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Electrical velocimetry as a tool for measuring cardiac output in small infants after heart surgery

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Abstract *Purpose:* Cardiac output (CO), the product of stroke volume (SV) and heart rate, is essential to guarantee organ perfusion, especially in the intensive care setting. As invasive measurement of CO bears the risk of complications there is a need for non-invasive alternatives. We investigated if electrical velocimetry (EV) and transthoracic Doppler (Doppler-TTE) are interchangeable for the non-invasive measurement of SV and able to reflect the post-surgical SV/CO trend. *Methods:* Comparison of SV measurements by EV and Doppler-TTE was performed in 24 newborns after switch operation ($n = 240$ measurements). Three subgroups of measurements (=periods) were created according to the patients' status in the course of post-surgical CO recovery. *Results:* Bland–Altman analysis found acceptable bias and limits of agreement for the interchangeability of the two methods. Mean overall SV was 3.7 ml with a mean overall bias of 0.28 ml (=7.6 %). The mean percentage error of 29 % was acceptable according to the method of Critchley and Critchley. Overall precision expressed by the coefficient of variation (CV) was 6.6 % for SV_{TTE} and 4.4 % for SV_{EV}. SV_{TTE} and SV_{EV} medians in the three periods were significantly different and documented the post-surgical CO trend. *Conclusions:* EV and Doppler-TTE are interchangeable for estimating SV. EV has the advantages of easy handling and allows continuous measurement.

Keywords Stroke volume · Cardiac output · Electrical velocimetry · Doppler transthoracic echocardiography · Pediatric cardiac intensive care unit

Introduction

Blood circulation transports oxygen and nutritional elements to the tissues. It is driven by the heart that, by ejecting the stroke volume (SV) with each heart action at the heart rate (HR), creates a circulating blood volume in time—the cardiac output (CO):

$$CO = SV \times HR. \quad (1)$$

When CO can not guarantee adequate tissue perfusion, we speak of heart insufficiency, which is particularly disastrous in critically ill patients. Thus, measuring the actual CO and its evolution is important [1] as the clinical estimation of a patient's circulatory status is often misleading [2]. Therefore, CO measurement techniques, invasive and non-invasive, have been developed.

Among the invasive techniques are Fick's method and thermodilution [3], considered as reference methods although not referring to the physiological output definition based on SV. Additionally, they suffer some inherent inaccuracies [4, 5], are technically demanding, expensive and likely to cause complications. This has initiated

intensive research into non-invasive alternatives. Among these are ultrasound and bioimpedance measurement of CO. Echocardiography mostly relies on the Doppler principle (CO_{TTE}) [6, 7]: the velocity time integral (VTI) of the blood flow through the aortic valve is measured and multiplied by its surface (CSA) to calculate SV_{TTE} [7–10]:

$$SV_{TTE} = CSA \times VTI \quad (2)$$

Bioimpedance measurement of cardiac output was mainly developed in the 1960s by Kubicek [11]. It presumes that the ejection of blood into the thorax would lower its resistance to a current emitted through it by electrodes. Kubicek related these impedance changes to intrathoracic vessel volume changes. With time, mathematical models were refined leading to more sophisticated algorithms such as the Osypka–Bernstein equation with the development of the electrical velocimetry (EV) [12, 13]. In contrast to Kubicek's volumetrical approach, EV correlates impedance changes with changes of the erythrocytes' orientation and the flow peak velocity in the ascending aorta, thus eliminating geometrical problems of the thorax–vessel relation (Fig. 1). Doppler-TTE and EV both aim to measure SV and calculate the CO thereof, based on the same physiological principle.

Invasive as well as non-invasive techniques have been evaluated vs the Fick principle or thermodilution as reference methods. EV has been criticized for not correlating well or lacking sufficient agreement with the reference methods [14, 15]. But there have been positive evaluations too [16–19]. And evidence is growing that there is already and will be more place for EV in daily practical work because it provides a steadily improving, more reliable and continuous overview of the patients' circulatory status [20, 21].

As invasive techniques are likely to cause complications in children, and Doppler-TTE needs an experienced examiner and can only be applied sporadically, EV becomes an interesting tool for the paediatric intensivist who wants information about CO non-invasively and continuously.

