^2=0.1, P=0.11) and individual haemoglobin concentration (r=0.002; P=0.38).

Discussion

Although infants and children have been studied with impedance cardiography in the past, its use in patients with congenital heart disease has rarely been reported. Using the previous equations, implemented by far less

Table 1 Patient characteristics. Hb, haemoglobin; VO_2, oxygen consumption; Sa_{O_2}, arterial oxygen saturation; Sv_{O_2}, mixed venous oxygen saturation; AS, aortic stenosis; CMP, cardiomyopathy; HLHS, hypoplastic left heart syndrome; LPA, left pulmonary artery; MR, mitral valve regurgitation; PA, pulmonary atresia; PDA, patent ductus arteriosus; PR, pulmonary valve regurgitation; PS, pulmonary valve stenosis; PHT, pulmonary hypertension; TA, tricuspid valve atresia; TOF, tetralogy of Fallot; VSD, ventricular septal defect

Patient	Age (yr)	Weight (kg)	Length (cm)	VO_2 index (ml kg^{-1} m^{-2})	Hb (g dl^{-1})	Sa_{O_2} (%)	Sv_{O_2} (%)	Diagnosis
1	0.23	5.6	59	101	8.9	99	71	Mild AS
2	2.67	16.7	97	110	11	97	75	Mild AS
3	5.31	17	106	92	14.5	97	65	CMP
4	1.35	11	80	141	14	88	65	HLHS (Glenn)
5	0.47	5.6	59	41	14.7	44	32	HLHS (Norwood)
6	5.68	18	111	89	13.5	97	76	LPA stenosis
7	3.85	11.9	97	181	12.2	97	66	MR
8	9.75	43	146	114	10	97	65	MR
9	15.92	53	160	93	12.8	95	72	PA (Fontan)
10	8.47	17	116	109	12	100	79	PDA
11	0.85	7	67	134	10.6	99	77	PDA
12	0.8	7.7	66	102	9.8	98	62	PHT
13	17.8	53	173	75	12.6	99	69	PR
14	4.34	11	93	116	11.1	99	74	PS
15	1.58	9	81	81	15.4	99	76	PS
16	0.3	6.1	60	69	11.2	97	72	PS
17	0.03	2.7	47	89	12.8	92	64	Shone complex
18	0.55	7.2	69	135	11.8	84	60	TA
19	0.08	3	51	186	9.9	66	45	TA
20	0.31	6	64	77	12.2	91	60	TA
21	10.98	24	135	94	17.3	68	54	TOF
22	0.33	5	58	122	10.6	96	66	TOF
23	0.17	5.1	57	186	9.3	96	60	TOF
24	0.3	3.9	52	116	8.5	99	74	VSD
25	0.47	6.3	60	130	8.5	99	69	VSD
26	0.35	5.1	59	61	10.1	99	67	VSD
27	0.3	5.8	60	56	11	86	62	VSD
28	14.76	54	165	99	14.2	99	77	VSD
29	0.46	3	48	68	10.8	93	59	VSD
30	0.47	4.8	60	111	10	97	62	VSD
31	0.33	4.9	60	87	9.9	98	72	VSD
32	1.05	7.2	71	146	9.1	97	66	VSD

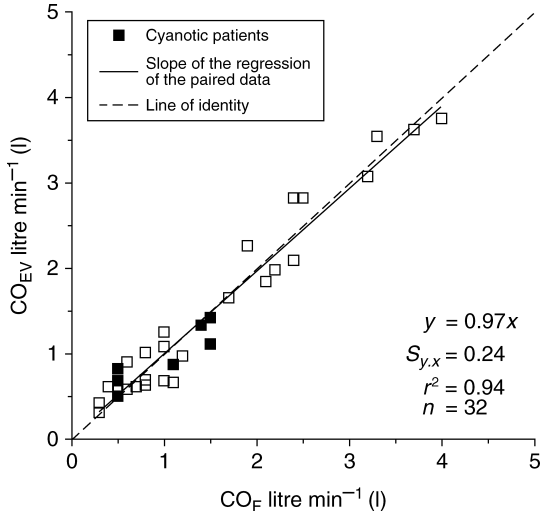

Fig 2 Scatter-plot of the data from 32 invasive measures of CO_F and corresponding CO_{EV} measurements.

sophisticated devices than AESCULON®, Miles and colleagues[17] found a good to very good correlation (r=0.70–0.89) between CO_F and CO_{ICG} in young children with a variety of congenital heart diseases. As with our results, correlation and agreement was lower in patients with a ventricular septal defect (VSD). Braden and colleagues[18] compared CO_F with CO_{ICG} in a group of children with congenital heart disease. Again in this study, correlation was highest (r=0.84) in patients without shunts and was appreciably lower (r=0.70) in patients with a VSD and left-to-right shunt.

To our knowledge, this report is the first study comparing CO_{EV} with CO_F in children with a variety of different heart lesions. The direct Fick-oxygen method is an established, but invasive gold-standard method of measuring cardiac output. Electrical velocimetry is a new technique which has several advantages compared with CO_F: it is non-invasive, safe, easy to apply, and provides continuous beat-to-beat estimation of cardiac output.

