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Comparison of bioreactance and echocardiographic non-invasive cardiac output monitoring and myocardial function assessment in primagravida women

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Abstract

Background. Non-invasive cardiac output monitoring (NICOM) using bioreactance (BRT) in pregnancy is gaining interest but lacks validation. We compared simultaneous cardiac output (CO) measurements obtained using the NICOM® (BRT-CO) and echocardiography (echo-CO), and assessed the relationship between maternal characteristics and myocardial performance.
Methods. Paired stroke volume (SV) and CO readings were obtained using NICOM® and echocardiography, in a group of healthy nulliparous women throughout a 15 min period. Agreement between NICOM® and echocardiography was assessed using Bland–Altman analysis and the intraclass correlation coefficient (ICC). Left ventricular (LV) function was assessed using systolic strain and tissue Doppler velocities (S′, E′, and A′ waves).
Results. Thirty-five women with a median [interquartile range] age, weight, and gestation of 29 [26–34] yr, 71 [64–79] kg, and 28 [21–29] weeks, respectively, were enrolled. There was good agreement between NICOM®-measured and echocardiographically measured SV [mean bias 6 ml (limits of agreement −18 to 29); ICC 0.8 (95% confidence interval 0.6–0.9), $P<0.001$] and CO [mean bias 0.2 litres (limits of agreement −1.3–1.7); ICC 0.8 (95% confidence interval 0.7–0.9), $P<0.001$; mean percentage error ±26%; coefficient of error (precision)=3.4%]. The mean (SD) LV S′ was 9.7 (2.3) cm s^{-1}. The mean (SD) LV strain was −18.6 (2.6)%. There was a negative relationship between BMI and LV diastolic function measured using the E′:A′ ratio ($r=-0.51$, $P<0.01$).
Conclusions. Stroke volume and CO measurements obtained using NICOM® were comparable to those obtained using echocardiography, with acceptable limits of agreement. Increased maternal BMI negatively impacts LV diastolic function measured using tissue Doppler imaging.

Key words: cardiac output; echocardiography; myocardial function

Haemodynamic assessment of healthy women in pregnancy has traditionally centred on maternal blood pressure and heart rate (HR). Further assessment of maternal haemodynamic profile has been limited because of the invasive nature of many methods, such as pulmonary artery catheter placement for thermodilution measurement of cardiac output (CO). Even some minimally invasive methods require arterial line placement, which limits elective use in healthy parturients. Early non-invasive methods of CO assessment were limited by poor signal-to-noise ratios and electrical interference in the case of

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Editor's key points

- Non-invasive measurements of cardiac output are potentially useful in obstetric patients but have not been validated in this population.
- The NICOM® bioreactance monitor of cardiac output was compared with standard transthoracic echocardiographic methods in 35 healthy primagravida.
- Stroke volume and cardiac output measurements were comparable between the two methods, validating the utility of non-invasive bioreactance monitoring in pregnant patients.

bioimpedance, or were time consuming and required an expert to perform and read the examination when using echocardiography. However, development of bioreactance has allowed detailed non-invasive assessment of maternal haemodynamics, on an outpatient basis if required, without the need for an expert to operate the device. Bioreactance technology uses the phase shift (or time delay) of an applied alternating current traversing the thoracic area to derive stroke volume (SV).[1]

Recent obstetric studies have used this technology to assess maternal haemodynamics in patients at high risk of pre-eclampsia and intrauterine growth restriction.[2 3] Bioreactance has been validated in many patient populations, against gold-standard techniques for the assessment of CO, and is robust enough to be used at rest and during exercise.[1 4 5] Until recently, however, bioreactance has not been validated in the obstetric population. The obstetric population has a unique and rapidly changing body habitus, particularly during the second and third trimesters. In addition, the impact of the uterus, amniotic fluid, and fetus on the bioreactance properties of the thorax are unknown. Therefore, extrapolating bioreactance validity data from other patient populations for use in the obstetric population is not necessarily justified.[6]

We compared simultaneous CO measurements obtained using the non-invasive cardiac output monitor NICOM® (Cheetah Medical, Newton, MA, USA) by means of bioreactance (BRT-CO) and echocardiography (echo-CO) in a group of healthy primigravid women, and assessed the relationship between maternal characteristics, cardiac output, and myocardial performance.

