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ORIGINAL ARTICLE

Comparison of noninvasive and central arterial blood pressure measurements in ELBW infants

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Objective: The objective of this study was to evaluate the difference between noninvasive and central arterial blood pressure measurements in extremely low-birth-weight (ELBW) infants.

Study Design: We conducted a retrospective cohort study of infants with birth weight $\leqslant$1000 g and who were admitted to a single center in 2005. Paired noninvasive and umbilical arterial blood pressure measurements obtained in the first 72 h were compared. The primary outcome was the differential between the paired measurements. Noninvasive blood pressure (NBP) measurements were defined as clinically acceptable if the differential between the pairs was 15% or lower.

Result: We obtained 146 pairs of measurements from 38 infants. The median absolute differences between noninvasive and arterial systolic, mean and diastolic blood pressure measurements were +18.5, +12 and +10 mm Hg, respectively (percentage differential of 43, 39 and 41%, respectively). In total 75% of the noninvasive measurements of mean blood pressure were clinically unacceptable. No patient or measurement characteristic was significantly associated with clinically unacceptable noninvasive measurements.

Conclusion: In ELBW infants, NBP measurements substantially overestimate systolic, mean and diastolic blood pressures compared with central arterial measurements.
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Introduction

Blood pressure can be monitored invasively through an arterial catheter or noninvasively by using a blood pressure cuff. In term infants, a central arterial catheter is believed to provide the most accurate blood pressure measurement,[1] but providers may often find that they must rely on noninvasive blood pressure (NBP) measurements.

Noninvasive blood pressure is measured in the neonatal population using the automated oscillometric method. In term infants, NBP measurements are comparable with arterial blood pressure measurements.[2–4] However, it is unclear how NBP and arterial blood pressure measurements compare in preterm infants.[5–12] Data on the correlation between NBP and arterial measurements in extremely low-birth-weight (ELBW) infants are particularly lacking. One small study, evaluating systolic NBP and arterial blood pressure measurements, showed discrepant NBP and arterial measurements in infants who weighed <750 g.[13] The aim of this study was to compare measurements of systolic, mean and diastolic blood pressures obtained using noninvasive means with measurements procured from a central arterial catheter in newborn ELBW infants.

Methods

Study population

We conducted a retrospective cohort study of ELBW infants admitted to The North Carolina Children's Hospital Newborn Critical Care Center from 1 January 2005 through 31 December 2005. We included infants who were inborn, had a birth weight of $\leqslant$1000 g and those who were managed using an umbilical arterial catheter (UAC). We excluded infants with a non-sinus arrhythmia documented on electrocardiogram or those with a congenital limb malformation.

Blood pressure measurements

Both NBP and UAC measurements were abstracted from the bedside nursing flow sheet. We defined a paired measurement as an NBP and a UAC measurement obtained within 5 min of each other. We included all paired measurements obtained within the first 72 h after delivery. NBP measurements were assessed on the basis of the oscillometric principle using a Spacelabs SL1700 monitor system (Spacelabs Healthcare, Issaquah, WA, USA). Central arterial measurements were obtained using a fluid-coupled pressure transducer (Transpac Neonatal Disposable Pressure Transducer; Hospira, Lake Forest, IL, USA), and the arterial measurements were

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displayed on the bedside monitor. All central arterial blood pressure measurements were obtained from a high-lying 3.5 French UAC (placement between the thoracic vertebrae 6 and 9, confirmed by radiography). NBP measurements were obtained using a blood pressure cuff (Critikon Neonatal Blood Pressure Cuff; General Electric, Waukesha, WI, USA) placed on either an arm or leg. The manufacturer's recommended cuff size, size 1 for an arm circumference of 3 to 6 cm or size 2 for an arm circumference of 4 to 8 cm, was used. We excluded measurements that were accompanied by a concern regarding the monitoring system, such as a dampened arterial waveform documented on the nursing flow sheet.

Outcomes
The primary outcome was the difference between systolic, mean and diastolic blood pressures obtained by noninvasive means from those obtained from an UAC, measured as the differential between the pairs. We constructed the differential by subtracting the UAC measurement from the NBP measurement, divided the difference by the UAC measurement and multiplied by 100. Our *a priori* definition of an acceptable NBP measurement was an NBP−UAC differential of 15% or lower, as this difference is clinically relevant and may alter medical management in the ELBW population.