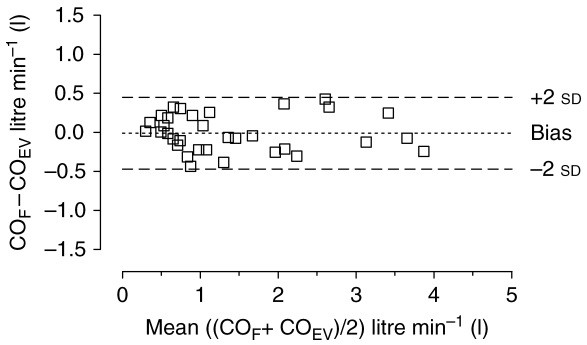

Fig 3 Bland and Altman analysis of cardiac output measured by electrical velocimetry (CO_{EV}) and that determined by the direct Fick-oxygen (CO_F) in 32 infants and children. Note: The cardiac output is not indexed but given in absolute values. The bias between CO_{EV} and CO_F was 0.01 litre min^{-1}. The upper and lower limits of agreement (±2 SD) were 0.47 and 0.45 litre min^{-1}, respectively.

The results from our study suggest that variations of the anatomical position of the great thoracic vessels in congenital heart disease do not substantially affect the accuracy of electrical velocimetry measurements. This is probably due to the fact that in early systole, electrical velocimetry detects the greatest systolic downslope of $\Delta Z(t)$, which is $dZ(t)/dt_{min}$. Since it is suggested that $dZ(t)/dt_{min}$ represents the greatest rate of change of blood resistivity, this value will always determine the magnitude of the stroke volume estimated by electrical velocimetry (SV_{EV}). Since, in the absence of a VSD and left-to-right shunt, the greatest systolic ohmic acceleration is always located in the ascending thoracic aorta and not the pulmonary artery; the actual position of the great vessels within the thorax is probably unimportant. This allows the use of an unfocused transthoracic current field, which interrogates the entire thoracic volume, and especially the intrathoracic blood volume. This is in contrast to Doppler velocimetry, where a precisely focused beam of ultrasound insonating the aortic root is necessary to detect the highest ascending aortic velocities for accurate determination of the systolic velocity integral. The robustness of the electrical velocimetry technique was evident in three patients studied after Norwood and Glenn operations, a circumstance where only one major artery arises from the heart.

Another interesting aspect of our study was the lack of correlation between haemoglobin concentration and the accuracy of electrical velocimetry when compared with the Fick principle determination of cardiac output. Since, by the new theory of electrical velocimetry, $dZ(t)/dt_{min}$ is dependent on the biphasic orientation of erythrocytes over the cardiac cycle, it seemed plausible that haemoglobin or haematocrit levels might affect the accuracy of electrical velocimetry. Our data show that over a range of haemoglobin concentrations of 8.5–17.3 g dl^{-1}, the agreement between the two methods was unaffected. This is consistent with the results of Quail and colleagues[19] and Wallace and colleagues[20] who found that the magnitude of impedance cardiography-derived stroke volume and cardiac output was unaffected by haematocrit over a wide range of values. It is also consistent with the observation by Visser and colleagues[21] that although the magnitude of $\Delta Z(t)$ is haematocrit-dependent, its maximum systolic upslope [i.e. $dZ(t)/dt_{min}$] is not.

The correlation and agreement between cardiac output determined by electrical velocimetry and our 'gold-standard' method was superior to that reported in the studies conducted in adults by Schmidt and colleagues[22] and Suttner and colleagues.[23] Possible reasons include their choice of reference methods. Schmidt and colleagues[22] studied patients undergoing cardiac surgery under anaesthesia before surgery using transoesophageal echocardiography (TOE) as their reference method. They reported excellent correlation (r^2=0.86) and limits of agreement of −0.99 to 1.36 litre min^{-1}. TOE-determined stroke volume has several sources for inaccuracy, which include minor errors in aortic

valve cross-sectional area measurement[24] and errors inherent in determining the systolic velocity integral. In the study by Suttner and colleagues,[23] thermodilution was employed as the reference method of cardiac output estimation in patients in intensive care after cardiac surgery. Their patients had the integrity of the chest wall interrupted by median sternotomy during surgery and were inherently more unstable. Despite this, they reported r=0.83 for cardiac index, a bias of 0.01 litre min^{-1} m^{-2}, and a precision of $\pm$0.57 litre min^{-1} m^{-2}. Sources of error associated with the thermodilution estimation of cardiac output are well documented,[2] especially in ventilated patients, where cardiac output differences over the respiratory cycle can be >20%. The clinical setting, reference method, and results of Suttner and colleagues[23] were not significantly different from those of Bernstein and Lemmens.[15] They studied a similar, but larger population of patients employing electrical velocimetry from raw data obtained from another proprietary impedance cardiography device. However, despite reference method inaccuracies, results from all these studies substantiate the interchangeability of CO_{EV} with their respective gold standards as it is now accepted that limits of agreement between methods of $\pm$30% imply comparability.[25]

Other concerns regarding the applicability of electrical velocimetry in patients with congenital heart disease include its accuracy in severe aortic stenosis or coarctation, SHONE complex, severe sub-aortic stenosis, severe narrowing of the aortic isthmus, right aortic arch, transposition of the great arteries, and in haemodynamically unstable paediatric patients after corrective surgery. Further studies are needed.

Conclusions

In young individuals with congenital heart disease, measurement of CO_{EV} by the AESCULON® monitor agreed well with measurement by CO_F in a steady-state clinical situation. This is true for the range of cardiac output from 0.4 to 4.0 litre min^{-1}. The results were not significantly influenced by the type of heart defect and were stable over the body weight and [Hb] range from 2.7 to 54 kg and 8.5 to 17.3 g dl^{-1}, respectively. Thus, the system seems appropriate for continuous cardiac output measurement, even under the abnormal haemodynamics of infants with a variety of congenital heart lesions.

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