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The Use of Electrical Cardiometry for Continuous Cardiac Output Monitoring in Preterm Neonates: A Validation Study

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Abstract

Background Electrical cardiometry (EC) is a continuous noninvasive method for measuring cardiac output (CO), but there are limited data on premature infants. We evaluated the utility of EC monitoring by comparing the results obtained using EC to measurements of CO and systemic blood flow using echocardiography (ECHO).

Methods In this prospective observational study, 40 preterm neonates underwent 108-paired EC and ECHO measurements.

Results There were correlations between EC-CO and left ventricular output (LVO, $p < 0.005$) and right ventricular output (RVO, $p < 0.005$) but not with superior vena cava ($r = 0.093$, $p = 0.177$). Both RVO and LVO correlated with EC with and without a hemodynamically significant ductus arteriosus ($p = 0.001$ and 0.008, respectively). The level of agreement was decreased in infants ventilated by high-frequency oscillation ventilators (HFOV). The bias in HFOV was also positive compared with the negative biases found in other modes of ventilation.

Conclusion Given the correlation of EC with LVO, RVO, and lack of confounding effects of the ductus, our results suggest that EC has promise for trending CO in the preterm infant. However, given the limitations with mode of ventilation and the lack of correlation at low LVO values, further study is needed before this technology can be for routine use.

Keywords
- neonatology
- cardiology
- echocardiography
- electrical cardiometry

The evaluation of hemodynamics is integral to the care of infants in the intensive care unit (ICU). Historically, physicians have used blood pressure and heart rate to assess the hemodynamic status of a sick neonate. These measures are limited by the assumption of a normal cardiac output (CO). Functional echocardiography (ECHO) has emerged as a useful bedside measure of CO and systemic blood flow.[1] The limitations of ECHO include the need to have trained providers and the noncontinuous nature of the CO measurement.

Recently, a noninvasive method known as electrical cardiometry (EC) has emerged as a continuous measure of CO. EC uses the properties of bioimpedance to noninvasively measure body composition and blood flow. By utilizing changes in thoracic impedance after delivery of a low-voltage current, CO can be derived using surface adhesive electrodes. EC assumes that erythrocytes are in random orientation before the aortic valve opening and then align in a parallel fashion with pulsatile blood flow.[2,3] This parallel state results in increased conductance and conversely decreased impedance. The difference in conductance between these two states provides the baseline data that allow the calculation of CO.

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The emerging literature from adult and pediatric populations provides evidence that EC may be another valuable tool for monitoring and assessing clinical status. Excellent correlations have been observed in animal models and pediatrics patients.[4–6] However, there is limited data on the utility of EC in the neonatal population, in particular, premature infants. Premature infants often have cardiac instability, which can be confounded by the need for mechanical ventilation as well as the presence of cardiac shunts that limit the usefulness of traditional measures such as left ventricular output (LVO). It is unclear under such circumstances, whether EC monitoring is measuring systemic blood flow or a composite of systemic and pulmonary blood flow. The purpose of this study was to prospectively evaluate the utility of continuous EC monitoring in very preterm neonates by comparing the results obtained using this technique to serial measurements of both right ventricular output (RVO) and LVO, and superior vena cava (SVC) flow using ECHO.

Methods

This was a prospective observational study approved by the University of California at San Diego Institutional Review Board. Infants enrolled were part of a larger trial evaluating the hemodynamic effects of umbilical cord milking.[7] Antenatal informed consent was obtained. The target population was premature infants born at less than 32 weeks gestation who were admitted to the neonatal ICU at the UC San Diego Medical Center. Exclusion criteria included congenital heart defects (except for small VSDs), inability to tolerate adhesive skin leads, and the presence of major congenital anomalies. Participants were recruited between July 2011 and January 2013.

EC electrodes were placed on enrolled neonates in the first few hours of life. Up to three echocardiograms were performed at 6, 18, and 30 hours of life. Optimal EC signal quality was maintained by replacing or readjusting the leads whenever possible.

Echocardiograms were performed using the Vivid E9 (GE Healthcare, Wauwatosa, WI) by an investigator (A.C.K.) trained in pediatric functional ECHO. Measures of systemic blood flow including SVC, LVO, RVO, and diameters of the patent ductus arteriosus (PDA) were collected on each exam. PDA diameters > 1.5 mm were considered to be hemodynamically significant (hsPDA). All measures were performed as previously described.[8,9]

Data Analysis and Statistics

Continuous data are presented as a median with a range. Paired *t*-tests were used for parametric data. The Pearson coefficient was also calculated to evaluate the correlation between the EC-LVO and the predetermined echocardiogram measurements. Data were analyzed using SPSS Statistics software (IBM, New York, NY) and a p value less than 0.05 was considered statistically significant.