In our study, we did not want to reproduce the basic comparisons of this method to invasive techniques. Our questions were rather:

1. Would there be acceptable agreement between Doppler-TTE and EV, making them interchangeable?
2. Would the precision of EV be sufficient?

Methods

Patients

In this prospective study, we enrolled 24 newborns (median age 10 (3–29) days, mean weight 3.3 ± 0.5 kg, mean extubation time 84 ± 17 h) in our pediatric cardiac intensive care unit (PCICU) after switch operation for simple transposition of the great arteries (TGA). We chose this cohort because of homogeneity in age, weight,

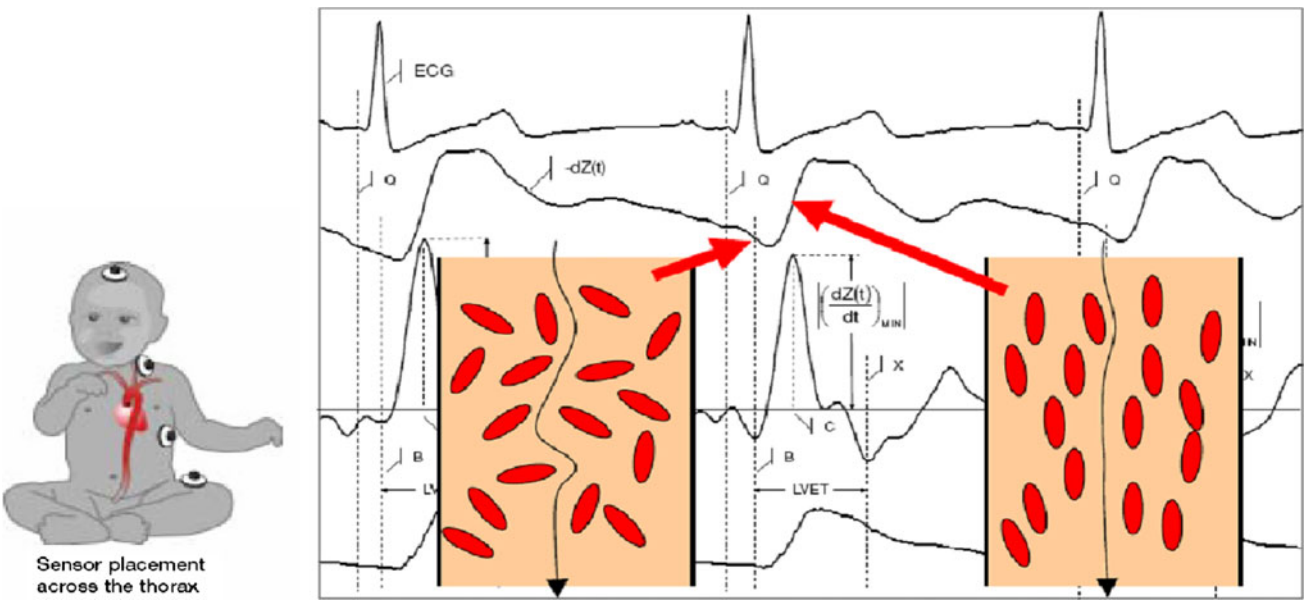

Fig. 1 EV—electrode placement in the small infant (*left*) and EV signals (*right*). It is important that the electrodes are separated by a sufficient distance to avoid interference and signal disturbance. ECG and EV signals must be clearly identified on the monitor as they correlate with the intrathoracic blood flow changes. Further explanations are given in the text. (With kind permission of Osypka Medical, Berlin, Germany and La Jolla, California, USA)

diagnosis, pre-surgical preparation, surgery and cardiopulmonary bypass, and because there is generally post-surgical temporary left ventricular insufficiency [22, 23] so that repeated measurements of SV would document changes in myocardial performance. During the post-surgical period of haemodynamic stabilisation (about 36 h) all patients received sufentanil (1 μg kg^{-1} h^{-1}) for analgesia, then were switched to morphine (20 μg kg^{-1} h^{-1}) and finally weaned from ventilation. Inotropic support was given by administering adrenaline (0.05 g kg^{-1} min^{-1}) and milrinone (0.35 μg kg^{-1} min^{-1}). There was no external cardiac pacing.

The local ethical committee's permission and informed parental consent were obtained.