Methods

This was a cross-sectional study conducted in the Rotunda Hospital, Dublin, with Institutional Research Ethics Board approval. Informed consent was obtained from all participants. Subjects were recruited from those participating in a large prospective study assessing the ability of NICOM® to predict the evolution of pre-eclampsia and intrauterine growth restriction (the HANDLE study). All low-risk primagravida patients attending the Rotunda Hospital for antenatal care of a singleton pregnancy were considered for inclusion. Those patients with multiple gestations, known fetal abnormality, pre-existing medical conditions, or hypertension at the first antenatal visit were excluded. Eligible subjects who were enrolled in the HANDLE study were then approached for consent to conduct simultaneous echocardiography assessments during NICOM assessments. Study participants underwent simultaneous echocardiography and NICOM assessment of cardiac output throughout a 15 min period. The echocardiographer was blinded at all times to the NICOM readings. None of the participants underwent multiple assessments. Maternal weight and height were noted at the time of the assessments to derive BMI.

NICOM® measurements

Cardiac output and SV measurements using bioreactance (BRT-CO and BRT-SV) were performed using the NICOM® monitor (Cheetah Medical). Bioreactance is a technique that uses four dual electrodes, each with a current-emitting and -sensing component. Electrodes are placed on the right and left shoulders and the posterolateral aspect of the left and right thorax, below the level of the heart. In this way, they 'box' the heart. An AC current, of known frequency, is then passed from the outer emitting electrodes and detected by the inner sensing electrodes. The phase shift in the sensed signal is proportional to the pulsatile blood flow in the thorax and is highly correlated with aortic blood volume.[1] The derivative of this signal over time provides information on aortic flow (i.e. SV). Stroke volume is calculated using the following formula: $SV = dX/dt \times VET$, where SV is the stroke volume, dX/dt the maximal flow, and VET the ventricular ejection time. Heart rate is obtained from an ECG signal sensed from the electrodes, and CO is then calculated as follows: $CO = SV \times HR$. The NICOM® display of haemodynamic measurements was shielded from view during echocardiographic assessment.

Echocardiographic measurements

Echocardiographic measurements of CO were performed at the same time as NICOM® using a Vivid S6 echocardiography machine and a 4 MHz multifrequency probe (General Electric, Milwaukee, WI, USA) using a standardized protocol adapted from recently published guidelines.[7] All patients were in a semi-recumbent position elevated at a 45° angle and placed in a slightly left lateral position. Cine loops were obtained at end expiration in raw DICOM format by two investigators (A.E.-K. and C.B.) and stored in an archiving system for later analysis (EchoPac, version 112 revision 1.3; General Electric). Offline analysis was conducted at the end of the study by a single investigator (A.E.-K.) who was blinded to the NICOM® values. Stroke volume and CO were measured as follows. The long axis parasternal view of the left ventricle was used to obtain the aortic root diameter to derive the aortic cross-sectional area (AoCSA) as follows: $AoCSA = \pi \times (\text{aortic root radius})^2$. The apical five-chamber view was used to obtain a pulsed-wave Doppler measurement of aortic blood flow at the aortic root to derive the velocity–time index (VTI). Heart rate was obtained using the RR interval from the ECG. Stroke volume was calculated using the following formula: $SV = AoCSA \times VTI$. Cardiac output was derived using the following formula: $CO = SV \times HR$.

