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Continuous non-invasive cardiac output measurements in the neonate by electrical velocimetry: a comparison with echocardiography

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ABSTRACT

Objective Electrical velocimetry (EV) is a non-invasive method of continuous left cardiac output monitoring based on measurement of thoracic electrical bioimpedance. The objective was to validate EV by investigating the agreement in cardiac output measurements performed by EV and echocardiography.

Design In this prospective observational study, left ventricular output (LVO) was simultaneously measured by EV (LVO_{ev}) using Aesculon and by echocardiography (LVO_{echo}) in healthy term neonates during the first 2 postnatal days. To determine the agreement between the two methods, we calculated the bias (mean difference) and precision (1.96×SD of the difference). As LVO_{echo} has its own limitations, the authors also calculated the 'true precision' of EV adjusted for echocardiography as the reference method.

Results The authors performed 115 paired measurements in 20 neonates. LVO_{ev} and LVO_{echo} were similar (534±105 vs 538±105 ml/min, p=0.7). The bias and precision of EV were −4 and 234 ml/min, respectively. The authors found the true precision of EV to be similar to the precision of echocardiography (31.6% vs 30%, respectively). There was no difference in bias and precision between the measurements obtained in patients with or without a haemodynamically significant patent ductus arteriosus.

Conclusions EV is as accurate in measuring LVO as echocardiography and the variation in the agreement between EV and echocardiography among the individual subjects reflects the limitations of both techniques.

What is known about this topic

- Echocardiography is the only non-invasive method of determining cardiac output in neonates in the clinical setting.
- EV, a non-invasive method of cardiac output monitoring, has been validated in adults and children but not in neonates.

What this study adds

- Cardiac output can be continuously and non-invasively estimated in neonates by EV.
- EV is comparable with echocardiography in estimating cardiac output.

INTRODUCTION

Blood pressure is determined by the interaction between two independent haemodynamic variables, the cardiac output and systemic vascular resistance (SVR). In clinical practice, blood pressure is routinely and continuously monitored in critically ill neonates by an indwelling arterial catheter. However, as blood pressure is the dependent haemodynamic variable, blood pressure monitoring alone only provides limited information on the independent haemodynamic variables, cardiac output and SVR and thus on systemic perfusion and tissue oxygen delivery. Therefore, accurate and continuous assessment of the cardiovascular status requires the ability to also monitor cardiac output, SVR or both. However, at present, direct and indirect assessments of cardiac output and tissue perfusion in the clinical practice are unreliable.[1] Moreover, in the clinical practice, cardiac output can only be measured intermittently with invasive (eg, thermodilution) or non-invasive (eg, echocardiography) methods. The capability to continuously monitor cardiac output non-invasively would be invaluable in clinical research and the management of neonates with haemodynamic compromise who require frequent adjustments in supportive care, volume administration and titration of vasoactive agents.

Electrical velocimetry (EV) is a method of continuous cardiac output monitoring based on impedance cardiography technology originally developed in 1964,[2] and modified in 1980. The Aesculon (Cardiotronic, La Jolla, California, USA) EV monitoring system uses a novel modification of impedance cardiography technology and has been validated against invasive methods of cardiac output measurements with excellent correlations in animals,[3] adult humans[4 5] and in children with congenital heart defects.[6] However, EV has not been evaluated in the newborn population. Therefore, in this study, we sought to compare EV using the non-invasive continuous cardiac output monitor (Aesculon) with echocardiography in estimating left ventricular output (LVO) in healthy term newborns during the first two postnatal days.

METHODS

This was a prospective observational study approved by the institutional review board at the Children's Hospital of the University of Oklahoma Health Sciences Center. Parental informed consent was obtained.

The aim of the study was to define the accuracy and precision of EV using the FDA-approved, non-invasive continuous cardiac output monitor (Aesculon) compared with echocardiography in estimating LVO in term neonates.