Doppler-TTE

SV_{TTE} measurement requires calculation of the aortic valve opening surface. Usually, the cross-sectional area of the aortic valve ($CSA_{annulus}$) is calculated as

$$CSA_{annulus} = d^2_{annulus} \times \frac{\pi}{4} \tag{3}$$

where $d_{annulus}$ is the aortic annulus diameter.

In 1996, Darmon et al. [7] described a new triangular approach for measuring the aortic CSA by TEE in adults, demonstrating the triangular opening of the aortic valve and calculating its CSA by measuring and averaging the three leaflets. Taking into account the difficulties of leaflet measurement in small infants due to the small dimensions and high heart rate we modified Darmon's technique by measuring the aortic valve circular surface with radius R at the leaflet level and hypothetically inscribing into it an equilateral triangle with the length a. It follows for the cross-sectional triangle area ($CSA_{triangular}$):

$$CSA_{triangular} = \frac{a^2\sqrt{3}}{4}. \tag{4}$$

R of the cross-sectional annulus area ($CSA_{annulus}$) is then

$$R = \frac{\sqrt{3}}{3} \times a \tag{5}$$

For the cross-sectional annulus area ($CSA_{annulus}$) we find

$$CSA_{annulus} = \pi \times R^2 = \pi\left(\frac{\sqrt{3}}{3} \times a\right)^2 = \pi \times \frac{a^2}{3} \tag{6}$$

and therefore

$$\frac{CSA_{triangular}}{CSA_{annulus}} = \frac{\frac{a^2\sqrt{3}}{4}}{\pi \times \frac{a^2}{3}} = \frac{3\sqrt{3}}{4 \times \pi} = 0.4135 \approx 0.41 \tag{7}$$

which means that the triangular valve opening surface is about 41 % of the aortic surface calculated by the circular model.

For VTI measurement, the ultrasound sample was placed directly behind the aortic valve, in line with the blood stream ejected from the left ventricle into the aorta. Five VTI measurements were made consequently by pulsed Doppler in the ascending aorta and averaged according to the algorithm chosen for the EV. SV_{TTE} was then calculated as

$$SV_{TTE} = CSA_{triangular} \times VTI. \tag{8}$$

The measurements were performed by an experienced specialist in paediatric cardiac ultrasound who was blinded to the SV_{EV} values simultaneously measured. All measurements were made in the short-axis or the five-chamber view (for the CSA) and from the subcostal view (for measuring VTI) using the Vivid 7 ultrasound machine (GE Healthcare, Chalfont St. Giles, Buckinghamshire, UK).

Electrical velocimetry

At the same time, SV was measured by EV. We used the AESCULON® bioimpedance monitor (Osypka Medical, Berlin, Germany and La Jolla, California, USA). The AESCULON® emits a current of high frequency (50 kHz) and low amperage (2 mA) through the thorax via two electrodes. The signal is received by two other electrodes after being modified by thoracic impedance. At the same time, an ECG is traced, and changes in thoracic impedance are related to it (Fig. 2).

Thoracic impedance and its changes are influenced by multiple factors: thoracic tissue, air in the lungs, intrathoracic fluid and blood. As electrical conductivity is highest in the blood, the other determinants for thoracic impedance changes play a minor role. In contrast to former bioimpedance equations, the AESCULON® takes into account changes in the orientation of the red blood cells from a random to an organized and oriented flow and the velocity of the aortic blood flow during systole, calculated by Bernstein and Lemmens [13]:

$$SV_{EV} = \frac{V_{ITBV}}{\varsigma}\sqrt{\frac{dZ(t)/dt_{max}}{Z_0}}T_{lve} \tag{9}$$

where: (1) $V_{ITBV} = K \times 16\ W^{1.02}$; (2) ζ = index of transthoracic aberrant conduction $(0 < \zeta \leq 1.0) = Z_c{}^2 - Z_cZ_0 + K/2Z_c{}^2 + Z_0{}^2 - 3Z_cZ_0 + K$, where Z_c is the critical level of Z_0, nominally ascribed a default value of 20 Ω, and K is a trivial constant → 0; (3) dZ/dt_{max} = the peak rate of change of the transthoracic cardiogenic impedance pulse variation (Ω s^{-2}); (4) Z_0 = the