Bland–Altman plots were made to evaluate the agreement of multiple paired data for each patient between echocardiogram measurements and LVO obtained by EC monitor. Bias was defined as the mean difference between the EC and ECHO measurements, whereas percentage error was defined as: 100% $\times$ (1.96 $\times$ standard deviation of the difference between EC and ECHO measurements)/average of the ECHO measurements. A percentage error of less than 30% is generally accepted to be clinically acceptable.[10]

Results

Of the 60 infants who were enrolled in the primary trial, 40 infants had EC leads placed with reliable signal quality for at least one echocardiogram. There was no difference in gestational age in the infants with EC data; however, infants who had reliable data were smaller (1,076 g $\pm$ 321 vs. 1,299 g $\pm$ 433, $p = 0.03$) and were more likely to be hypotensive requiring pressors (17/40 vs. 3/20, $p = 0.03$). In total there were 109 paired EC and ECHO measurements. The baseline clinical characteristics are described in ►**Table 1**. Fifty-four paired measurements were nonventilated (continuous positive airway pressure [CPAP]) infants and 55 paired measurements were in ventilated infants (39 synchronized intermittent mechanical ventilation [SIMV], 8 high-frequency oscillation ventilators [HFOV], and 8 high-frequency jet ventilation). The mean age and weight (range) were 27 weeks (23–31 weeks) and 1,072 g (530–1,596 g), respectively.

Paired measurements of EC-derived CO (EC-CO) with LVO, RVO, and SVC were analyzed separately. The average measurement of EC-CO was 201 mL/kg/min with average measurements of LVO, RVO, and SVC being 218, 227, and 151 mL/kg/min, respectively. There were correlations between EC-CO and LVO ($r = 0.326$, $p < 0.005$) and RVO ($r = 0.378$, $p < 0.005$) but not with SVC ($r = 0.068$, $p = 0.485$). For LVO and RVO, correlations were significant within the overall patient population and when separated into nonventilated and ventilated groups (►**Table 2**). Infants ventilated with SIMV had significant correlations between both outputs (RVO and LVO) with EC-CO while those ventilated with high-frequency ventilation did not. Infants with low LVO ($\leq$200 mL/kg/min) had no correlation with EC-CO ($r = 0.061$, $p = 0.722$) compared with those with normal outputs (>200 mL/kg/min, $r = 0.285$, $p = 0.014$). Similarly,

Table 1 Patient characteristics

Patients	40
Mean gestational age (range)	27 (23–31)
Mean birth weight (range)	1,072 (530–1,596)
Mean 1 min Apgar score (range)	5 (1–9)
Mean 5 min Apgar score (range)	7 (3–9)
Male (%)	26/40 (65)
Cesarean section (%)	27/40 (68)
Receiving antenatal steroids (%)	33/40 (85)
Maternal chorioamnionitis (%)	7/40 (21)
Surfactant	25/40 (63)
Patent ductus arteriosus	38/40 (95)

Table 2 Correlation between EC and LVO or RVO

	LVO		RVO	
	Correlation	*p* value	Correlation	*p* value
Overall	0.326	< 0.005	0.378	< 0.005
Nonventilated	0.296	0.030	0.317	0.020
Ventilated	0.347	0.009	0.508	< 0.005
Conventional	0.387	0.015	0.485	< 0.005
High frequency	0.122	0.653	0.524	0.037
PDA	0.353	< 0.005	0.374	< 0.005
No PDA	0.322	0.045	0.385	0.015

Abbreviations: EC, electrical cardiometry; LVO, left ventricular output; RVO, right ventricular output.

infants with low RVO (≤200 mL/kg/min) did not significantly correlate with EC-CO ($r = 0.312$, $p = 0.077$) in contrast to those with higher RVO (> 200 mL/kg/min) ($r = 0.264$, $p = 0.021$).

There were a total of 70-paired measurements that had hsPDAs. The correlation of CO measurements between EC-CO and LVO and EC-CO and RVO were independent of the presence of the PDA (►**Table 2**).

►**Table 3** shows the level of agreement and bias by Bland–Altman analysis by different modes of ventilation. The level of agreement was low in infants ventilated by HFOV. The bias in HFOV was also positive compared with the negative biases found in other modes of ventilation (►**Fig. 1**).

Percentage error of CO measurement by ECHO and EC are shown in ►**Table 4**. The acceptable level of percentage error being less than 30% is only found in the LVO subset of neonates in room air. The magnitude of percentage error increases with respiratory support and reaches maximum percentage error when receiving high-frequency ventilation.

Discussion

This study is the first comparison of EC with ECHO in preterm neonates.