We enrolled healthy term neonates in the first postnatal day. We excluded newborns with conditions that could affect cardiac function such as known congenital heart defects other than a patent ductus arteriosus (PDA) or patent foramen ovale, low Apgar scores (<7 at 5 min), being born to a mother with diabetes, and presenting with major congenital anomalies. As EV is designed to estimate LVO by assessing blood flow primarily in the ascending aorta,[5 6] we included subjects with a PDA irrespective of the potential haemodynamic significance of ductal shunting. At three time points within a 30-min period, each subject had simultaneous measurements of LVO using EV (LVO-ev) and echocardiography (LVO-echo) on the first day of postnatal life. As the measurements were repeated on the second postnatal day, each subject had six pairs of data points over the first two postnatal days. Each LVO_{ev} measurement was an average of 10 s. During the 10-s period of the LVO_{ev} measurement, blood velocity at the aortic valve was also constantly sampled by a pulsed wave Doppler. A still frame was acquired if the Doppler tracing was similar in shape and size and each LVO_{echo} measurement was an average of the data obtained over three to five cardiac cycles during the corresponding 10 s of the LVO_{ev} data collection. The 10 s of data collection for the LVO_{ev} measurement was only accepted if the signal quality index was ≥80%. The signal quality index is a composition of two measures. First, the signal has to meet certain shape and timing requirements. Second, the magnitude derived from the signal has to fall within statistically predetermined limits. Therefore, the signal quality index is an indication for signal strength over a number of cardiac cycles. For example, a signal quality index of 80% means that 8 of 10 consecutive cardiac cycles met the established criteria and thus were acceptable.

The principles and method of estimation of cardiac output using EV by Aesculon have been described elsewhere in detail.[3] Briefly, body mass is calculated based on weight and height. Four surface EKG electrodes are placed over the skin (forehead, left side of the neck, left mid-axillary line at the level of xiphoid process and left thigh). A small alternate electrical current flows through the thorax from the outer EKG electrodes and the resulting voltage is measured by the inner electrodes. A major contributing factor to conductance (1/impedance) of the current is blood flow in the ascending aorta. The impedance to the flow of current varies according to the alignment of red blood cells in the ascending aorta. As red blood cells are aligned during systole and misaligned during diastole, there is a difference in the measured voltage during systole and diastole. This difference serves as the basis for the model that estimates the cardiac output. The mean velocity index empirically derived from a peak amplitude measurement is assumed to be an index of peak aortic acceleration of blood flow. EV by Aesculon uses an algorithm which estimates stroke volume in millilitres based on the mean velocity index, the flow time and the body mass. Stroke volume multiplied by heart rate yields cardiac output in millilitres per minute. In the algorithm, the computerised calculation of body mass for neonates was adjusted based on preliminary data obtained from EV assessment of cardiac output in 50 preterm and term neonates with body weight between 0.5 and 4 kg (data not shown).

LVO_{echo} was measured by using a SONOS 7500 echocardiography machine (Philips, Andover, Massachusetts, USA) equipped with 8-MHz and 12-MHz transducers. All echocardiograms were performed and analysed by one of the authors (SN) trained and certified in paediatric echocardiography. The ultrasound and Doppler measurements were done off-line weeks after enrolling all the subjects and SN was blinded to the Aesculon results. LVO_{echo} was calculated using the aortic diameter (D) and velocity time integral (VTI) measured at the aortic valve annulus from parasternal long axis and apical views, respectively.[7] The machine's built-in software uses the formula '$(\pi D^2/4)\times VTI\times$heart rate' to calculate the flow. Dividing the calculated flow by the infant's weight yields LVO in ml/kg/min. We also assessed the status of the ductus arteriosus.[8] Several factors play a role in determining the potential haemodynamic significance of left-to-right shunting across the ductus arteriosus and there is no evidence-based agreement in the literature on the definition of haemodynamic significance of the PDA.[9] However, in preterm infants, a ductus arteriosus of <1.5 mm in diameter is considered haemodynamically insignificant.[8] By extrapolation, in our population of term infants, we arbitrarily chose a cut-off of 2 mm of ductal diameter measured at the pulmonary artery to classify a ductus arteriosus as haemodynamically significant.