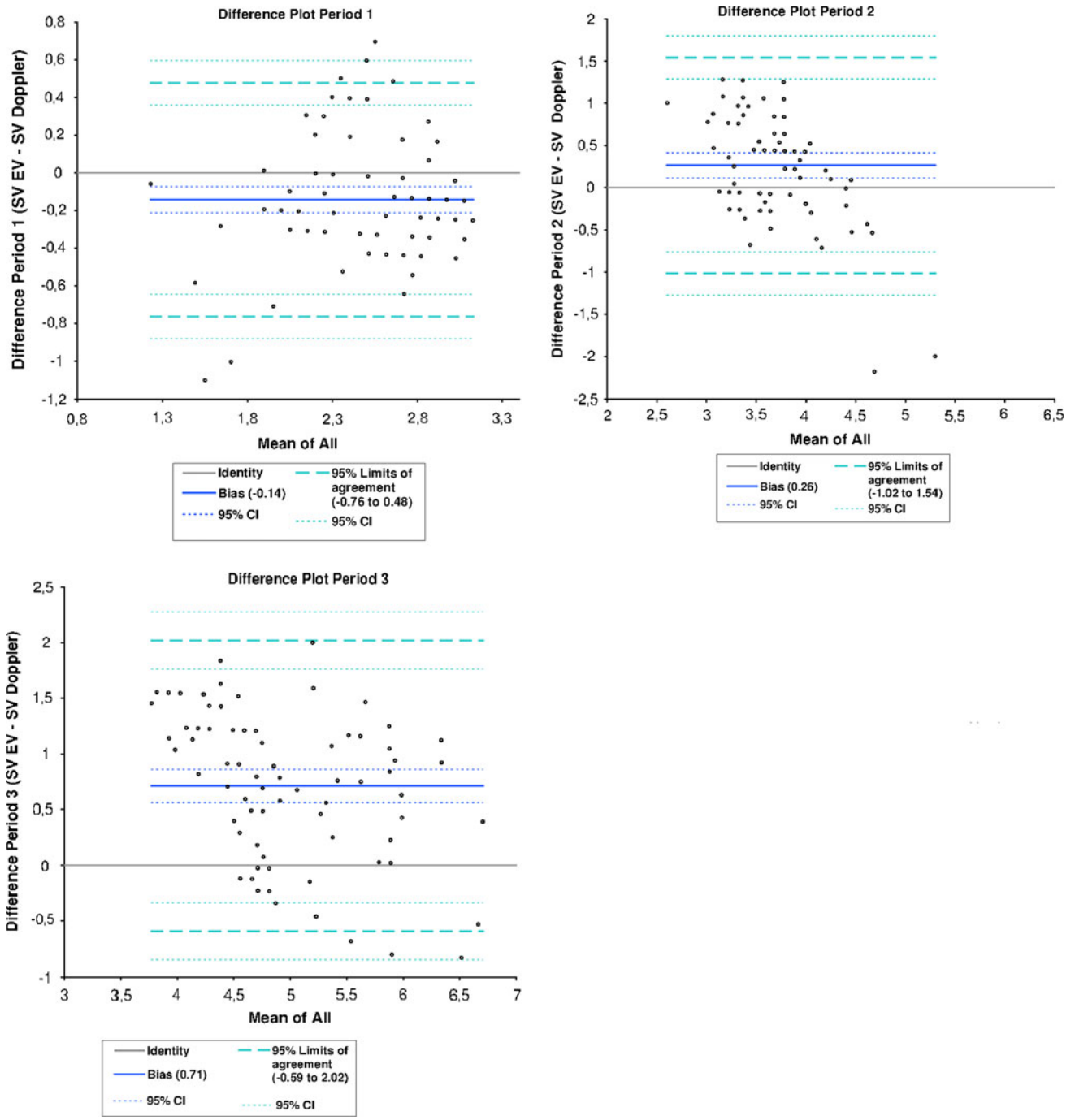

Fig. 2 Bland–Altman plots (periods 1–3) for the evaluation of stroke volume measurement by EV vs Doppler-TTE. Acceptable bias and agreement for the two methods were obtained in all periods. All values in millilitres. Details in the text and in Table 1

transthoracic quasi-static base impedance (Ω) and T_{lvc} = left ventricular ejection time (s).

Respiratory changes of thoracic impedance are suppressed by a filter. In total, changes in intrathoracic impedance are due to changes caused mainly by the blood flow in the aorta as the leading vessel and thus reflect SV.