Although there was a correlation between EC measurements and echocardiogram measurements, there were fairly wide levels of agreement. The wide range was also demonstrated in a term infant study of EC and ECHO.[11] It is possible that the use of EC in an infant whether term or preterm may be confounded by the presence of fetal shunts. Interestingly in our study, EC had a correlation with LVO independent of the presence of a significant PDA. This observation concurs with those of Noori et al who demonstrated the lack of an effect of a PDA with EC measurements in term infants.[11] This suggests that the descending aorta provides a stronger signal compared with the smaller segment of the ascending aorta. However, while significant, the correlation between RVO and LVO with EC was low (r values approximately 0.3) suggesting that the relationship between ECHO derived COs and EC are not similar.

ECHO has its own limitations in estimating CO. LVO has a precision of approximately 30% when compared with thermodilution and Fick methods.[5,6] Similarly, ECs algorithm for calculating CO is based on a hemodynamic model in adults. While we adjusted the body mass calculation for neonates in our study, it is possible that in very small preterm infants this calculation may need further adjustments. This could also explain why there was no correlation with EC when LVO

Table 3 Agreement between LVO measured by ECHO and EC calculated by Bland–Altman analysis

	Bias	SD	Lower limit of agreement	Upper limit of agreement
Overall	− 18.8	67.7	− 151.6	113.8
Nonventilated	− 20.4	53.5	− 124.9	84.1
Room air	− 25.0	22.8	− 69.7	19.7
CPAP	− 18.2	63.7	− 143.1	106.7
Ventilated	− 17.5	79.8	173.9	138.9
SIMV	− 30.2	73.8	− 174.8	114.4
HFJV	− 10.9	81.7	− 171.0	149.2
HFOV	38.2	91.4	− 140.9	217.3

Abbreviations: EC, electrical cardiometry; ECHO, echocardiography; CPAP, continuous positive airway pressure; HFJV, high-frequency jet ventilation; HFOV, high-frequency oscillation ventilators; LVO, left ventricular output; SD, standard deviation; SIMV, synchronized intermittent mechanical ventilation.