Table 1 Clinical characteristics of the study population

N	20
Gestational age (week)*	39.2±1.1
Birth weight (g)*	3094±338
Apgar at 1 min†	8 (5–9)
Apgar at 5 min†	9 (8–10)
C-section	15
Male gender (%)	50
Small for gestation (%)	10

*Mean±SD.
†Median (range).

Data analysis and calculations

As each subject had multiple paired data, agreement between LVO_{echo} and LVO_{ev} was assessed using the Bland-Altman plot, which takes into account multiple observations per individual.[10] The bias and precision were defined as the mean difference and 1.96×SD of the difference between LVO_{echo} and LVO-ev, respectively.[11] The bias represents the accuracy or degree of closeness of a method (EV) compared with another method (echocardiography). Lower bias values represent better accuracy. Precision represents the reproducibility or repeatability of the method, and is depicted on the Bland-Altman plot as the limits of agreement (bias±precision). Narrower limits of agreement represent better repeatability, that is, higher precision of a method (EV) compared with another method (echocardiography).

To take into account the population mean in assessing the limit of agreement between the two methods, we calculated the error percentage as follows: 100%× (1.96×SD)/mean LVO.[12 13] An error percentage of less than 30% is generally considered clinically acceptable.[13] As the reference method for comparison (echocardiography in our case) has its own limitations in estimating cardiac output, the precision of the new method (EV in our case) can be underestimated.[13] However, the true precision can be calculated by the following equation: $\text{precision}_{EV}=\sqrt{((EP)^2-(\text{precision}_{echo})^2)}$, where precision_{EV} is the true precision of EV, EP is the error percentage and precision_{echo} is the precision of echocardiography compared with the gold standard methods.[13] Review of the literature indicates that the precision_{echo} is around 30%.[14]

Statistics

Continuous data are presented as median (range) or mean ±SD. Parametric (paired t test) and non-parametric (Wilcoxon signed-rank) statistical methods were used as appropriate. A $p<0.05$ was considered statistically significant.

RESULTS

Twenty healthy neonates were enrolled in the study. Clinical characteristics of the study population are shown in table 1.

A total of 115 pairs of LVO_{ev} and LVO_{echo} were analysed. There was no significant difference between the mean LVO_{ev} and LVO_{echo} (534±105 vs 538±105 ml/min, p=0.7; figure 1). The average cardiac output of all measurements (both groups) was 536 ml/min and the mean difference and SD of the difference were 4 and 119 ml/min, respectively. Thus, the bias and precision of EV in measuring LVO using echocardiography as the reference method were −4 and 234 ml/min, respectively (figure 2). As it might have more clinical relevance, the bias and precision expressed in ml/kg/min are shown in figure 3.

Using the equation '100%×(1.96×SD)/mean LVO',[12] the error percentage of EV was 43.6% and, since the precision of echocardiography is estimated to be 30%,[14] we calculated the true precision of EV using the equation $precision_{EV}=\sqrt{((EP)^2-(precision_{echo})^2)}$. We found the true precision of EV to be 31.6%, a value almost identical to the estimated precision of echocardiography.[14]

A haemodynamically significant PDA (>2 mm) was noted in eight neonates at the time of the study (in seven neonates on day #1, and in one neonate on day #2). Shunt across the PDA was left to right in all cases. There was no difference in bias (12 vs 2 ml/min) and precision (296 vs 218 ml/min) between those with or without a haemodynamically significant PDA, respectively (p=0.8).

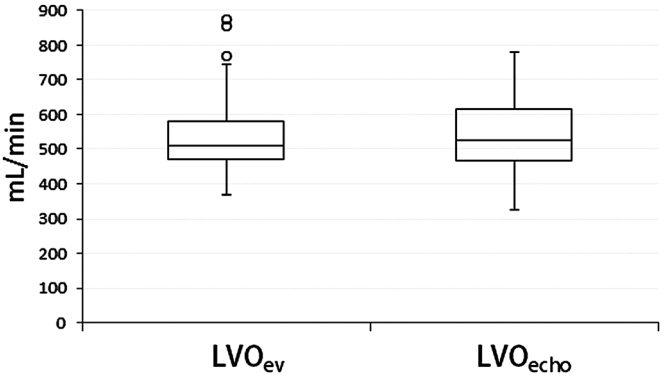

Figure 1 Box and whisker plot for left ventricular output as measured by electrical velocimetry and echocardiography. The box represents the IQR, the horizontal line in the box is the median, the bars are the IQR×1.5 or max/min values whichever smaller and the circles are the outliers.