We examined infant demographic factors and measurement characteristics that potentially influenced the difference between NBP and UAC measurements. We analyzed birth weight, gestational age, sex and race, as well as various mechanical, physiological and respiratory measurement characteristics. The mechanical factors were cuff size (1 or 2) and cuff location (an arm or leg). Physiological factors included low temperature (defined as skin temperature of $<36\,^{\circ}$C), urine output (ml per kg per hour during the 6 h before measurement), heart rate, age at the time of measurement (in hours), time of day (in hours), presumed sepsis (defined as having a negative blood culture, but either clinical signs or laboratory values concerning for sepsis and treatment with antibiotics for $\geqslant 5$ days) and receipt of hydrocortisone, dopamine, dobutamine or fentanyl. Respiratory factors were peak inspiratory pressure, positive end expiratory pressure and mean airway pressure.

The study was approved by the Institutional Review Board of the University of North Carolina at Chapel Hill.

Statistical analysis
We compared the magnitude of differentials between the pairs of NBP and UAC systolic, mean and diastolic measurements using a modified Bland−Altman analysis adjusted for multiple observations per patient.[14] The Bland−Altman analysis uses LOA (limits of agreement), which are the limits that contain 95% of the measurement differences. We plotted the NBP−UAC differential against the UAC measurement.

Patient demographic factors
To examine which patient demographic factor might be associated with a greater difference between the pairs of NBP and UAC measurements, we calculated the difference between the median NBP and UAC blood pressure measurements for each patient. We then entered the difference between values as a continuous variable into a multiple linear regression model using a backward-stepwise selection procedure to determine infant demographic variables that were associated with a higher difference in NBP and UAC measurements.

Measurement characteristics
Multiple linear regression was used to select variables within each category (mechanical, physiological and respiratory) that were independently associated with a NBP and UAC measurement difference at a level of $P<0.20$. These variables were then entered into a final linear regression model using the backward selection procedure. The final model was determined after adjustment was made for significant patient demographic variables.

The regression models were cross-validated using a bootstrapping technique.[15] Measurement characteristics were chosen with 200 iterations of stepwise regression (removal of variables at a *P*-value of 0.15 and addition of variables at a *P*-value of 0.05).[16] We deleted measurements with missing variables before analysis. Variables included in more than 50% of the models were then entered into a final regression model with backward selection, after adjustment for significant patient demographic variables.

Risk factors for clinically unacceptable NBP measurement
To determine measurement characteristics associated with increased risk of a clinically unacceptable NBP measurement (defined as a differential of more than 15%), we carried out a backward stepwise logistic regression analysis, using a *P*-value of 0.15 as a cutoff for removal and a *P*-value of 0.05 for addition of variables to the models. The final model was determined after adjustment for significant patient demographic variables. Low temperature was not included because all infants with a low temperature had clinically unacceptable NBP measurements, thus making the model unstable.

All statistical calculations were carried out using Stata 9.0 (StataCorp LP, College Station, TX, USA).

Results

Study population
Of the 71 ELBW infants admitted to the neonatal unit during the study period, 38 met the eligibility criteria for inclusion in the study. Among the ineligible infants, 28 did not have a UAC and 5 did not have paired blood pressure measurements. The median birth weight of the study cohort was 754 g (range: 435 to 996 g), and the median gestational age was $25^{6/7}$ weeks (range: $23^{4/7}$ to $29^{4/7}$ weeks). Thirteen (34%) infants in the cohort were males. Nineteen (50%) infants were black, 12 (32%) were white and 7 (18%) were Hispanic. We obtained 146 pairs of measurements from the 38 infants in the study (Table 1).

Table 1 Measurement characteristics

Total number of measurements	*146*
Number of paired blood pressure measurements per patient, median (range)	4 (1–10)
Location of cuff, n (%)	
Arm	9 (6)
Leg	137 (94)
Size of cuff, n (%)	
1	61 (42)
2	85 (58)
Respiratory support, n (%)	
None	0
Nasal continuous positive airway pressure	23 (16)
Mechanical ventilation	123 (84)
Medications,[a] n (%)	
Dopamine	7 (5)
Dobutamine	20 (14)
Fentanyl	25 (17)
Hydrocortisone	18 (12)
Presumed sepsis, *n* (%)	73 (50)
Temperature <36 °C, *n* (%)	5 (3)

[a]Some infants received multiple medications.