As the emitted and registered currents are weak, and signal quality is crucial, the utmost attention was paid to the best signal force indicated optically and an optimal

ECG and d*Z*/d*t* curve on the AESCULON® monitor (Fig. 1).

As electrode quality proved to be important for the expression of the signal, we tested and chose MEDITRACE® Ag/AgCl wet gel electrodes (Tyco Healthcare, Mansfield, USA) as these gave the best signal in our setting; the electrodes were cut into appropriate dimensions for newborns. Electrode placement followed exactly the recommendations for the use of the AESCULON® in small children (Fig. 1). SV_{EV} and CO_{EV} were measured synchronously with the Doppler-TTE evaluations. We chose an averaging of five consecutive impedance waves according to the Doppler measurements.

Following our experience of the status of the patients' recovery from surgery, we divided the measurements into three subgroups or periods—up to 36 h, the haemodynamically instable period 1 ($n = 84$ measurements); 36–72 h, the stabilisation period 2 ($n = 77$ measurements); and beyond 72 h after surgery, the period 3 leading to extubation ($n = 79$ measurements)—in order to evaluate if both methods would reflect haemodynamic amelioration. Precision of the methods, expressed by the coefficient of variation (CV), was calculated for each patient and period and then averaged per period and for the whole observation time.

Statistics

Method comparison using Bland–Altman analysis and precision calculation [24–26] were performed by Analyse-it software version 2.21 (Analyse-it Software Ltd, Leeds, UK), descriptive statistics and ANOVA on ranks for SV by SigmaPlot software, version 11.0 (Systat Software, Chicago, Illinois, USA). Differences between the values were considered as significant at $p < 0.05$, unless indicated otherwise.

Results

Descriptive statistics and precision

Data for descriptive statistics are given in Table 1.

Twenty-four patients after switch operation for simple TGA were enrolled in the study. After a period of compromised CO with a median cardiac index (CI) 2.1 (EV) in period 1, the patients recovered progressively to normal CO (median CI 3.0 and 4.05 in period 2 and 3, respectively).

ANOVA analysis on ranks of SV_{TTE} and SV_{EV} showed significant differences between the different periods ($p < 0.05$).

CVs in the different periods were 5.5, 7.6 and 6.6 % (SV_{TTE}), and 5.4, 4.1 and 3.8 % (SV_{EV}) for periods 1, 2 and 3, respectively. HR was 164 ± 8, 157 ± 4 and 154 ± 4 bpm in periods 1, 2 and 3, respectively, with statistically significant differences ($p < 0.05$ %).

Method comparison

Data for method comparison are given in Table 2.

Bias of SV_{EV} vs SV_{TTE} was acceptable in the different subgroups with acceptable SD of differences between single measurements and limits of agreement. The confidence intervals were narrow.

The percentage error between the two methods was 24, 35 and 28 % in the different subgroups with an average of 29 % for all measurements.

Table 1 Descriptive statistics of SV measurement by CO-Doppler and EV, precision calculation and heart rates

Parameter	Measurement					
	SV–TTE 0–36 h (period 1)	SV–EV 0–36 h (period 1)	SV–TTE 36–72 h (period 2)	SV–EV 36–72 h (period 2)	SV–TTE >72 h (period 3)	SV–EV >72 h (period 3)
Mean	2.6	2.4	3.6	3.8	4.5	5.3
SD	0.4	0.5	0.7	0.4	0.9	0.7
SE	0.05	0.05	0.1	0.0	0.1	0.1
CI of mean	0.1	0.1	0.2	0.1	0.2	0.1
Median	2.6	2.5	3.5	3.9	4.6	5.1
Min	1.3	1	2.1	3	3.0	4
Max	3.3	3	6.3	4.5	6.9	6.9
CV (%)	5.5	5.4	7.6	4.4	6.6	3.8
HR (bpm)	164 ± 8		157 ± 4		154 ± 4	

Table showing the mean and median value for stroke volume measured by TTE and EV. There was no significant difference between SV–EV and SV–TTE median values in the same period. Differences for SV–EV and SV–TTE medians of different periods were significant