Left ventricular (LV) function was measured using tissue Doppler imaging to derive mitral valve annular systolic velocity (S′) and early (E′) and late (A′) diastolic velocities of the LV lateral wall. Diastolic E′ and A′ waves were expressed as a ratio (E′:A′) to assess diastolic function. Speckle tracking echocardiography was used to derive LV strain. Tissue Doppler imaging values were obtained from the apical four-chamber view using a pulsed-wave Doppler sample gate of 2–4 mm at the level of the mitral valve annulus. The cursor was aligned with the longitudinal plane of LV motion to maintain an angle of insonation $<20°$. Left ventricular S′ was obtained from averaging three consecutive waves. For longitudinal strain analysis, grey-scale

images were recorded from the apical four-chamber view at a frame rate of 80 frames s^{-1}. Images were optimized to view the myocardial walls. To derive longitudinal LV strain, the endocardial border was manually traced at end systole. The region of interest was maintained within the myocardial wall. The software divides the LV lateral wall and the septal wall into three segments (basal, mid, and apical) each and calculates the strain in each segment. An average strain for the entire LV in the four-chamber plane calculated from the six segments is provided. The analysis was accepted after visual inspection and when the software indicated adequate tracking. If tracking was suboptimal, the endocardial border was retraced. If satisfactory tracking was not accomplished within 5 min, the non-tracking segments were excluded from analysis. End-systolic strain values were measured at the time of aortic valve closure. The BRT-CO and BRT-SV measurements were timed to the same minute of acquisition of the echo-CO and echo-SV.

Statistical analysis

Continuous variables were tested for normality using the Shapiro–Wilk test and presented as the mean (SD) or median [interquartile range] as appropriate. Paired data were compared using Student's paired *t*-test or the Wilcoxson signed-rank test as appropriate. Independent data were compared using Student's unpaired *t*-test or a Mann–Whitney *U*-test as appropriate. Correlations were tested using the Pearson correlation coefficient. Agreement between echocardiography- and bioreactance-measured SV and CO was tested using Bland–Altman analysis [to derive bias and limits of agreement (LOA) between the two methods] and intraclass correlation coefficient (ICC). We calculated the percentage error between SV and CO measurements obtained from bioreactance and echocardiography using the following formula: mean percentage error=(100×1.96×SD of bias between the two methods)÷mean between the two methods.[8] Mean percentage error is considered acceptable if <30%.[9] We demonstrated the precision of BRT-CO and BRT-SV measurements (15 readings obtained 1 min apart for each subject during quiet rest) using the coefficient of error (CE).[10] The following formula was used: CE=coefficient of variation (COV)÷$\sqrt{n}$, where n represents the number of repeated measurements. The COV was calculated as follows: (SD of absolute differences between repeated measurements÷mean of all repeated measurements)×100%. SPSS (IBM, version 23) was used to conduct the analysis. We accepted $P<0.05$ as statistically significant.

Results

Thirty-five women with a median [range] age and weight of 29 [19–40] yr and 71 [56–107] kg, respectively, underwent paired echocardiographic and NICOM® assessments at a median [interquartile range] gestation of 28 [21–29] weeks. Table 1 illustrates the SV, CO, and HR values obtained. There was no difference between echo-CO and BRT-CO or between echo-HR and BRT-HR. The BRT-SV was lower than echo-SV, but this difference was small (Table 1). In addition, there were no differences in CO or SV between women in the lowest (first) and highest (fourth) quartiles of gestational age (all $P>0.5$).

There was good agreement between echo-SV and BRT-SV, with a mean bias of 6 ml (LOA −18 to 29) and an ICC of 0.8 (95% confidence interval 0.6–0.9, $P<0.001$). Likewise, there was good agreement between echo-CO and BRT-CO, with a mean bias of 0.2 litres (LOA −1.3 to 1.7) and an ICC 0.8 (95% confidence interval 0.7–0.9, $P<0.001$). The mean percentage error of CO measurements between the two methods was ±26%. There was a strong correlation between echocardiography- and bioreactance - measured SV and CO (Fig. 1). There was no difference in the mean bias of CO (0.21 *vs* 0.24 litres) or SV (5 *vs* 6 ml) between subjects assessed during the second *vs* third trimester (all $P>0.5$). Likewise, there was no difference in the mean bias of CO or SV between the lowest and highest age quartiles (all $P>0.4$). The coefficient of error (CE) representing the precision of BRT-CO was 3.4% (Table 2).