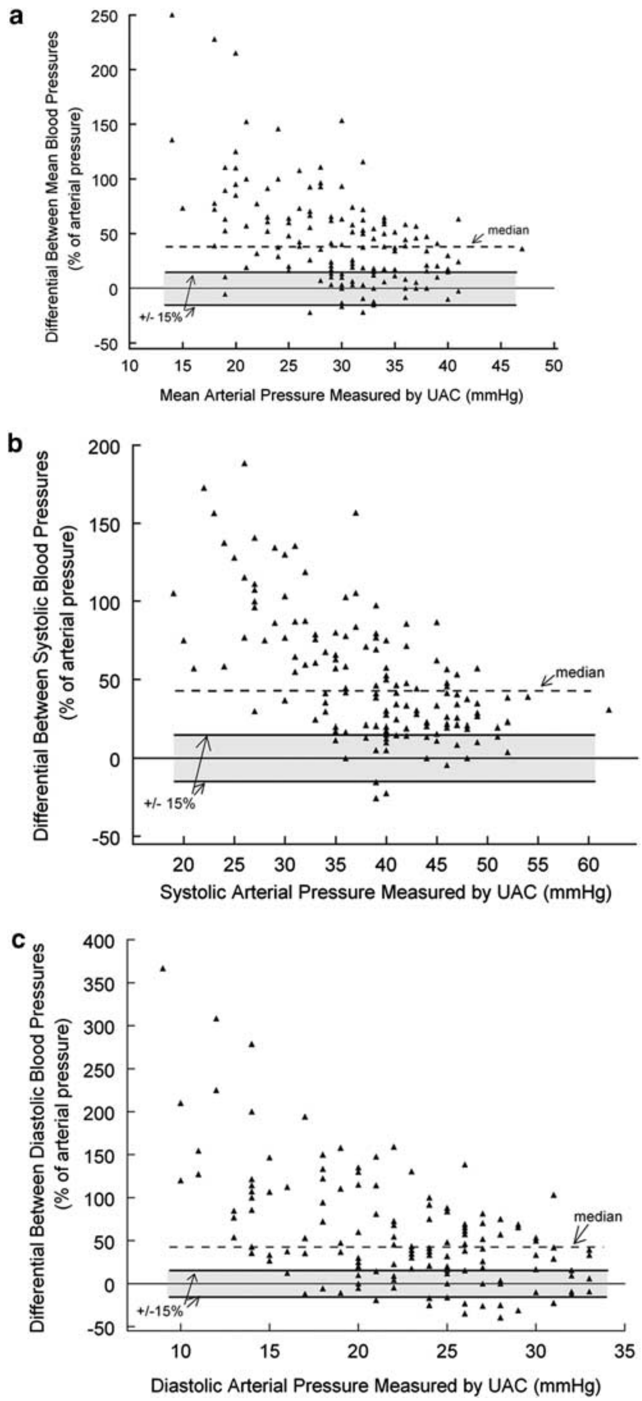

Figure 1 (**a**) Depicts the differential between noninvasive and umbilical arterial mean arterial blood pressure measurements. (**b**) The differential between noninvasive and umbilical arterial systolic blood pressure measurements is shown. (**c**) Shows the differential between noninvasive and umbilical arterial diastolic blood pressure measurements.

Comparison of NBP and central arterial blood pressure measurements

Noninvasive blood pressure and UAC systolic ($r = 0.26$, $r^2 = 0.07$), mean ($r = 0.19$, $r^2 = 0.04$) and diastolic ($r = 0.11$, $r^2 = 0.01$) blood pressure measurements were weakly correlated in this sample. The median absolute difference between NBP and UAC mean blood pressure measurements was +12 mm Hg (Bland–Altman LOA: −9.5, 34). The median NBP−UAC percentage differential obtained from mean blood pressure measurements was +39% (IQR (interquartile range): 13 to 64%) (Figure 1a).

Results were similar for systolic and diastolic measurements, with a median absolute difference of +18.5 mm Hg (LOA: −5.8, 42.8) and +10 mm Hg (LOA: −11.5, 33.5), respectively. The median systolic percentage differential was +43% (IQR: 21 to 77%), and the median diastolic percentage differential was +41% (IQR: 14 to 92%) (Figures 1b and c). The mean, systolic and diastolic differentials were larger at lower blood pressures ($P < 0.001$).