CI confidence interval, *CV* coefficient of variation, *HR* heart rate, *SD* standard deviation, *SE* standard error, *SV–EV* stroke volume measured by electrical velocimetry (EV), *SV-TTE* stroke volume measured by transthoracic echocardiography (TTE)

Table 2 Agreement between SV-TTE and SV-EV calculated by the Altman–Bland analysis

Parameter	Measurement		
	SV–TTE versus SV–EV (period 1)	SV–TTE versus SV–EV (period 2)	SV–TTE versus SV–EV (period 3)
Bias	−0.14	0.26	0.71
95 % CI	−0.21 to −0.07	0.11 to 0.41	0.56 to 0.86
SE	0.035	0.074	0.075
P	<0.0001	<0.0007	<0.0001
SD of differences	0.32	0.65	0.67
Lower limits of agreement	−0.76	−1.02	−0.59
Upper limits of agreement	0.48	1.54	2.02

Table showing the mean and median value for stroke volume measured by TTE and EV. There was no significant difference between SV–EV and SV–TTE median values in the same period. Differences for SV–EV and SV–TTE medians of different periods were significant

CI confidence interval, *CV* coefficient of variation, *HR* heart rate, *SD* standard deviation, *SE* standard error, *SV–EV* stroke volume measured by electrical velocimetry (EV), *SV–TTE* stroke volume measured by transthoracic echocardiography (TTE)

Overall correlation was good with $r = 0.86$. Linear regression for all measures showed a slope of $SV_{EV} = 0.204 + (1.018 \times SV_{TTE})$, i.e. near the line of identity, thus highlighting the good predictability for the two methods, albeit a little less well than that found by Schmidt et al. [16] and Norozi et al. [18].

Discussion

Agreement of two non-invasive methods for measuring cardiac output in a paediatric intensive care unit

Our results show that bias and limits of agreement for SV measurement by EV versus Doppler-ETT were acceptable. The percentage error (overall average error 29 %) in periods 1 and 3 lay within the clinically accepted limits for method comparison as stipulated by Critchley and Critchley [25]; in period 2 the error was slightly beyond these limits. Therefore, the two methods can be considered as generally interchangeable.

Our findings are in accordance with the results of other studies: Schmidt et al. [16] described the interchangeability of EV and transoesophageal aortic Doppler in a homogenous cohort of 37 patients undergoing coronary surgery. Suttner et al. [17] reported good correlation and acceptable agreement between EV and pulmonary artery thermodilution in adult patients after cardiac surgery. Norozi et al. [18] found good agreement between the Fick method and EV, the latter offering easy handling and beat-to-beat estimation of CO. Schubert et al. [19] described the usefulness of EV compared to TTE but with a percentage error of 48.2 %. Then, there are studies that describe negative results: Tomaske et al. [14, 15] found unacceptable agreement between EV and thermodilution with a percentage error of 48.9 % and a lack of correlation between EV and subxiphoidal Doppler flow. Schmidt et al. [17], Suttner et al. [18] and Schubert et al. [19] were the only authors to give pathology details of the patients enrolled in their studies. The studies investigating patients with congenital heart disease [14, 15, 20–22] integrated a large variety of different ages and weights.

Our results show less percentage error than the studies mentioned above. This may in part be due to a more rigid selection of patients, homogenous for age, weight and pathophysiology. Yet, in period 2, we found a percentage error (35 %) slightly above the criteria of Critchley and Critchley (30 %) who had described in their meta-analysis a similar value for bioimpedance measurements with a CO of 37 %. They attributed this finding to excess lung fluid in critical care situations. One can imagine that this could also have played a role in our patients as there may be important volume shifts due to volume substitution in the post-operative course.

As CV values stayed under 20 % for SV_{EV} and SV_{TTE} in all periods, both methods can be regarded as reflecting the evolution of CO in time correctly, an argument additionally supported by an overall good correlation ($r = 0.86$) and an overall linear regression close to identity. Only four values of the 240 measurements were found outside the prediction interval limits, indicating a good repeatability of EV measurement.

Usefulness of EV as a tool for monitoring cardiac output and for detection of acute heart failure: method discussion and critique

Though Doppler-TTE and EV correlate and agree well and therefore are interchangeable, nothing has been said about their ability to correctly reflect the "true" CO. But even the invasive methods, regarded as a reference, have their weak points: indirect CO measurement not referring to SV, errors due to erroneous handling and false calculation and interpretation particularly in critically ill patients [4, 5]. So, in fact, there is no real "gold standard" for CO measuring, especially in the clinical setting.