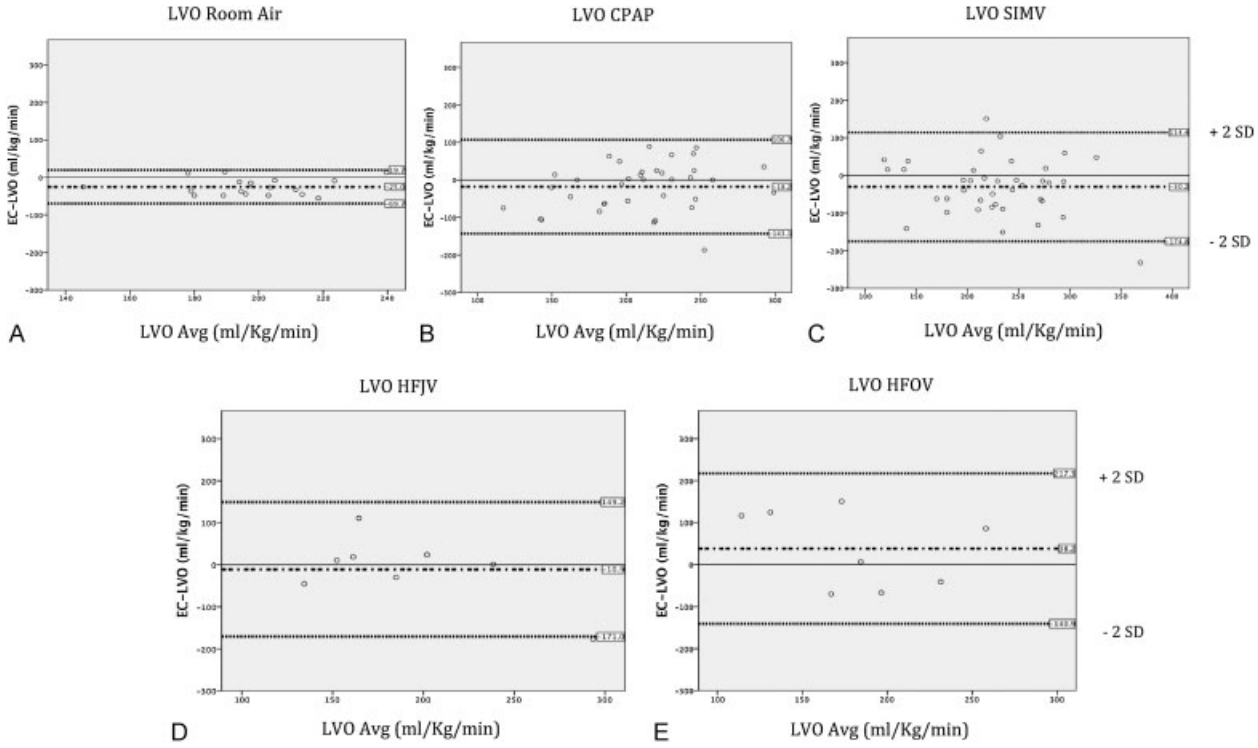

Fig. 1 Bland–Altman graphs (A) nonventilated infants, (B) infants on continuous positive airway pressure (CPAP), (C) infants on synchronized intermittent mechanical ventilation (SIMV), (D) infants on high-frequency jet ventilation (HFJV), and (E) infants on high-frequency oscillation (HFOV). Dotted lines represent ± 2 SD. LVO, left ventricular output; SD, standard deviation.

was < 200 mL/kg/min. Infants with low LVO also had very low SVC (< 50 mL/kg/min) and RVO (< 150 mL/kg/min) outputs (data not shown) indicating that the low LVO was unlikely to be due to ECHO measurement error rather an issue with detection at lower outputs.

Although there was a correlation between EC and LVO in ventilated infants as a group, there was a lack of correlation when infants were ventilated by high frequency. This observation is further emphasized when evaluating the percentage error during different respiratory states. Noori et al demonstrated a lower percentage error in healthy term infants compared with our preterm population (43.6 vs. 60.2%).[11] Interestingly, our percentage error was very similar when we compared nonintubated neonates (48.4%). However, the percentage error increased with different modes of ventilation, such that the highest percentage error occurred with high-frequency ventilation. This is of concern since often the most hemodynamically compromised infants are often placed on high-frequency ventilation. Reasons for the poor correlation are likely due to a variety of factors. One possibility may be that the oscillations from the high-frequency ventilator are at a similar frequency than the frequency used by EC to calculate a CO (12 Hz). Another possibility is that the high-frequency ventilation contributed to increased intrathoracic pressure thereby increasing the distance from the electrodes to the descending aorta. Also, since EC measurement algorithms are dependent on changes in electrical impedance in the thorax, it is plausible that the higher expansion in the lungs provided by high-frequency ventilation diminishes the bioimpedance signal substantial enough to cause the poor correlation between the devices.

Table 4 Percentage error measured by ECHO and EC calculated by Bland–Altman analysis

	LVO Percentage error (%)	RVO Percentage error (%)
Overall	60.2	59.4
Nonventilated	48.4	53.2
Room air	21.3	38.5
CPAP	57.0	59.3
Ventilated	69.7	59.2
SIMV	59.6	55.0
HFJV	81.3	57.9
HFOV	110	63.8

Abbreviations: EC, electrical cardiometry; ECHO, echocardiography; CPAP, continuous positive airway pressure; HFJV, high-frequency jet ventilation; HFOV, high-frequency oscillation ventilators; LVO, left ventricular output; SIMV, synchronized intermittent mechanical ventilation.

There were several limitations to this study. Although we had intended for each patient to have serial three echocardiograms with correlating COs on the EC monitor, this was not always possible. There were instances where the EC monitor was not able to record the CO due to a variety reasons such as subjects inability to tolerate the leads or poor signal quality that did not provide accurate measures. Twelve infants had fewer than three EC-echo paired measurements. To evaluate whether the effect of some infants having all three paired

measurements could have biased our results, the correlations were recalculated after their exclusions. The correlations were found to be similar whether or not these patients were excluded. There were no differences in overall LVO and RVO correlations to ECHO measurements as well as in nonventilated and ventilated patients. There was no difference in gestational age in the infants with EC data; however, infants who had reliable data were smaller and sicker. Most of the artifact with EC tended to be movement and smaller sicker infants had less motion affecting the EC signal quality indicating its use to be more reliable in this group of neonates. Both of these situations contributed to the dropout seen in our trial. This also limited our ability to detect acute changes with ventilation (e.g., extubation to CPAP or conversion from SIMV to HFOV). The effects of ventilation on EC measurements could have been better defined if we had been able to analyze these data.

Conclusion

Our results demonstrate that, in the preterm infant, EC correlates with both RVO and LVO, with limitations of detection at low output and with high-frequency ventilation. EC monitoring provides continuous trending of cardiac hemodynamics that is independent of the confounding presence of an hsPDA. It is conceivable that EC may assist with clinical decisions where trending CO is needed in the preterm infant. However, this still needs prospective study and, in particular, more studies are needed to test the sensitivity of EC to detect acute changes in hemodynamics before routine clinical integration.

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What Is Already Known on This Topic

Cardiac output can be measured in healthy full-term infants by electrical cardiometry.

What this study adds: Electrical cardiometry can be used to trend cardiac output in premature infants. However, there may be limitations by mode of ventilation and detection at low cardiac outputs in this population.

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