Overall 75% (110/146) of NBP measurements of mean blood pressure were clinically unacceptable. In all, 87% (127/146) of systolic and 82% (120/146) of diastolic NBP measurements were clinically unacceptable.

Patient demographic factors

In multivariate regression analysis, lower birth weight was associated with discrepant systolic, but not with mean or diastolic NBP and UAC measurements, although the coefficient of determination was low ($r = 0.34$, $r^2 = 0.12$, $P < 0.04$). Gestational age, sex and race were not associated with discrepant NBP and UAC measurements for any blood pressure parameter.

Measurement characteristics
Given that each blood pressure measurement had uniquely associated clinical parameters, further analysis was conducted to determine whether any measurement characteristics could predict a difference between NBP and UAC measurements. We first determined that there were no significant intra-patient correlations between measured arterial pressure and the difference between NBP and arterial pressure (data not shown), suggesting that these measurements behave in an independent manner.

In both the two-step procedure and bootstrap regression analyses, smaller cuff size, low temperature and the absence of presumed sepsis were associated with discrepant NBP and UAC mean blood pressure measurements (Table 2). Discrepant systolic measurements were associated with smaller cuff size, higher heart rate, later time of day and non-receipt of hydrocortisone. Discrepant diastolic measurements were associated with low temperature and non-receipt of hydrocortisone (two-step procedure and bootstrap method), as well as smaller cuff size, higher heart rate and lack of dopamine use (bootstrap method only). The coefficient of determination was <0.3 in all analyses. Respiratory factors were not significantly associated with discrepant NBP and UAC measurements.

Table 2 Measurement characteristics associated with discrepant noninvasive and central arterial measurements by stepwise linear regression

Mean blood pressure ($r^2=0.20$)	Small cuff size[a,b]
	Temperature <36 °C[a,b]
	Absence of presumed sepsis[a,b]
Systolic blood pressure ($r^2=0.29$)	Small cuff size[a,b]
	High heart rate[a,b]
	Later time of day[a,b]
	No hydrocortisone use[a,b]
Diastolic blood pressure ($r^2=0.27$)	Small cuff size[b]
	Temperature <36 °C[a,b]
	High heart rate[b]
	No hydrocortisone use[a,b]
	No dopamine use[b]

[a]Two-step method of variable selection.
[b]Bootstrap method of variable selection.

Risk factors for clinically unacceptable NBP measurement
A higher heart rate was a risk factor for clinically unacceptable systolic and mean NBP measurements (Table 3). Each 10-b.p.m. (beats per minute) increase in the heart rate was associated with a 1.6- and 1.5-fold increase in the risk of clinically unacceptable systolic and mean NBP measurements, respectively. Treatment with hydrocortisone was independently associated with a lower risk of clinically unacceptable mean and diastolic NBP measurements (odds ratio: 0.3; confidence interval: 0.10,0.93 and odds ratio: 0.16; confidence interval: 0.04,0.65, respectively). After adjusting for birth weight and arterial pressure, only treatment with hydrocortisone remained significantly associated with a lower risk of clinically unacceptable diastolic NBP measurements. (odds ratio: 0.32; confidence interval: 0.10,0.98, $P<0.05$).

Discussion

We studied a cohort of ELBW infants in the first 72 h after birth and found that NBP measurements frequently overestimated

Table 3 Multiple logistic regression analysis of risk factors for clinically unacceptable (>15% differential) noninvasive blood pressure

Measurement characteristic	*Model 1*[a]			*Model 2*[b]		
	Odds ratio	*95% CI*	P-*value*	*Odds ratio*	*95% CI*	P-*value*
Clinically unacceptable systolic NBP[c]						
Age at measurement, h[d]	0.87	0.75–1.00	0.055	0.91	0.77–1.07	0.3
Heart rate, b.p.m.[e]	1.64	1.06–2.53	<0.02	1.54	0.98–2.44	0.06
Hydrocortisone	0.27	0.07–1.02	0.053	0.27	0.07–1.03	0.07
Clinically unacceptable mean NBP[c]						
Heart rate, b.p.m.[e]	1.51	1.06–2.15	<0.02	1.29	0.92–1.82	0.15
Hydrocortisone	0.30	0.10–0.93	<0.04	0.38	0.12–1.15	0.09
Clinically unacceptable diastolic NBP[c]						
Hydrocortisone	0.16	0.04–0.65	<0.01	0.32	0.10–0.98	<0.05