Table 1 Difference between NICOM® and echocardiography readings. Values are presented as the mean (SD) and compared using Student's paired *t*-test. NICOM®, non-invasive cardiac output monitoring

Parameter	Echocardiography	NICOM	P-value
Stroke volume (ml)	75 (18)	69 (15)	0.01
Cardiac output (litres min^{-1})	6.4 (1.1)	6.1 (1.1)	0.1
Heart rate (beats min^{-1})	87 (14)	88 (13)	0.6

Image acquisition and analysis was possible in all study participants. The mean (SD) LV S′, E′, and A′ in the cohort were 9.7 (2.3), 17.3 (2.7), and 8.5 (2.3) cm s^{-1}, respectively. The median [interquartile range] E′:A′ was 2.0 [1.5–3.0]. The mean (SD) LV strain in the cohort was −18.6 (2.6)%. The group was divided into those with a BMI <25 kg m^{-2} (n=23, 66%) and those with BMI ≥25 kg m^{-2} (n=12, 34%). Subjects with a BMI ≥25 kg m^{-2} had a higher A′ wave [10.3 (1.6) *vs* 7.5 (2.0) cm s^{-1}, $P<0.01$] and a lower E′:A′ ratio [1.6 (0.3) *vs* 2.6 (0.9), $P<0.01$]. There was a negative linear correlation between BMI and E′:A′ ($r=-0.51$, $P<0.01$). There was no difference in LV strain between the higher and lower BMI groups [17.4 (3.1) *vs* 19.2 (2.2)%, $P=0.19$], although a negative correlation between LV strain and BMI was present ($r=-0.54$, $P=0.03$).

Discussion

Bioreactance-measured CO and SV obtained during the second trimester of pregnancy demonstrated acceptable agreement with echocardiography-measured values. A higher maternal BMI appeared to have a negative impact on measures of diastolic function using E′:A′ ratio.

The use of non-invasive CO monitoring by the bioreactance technique has gained considerable interest recently. Early work on NICOM® focused on establishing its reliability and validity in a variety of populations spanning neonates to adults.[11–14] In patients after cardiac surgery, NICOM® had good agreement with thermodilution (the currently accepted gold standard). In addition, NICOM® possessed a high sensitivity and specificity for predicting significant haemodynamic changes in this population.[13] Likewise, NICOM® has acceptable accuracy, precision, and responsiveness in a wide range of circulatory situations in the intensive care setting when compared with thermodilution.[1] Bioreactance also demonstrates good test–retest reliability for estimating cardiac output at rest and during exercise in the healthy population.[15] When compared with oesophageal Doppler for goal-directed fluid therapy, bioreactance offered similar clinical outcomes and increased ease of use, with fewer missing data points.[16]