DISCUSSION

In evaluating EV, we found excellent accuracy with a mean bias of only 4 ml/min using echocardiography as the reference method. However, the precision of EV was less robust (234 ml/min, 44%). In other words, while the average LVOs of the two methods were very close, there was a wide variation in the agreement between each data pair. There are several possible explanations for this finding. First, echocardiography has its own significant limitations in estimating LVO. Echocardiography has a precision of around 30% compared with the thermodilution and Fick methods.[14 15] As we used echocardiography as our reference method, its 30% precision can lead to a significant underestimation of the precision of EV.[13] Accordingly, after adjusting for the precision of echocardiography, EV's true precision was found to be 31.6%, a value similar to that of echocardiography. Of note is that true precision for a method in the 30% range is thought to be in the acceptable range for clinical application.[11 13] Second, EV has its own shortcomings as well. The cardiac output calculation is based on a haemodynamic model in adults. Although computerised body mass calculation for neonates was adjusted by the company using our recommendations, it is possible that other assumptions in the model also need adjustments to improve precision. Again, the finding of a similar variability in cardiac output estimated by EV and echocardiography (both had SD at 105 ml/min) suggests that some of the disagreement between the two methods stems from the limited precision of each technique. Finally, it is worth noting that, although we evaluated cardiac output in a population with a relatively narrow range of LVO (326 to 781 ml/min), the bias and precision of EV measurements were comparable with what is described in the literature for the invasive methods of cardiac output measurements.[14 16]

This is the first study to evaluate the validity of EV in estimating cardiac output in the neonatal population. Several studies have tested the accuracy and precision of EV in older

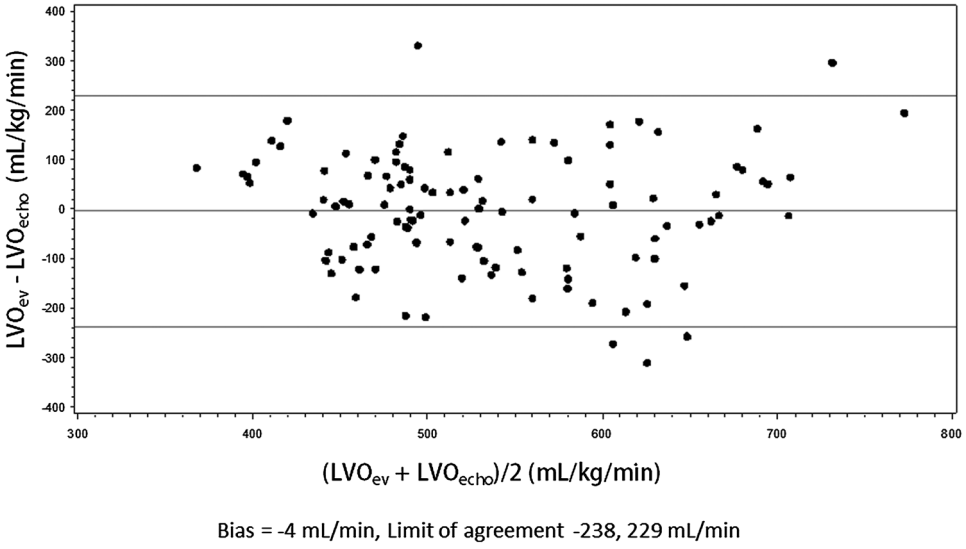

Figure 2 Bland-Altman plot depicting the agreement expressed in millilitre per minute between the left ventricular output estimated by echocardiography and electrical velocimetry. Left ventricular output (LVO) echo: left ventricular output measured by echocardiography; LVOev, left ventricular output measured by electrical velocimetry.