b.p.m., beats per minute; CI, confidence interval; NBP, noninvasive blood pressure; UAC, umbilical arterial catheter.
[a]Backwards stepwise logistic regression using significant risk factors.
[b]Backwards logistic regression using significant risk factors and adjusting for birth weight and arterial pressure.
[c]NBP–UAC differential of >15%.
[d]Advancing age, analyzed in 6-h increments.
[e]Increasing heart rate, analyzed in 10-b.p.m. increments.

systolic, mean and diastolic blood pressures compared with UAC measurements. We also found that a majority of NBP measurements met our *a priori* definition of a clinically unacceptable measurement (defined as a differential of more than 15%). Although NBP monitoring has advantages, such as ease of access, less frequent handling of sick infants and avoidance of central lines, we found that NBP and UAC measurements were not comparable in the ELBW population.

Although NBP and arterial blood pressure measurements in term infants have been shown to be comparable,[2–4] the correlation between NBP and arterial measurements in preterm infants has been unclear. Previous studies included both term and a mixed population of small and large preterm infants.[6–8,12] In these studies, NBP measurements generally correlated with arterial measurements, with the correlation coefficients for mean blood pressure ranging from 0.67 to 0.92. In a cohort of 12 very-low-birth-weight infants, NBP measurements overestimated blood pressure, especially at the lower end of the blood pressure range. In our ELBW population, the discrepancy in measurement was most pronounced at lower blood pressure levels.

With the exception of birth weight, no patient demographic factor was associated with discrepant NBP and arterial measurements. A previous study of term and preterm infants showed that the measurement discrepancy between NBP and arterial measurements may be related to infant size, with smaller infants having a larger measurement discrepancy.[9] We found that a lower birth weight was associated with a larger differential in systolic NBP and UAC measurements, but we did not find this association in mean or diastolic blood pressure measurements. Systolic blood pressure may be more strongly influenced by birth weight, or the lack of association between mean and diastolic differentials and low birth weight may be caused by the fact that our cohort was limited to small infants, in which NBP measurements were inaccurate across the entire birth weight range.

We found that a variety of mechanical and physiological factors were associated with NBP and UAC measurement discrepancies, including smaller cuff size, low temperature and hydrocortisone use. A proper cuff size is essential for the accurate measurement of NBP. In previous studies, it has been observed that smaller cuff size has been associated with NBP and UAC measurement discrepancies for all blood pressure parameters.[8,11] Although we found a similar association, the overall predictive value of cuff size, even when combined with other variables, was low ($r^2 < 0.3$). Cuff location was not associated with NBP and UAC measurement discrepancies, with a large majority of NBP measurements obtained from the lower limbs. When we attempted to identify physiological factors associated with clinically unacceptable NBP measurements (measured as a differential of more than 15%), we found only one statistically significant relationship. After adjusting the model for arterial pressure and birth weight, non-receipt of hydrocortisone remained associated with a clinically unacceptable diastolic measurement.

In newly born preterm infants, blood pressure changes over time, gradually increasing over the first 24 h after birth.[17] Thus, comparisons between NBP and UAC measurements require blood pressure readings be recorded at, or nearly at, the same time. We believed that readings documented within 5 min of each other were nearly simultaneous, although minor variations in blood pressure could have occurred within that time period. We excluded any measurement that had a documented association with an error in the invasive or noninvasive monitor system. However, because we examined this cohort retrospectively, we cannot be certain that all sources of error (that is, air bubbles in the arterial line or incorrect application of the blood pressure cuff) were excluded. Finally, the study compares NBP and arterial measurements from a Spacelab monitor system; therefore, these results may not be applicable to other monitor systems.

Noninvasive blood pressure measurements are not comparable with central arterial blood pressure measurements in the ELBW population. We did not find other factors that were associated with clinically unacceptable NBP measurements. No manner of adjustment provided a ‘correction factor’ to render the NBP measurements accurate. These findings have important clinical implications, as blood pressure is a widely used clinical marker of cardiovascular stability and often guides medical therapy.

Conflict of interest

The authors declare no conflict of interest.

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