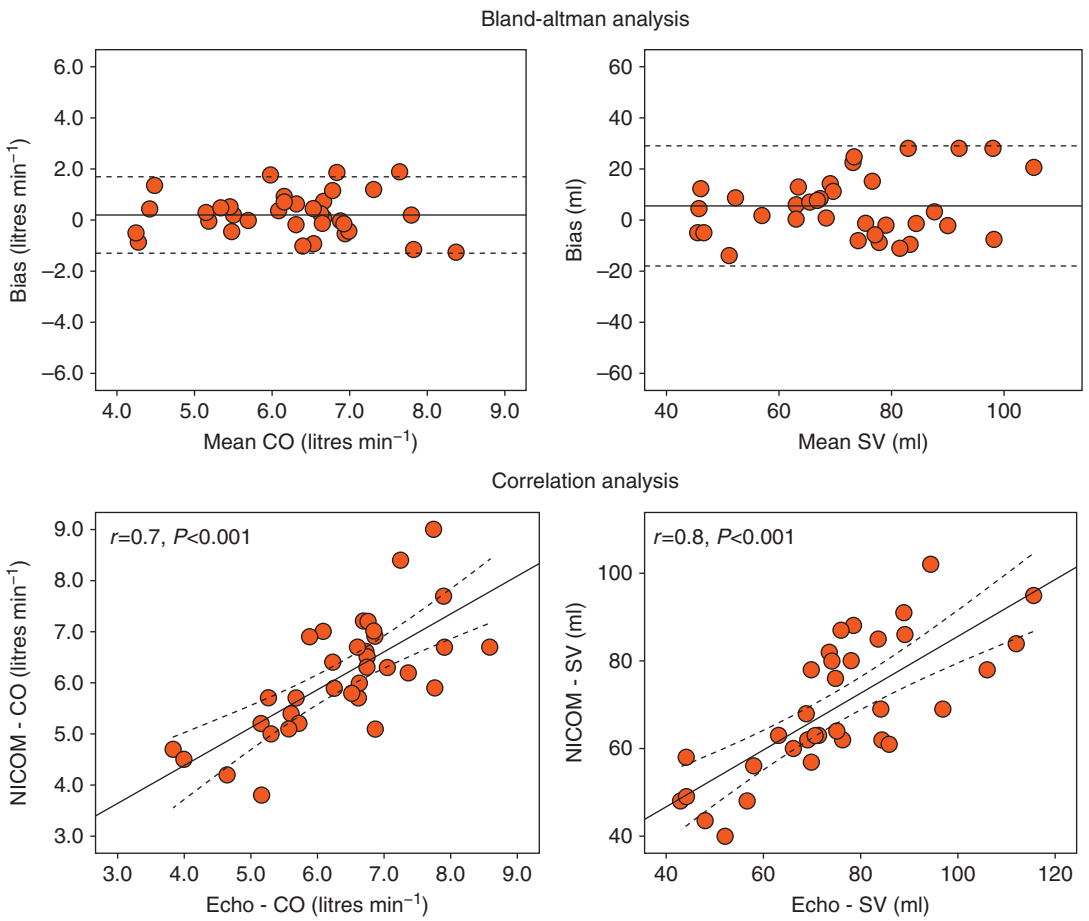

Figure 1 Bland–Altman and correlation analyses between cardiac output and stroke volume. CO, cardiac output; SV, stroke volume.

Table 2 Agreement between echocardiography and NICOM® measurements. *Bland–Altman analysis. ICC, intraclass correlation coefficient; NICOM®, non-invasive cardiac output monitoring

Measurement and type of analysis	Result
Stroke volume	
Bias and limits of agreement*	6 ml (−18 to 29)
ICC (95% confidence interval)	0.8 (0.6–0.9)
Correlation (r, P-value)	0.8, P<0.001
Mean percentage error	±29%
NICOM® coefficient of error (precision)	3.9%
Cardiac output	
Bias and limits of agreement*	0.2 litres min^{-1} (−1.3 to 1.7)
ICC (95% confidence interval)	0.8 (0.7–0.9)
Correlation (r, P-value)	0.7, <0.001
Mean percentage error	±26%
NICOM® coefficient of error (precision)	3.4%

Use of NICOM® in the obstetric population is increasing. Recent studies have demonstrated that NICOM® can identify distinct haemodynamic profiles associated with placental disease, consistent with the findings of more invasive methods.[3] Haemodynamic assessment using NICOM® can predict the evolution of clinical pre-eclampsia and detect different evolving haemodynamic profiles in women with pre-eclampsia and intrauterine growth restriction *vs* normal control subjects.[2] In addition, NICOM® has also been used to devise an optimal dosing regimen of phenylephrine to prevent hypotension during spinal anaesthesia in patients undergoing Caesarean section, demonstrating no clinical difference from administering phenylephrine as an infusion *vs* a bolus regimen in a randomized controlled setting.[17] Despite its emerging use in the obstetric population, there remains a lack of studies assessing its validity in this setting. The challenge to validating NICOM® in pregnant women stems from the impracticality and risk associated with recognized gold standards, such as thermodilution. As a result, we chose to use echocardiography (echo), which has recently been validated against thermodilution in pregnancy and has been suggested as a reference for the validation of other CO techniques in pregnant women.[18]