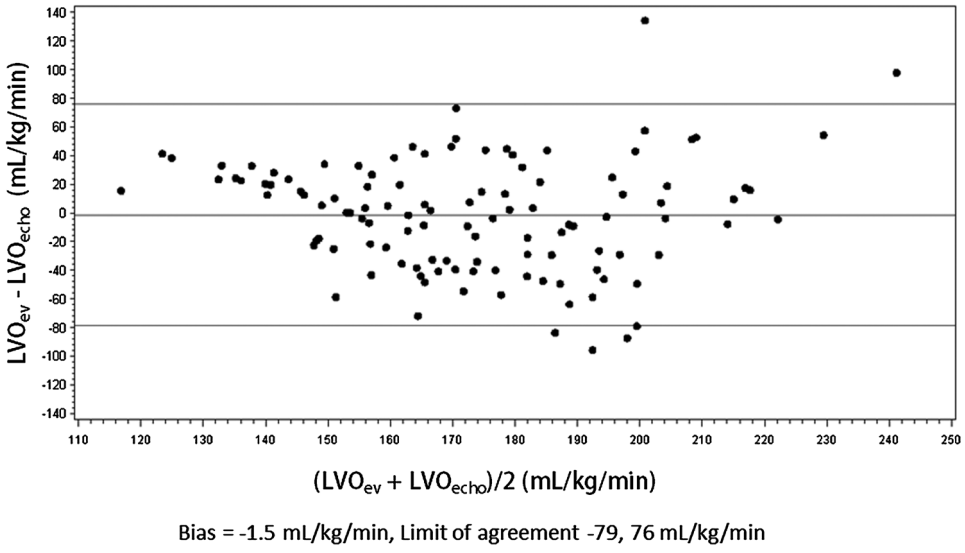

Figure 3 Bland-Altman plot depicting the agreement expressed in ml/kg/min between the left ventricular output estimated by echocardiography and electrical velocimetry.

children and adults.[4–6] In infants and children with congenital heart defect, cardiac output measurements by EV had an excellent correlation with those derived from the direct Fick-oxygen principle (r^2=0.94).[6] The bias and precision were 10 and 230 ml/min, respectively. When the population of infants was analysed separately, the correlation was still quite good (r^2=0.8). In adult subjects cared for in a surgical intensive care unit, cardiac output was assessed by thermodilution and compared with simultaneous measurements using EV.[5] The authors of this study also concluded that the bias (10 ml/min/m^2) and precision (570 ml/min/m^2) were clinically acceptable. Another study in critically ill adults found similar results with percentage error of <30%.[4]

There are several limitations to our study. We used echocardiography to assess the validity of EV in estimating cardiac output. We acknowledge that echocardiography is not the gold standard and as discussed earlier, it has its own significant limitations in estimating cardiac output. At present, the most accurate method of cardiac output measurement is believed to be thermodilution. However, the risks associated with this invasive method preclude its use for validation purposes in the normal or even the critically ill neonatal population. Another limitation of our study is the narrow range of cardiac output in our population likely leading to overestimation of the error percentage found in cardiac output measurements between EV and echocardiography. Finally, although we did not find any difference in agreement between those with and without a PDA >2 mm, further studies are needed in neonates with a larger and thus haemodynamically likely more significant PDA (eg, preterm infants with a PDA >2 mm) to better assess the impact of the ductus arteriosus on the bias and precision of EV.

In summary, we found continuous cardiac output monitoring using non-invasive EV to have comparable accuracy and precision to echocardiography in estimating cardiac output in healthy term neonates. Additional studies in preterm and term neonates with haemodynamic instability are needed to further define the validity and utility of this non-invasive cardiac output monitoring system in detecting changes in cardiac output during provision of intensive care. To this end, we have initiated a prospective study investigating the value of EV in assessing changes in cardiac output in critically ill preterm and term infants in response to initiation of cardiovascular supportive care.

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Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

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Notes