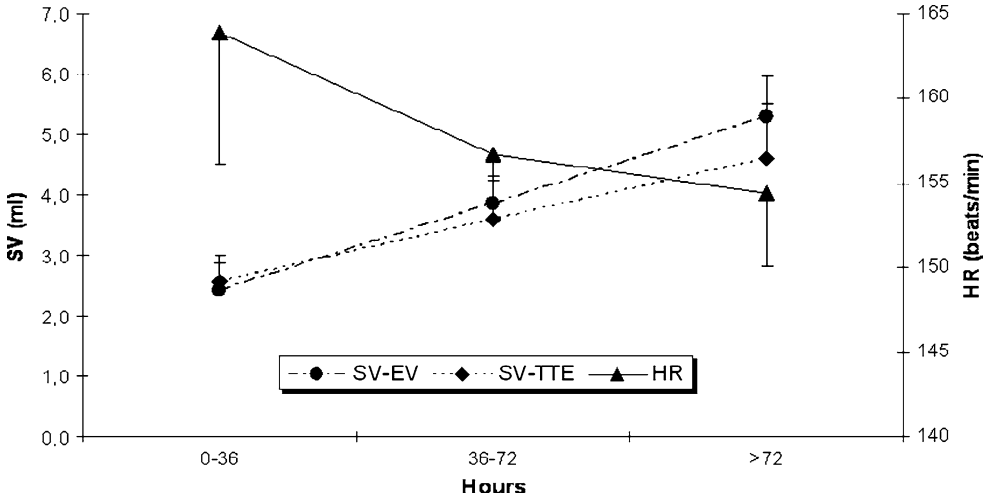

Fig. 3 Relationship between heart rate and SV_{TTE}/SV_{EV} in the post-operative course. As stroke volume and therefore cardiac output rise, heart rate decreases, indicating circulatory recovery of the patients after heart surgery

Non-invasive techniques are more sensitive to external interferences than invasive techniques. As to EV, from our experience, besides electrode placement, much depends on the quality of the electrodes in order to obtain an optimal ECG and d*Z*/d*t* signal that are essential for the reliable interpretation of SV by EV. Unfortunately, the previous studies cited earlier did not place much emphasis on this technical aspect.

As to Doppler-TTE, errors in the determination of the aortic annulus diameter, especially in small infants, may falsify CSA significantly by squaring the error. CSA should be corrected by following the triangular model [7]. Otherwise SV might be overestimated. Aortic flow velocity might be underestimated according to the cosine function of the angle between the ultrasound beam and vessel. Therefore, for measuring correct SV values, signals for aortic diameter and flow must be optimal.

Finally, as all methods, invasive and non-invasive, measure either CO or SV indirectly, they all suffer from problems that are inherent in the relation between the objective, i.e. CO as a function of SV, which can not simply be materialized, and the operator. Only the knowledge of the weak points of this interaction can help one to mind the pitfalls.

Regardless of these considerations, this study was not designed to evaluate electrical velocimetry in order to find the "true" CO. We merely wanted to investigate if electrical velocimetry could be a valuable tool in the hands of the paediatric intensivist dealing with heart insufficiency. Would it perhaps not replace, but complement echocardiography as a non-invasive tool especially in small infants and under conditions that make echocardiography less available? Our results indicate that this is indeed the case. First, we found that the two methods were interchangeable. Secondly, we found that they reflected the CO trend similarly and correctly. Looking at Fig. 3, we can see that SV increases continuously, whereas HR, initially compensating low cardiac output by tachycardia, decreased inversely in response to the increase of SV, indicating the amelioration of the haemodynamic situation.

Of course, the system is not yet perfect. In particular, the original signal may be altered when electrodes are not perfectly placed or not functional, or in the case of external interference like extravascular fluid, external currents, and patient movement. Then experienced interpretation of the signal and correction are needed.

Nevertheless, the results of this study are encouraging. EV may be a tool for continuous cardiac output measurement in critically ill infants with heart failure, as a monitoring complementary to echocardiography or as a replacement if echocardiography is not available. It may help to detect acute heart insufficiency as well as trends and may eventually help the intensivist in decision-making.

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