Our results suggest that NICOM® is a valid method for assessing CO in the pregnant population when compared with echocardiographically measured CO. The mean percentage error obtained in our study was 26%, which is less than the recommended cut-off of 30%. However, is it important to emphasize that while LOA ranging between −1.3 and 1.7 litres may be acceptable when the mean CO in the study population is 6.2 litres, those LOAs would be too wide for a population with a lower average CO. Therefore, the results of our study are applicable only to pregnant women of a similar range of BMI and COs in the general population. We also assessed the precision of the NICOM® device when obtaining repeated measures in the subject while at rest, when their CO is assumed to be stable. We found relatively low CE, suggesting that the bioreactance method demonstrated very good precision in pregnant women during the second and third trimesters.

Although echocardiography is a low-risk and non-invasive method of CO and SV assessment in this low-risk population, it requires expert training in order to acquire appropriate images and expertise in reading in order to estimate SV and CO. In contrast, NICOM® requires minimal training in order to obtain the necessary data. It is completely non-invasive, essentially operator independent, and can provide continuous SV and CO assessment. As a result, NICOM® can provide useful haemodynamic data on low-risk pregnant women, in both inpatient and outpatient settings. Vinayagam and colleagues[19] recently assessed 98 patients in all three trimesters using NICOM® and echocardiography, but found acceptable agreement only during the third trimester. This group suggested that NICOM® was primarily of use intrapartum and at advanced gestations.[19] Owing to the contrasting findings to our results, further studies are required to clarify the validity of NICOM® in this population.

We also evaluated LV function using tissue Doppler imaging and speckle tracking echocardiography. Tissue Doppler imaging is a quantitative echo modality that measures the velocity of cardiac muscle movement directly. We found that an increased maternal BMI is associated with diastolic dysfunction (measured by E′:A′). Recently, Melchiorre and colleagues[20] presented serial echocardiographic measurements of function and haemodynamics in a relatively large group of nulliparous healthy women. They found comparable CO (5.9 [5.0–7.3] litres min^{-1}) and SV (78 [67–93] ml) to our results. In addition, their systolic and diastolic function parameters measured using tissue Doppler imaging were very similar to those we obtained: S′=7.5 [6.0–9.0] cm s^{-1} and E′:A′=2.3 [1.5–3.0].[20] The negative correlation between increasing maternal BMI and LV diastolic function parameters is interesting. An association between obesity and LV diastolic dysfunction is well recognized and is likely to be a result of various neurohormonal and metabolic changes associated with obesity.[21 22] This relationship in the context of pregnancy and its potential contribution to placental disease warrant further study.

Our study is limited by a relatively small sample size and the narrow window of measurement during the gestational period. In addition, haemoglobin concentration and haematocrit can influence the accuracy of BRT-CO when compared with thermodilution, with concentrations haemoglobin <140 g $litre^{-1}$ increasing the bias between the two methods.[13] We did not measure haemoglobin concentrations in our cohort and were therefore unable to explore this relationship. The sample size was too small to make any meaningful associations between the functional parameters and important maternal characteristics. However, it appears that non-invasive CO assessment using bioreactance is a viable option for monitoring haemodynamic status during pregnancy. Further studies are required in a larger sample size and across a wider time period during pregnancy to confirm this.

Authors' contributions

Study design: A.D., A.E.-K., E.K., E.T., F.M., P.T.
Patient recruitment: C.M., L.M.
Data collection: A.D., A.E.-K., C.M., L.M., C.B., P.T.
Data analysis: A.E.-K., C.B.
Writing the first draft of the manuscript: A.D., A.E.-K.
Review of the manuscript before submission: C.M., L.M., C.B., E.K., E.T., F.M., P.T.

Declaration of interest

None declared.

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