Accuracy of Indirect Measurement of Blood Pressure in Neonatal Foals

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The objectives of this study were to assess, in anesthetized neonatal foals, the accuracy of 2 automated indirect oscillometric monitors for measurement of mean arterial pressure (MAP), to determine the optimal site of cuff placement for MAP monitoring, and to determine the relationship between arterial blood pressure and cardiac output. Ten neonatal foals were anesthetized and instrumented with a catheter in the metatarsal artery for direct MAP monitoring and measurement of cardiac output by lithium dilution. Concurrent MAP measurements were obtained with Cardell and Dinamap oscillometric monitors with cuffs placed at 3 different sites (coccygeal, metatarsal, and median arteries). Blood pressure was manipulated by varying the depth of anesthesia and by administration of dobutamine or phenylephrine. A statistically significant (P = .025) interaction was found between the type of monitor and cuff placement site. With the Cardell monitor, placement of the cuff over the coccygeal artery resulted in a significantly lower bias than placement over the median or dorsal metatarsal artery (P < .0001 and P = .0149, respectively). No significant difference in bias was found with cuff placement site when using the Dinamap monitor. The correlation coefficient (r) between MAP and cardiac output was 0.47. Indirect oscillometry with a cuff placed over the coccygeal artery or dorsal metatarsal artery is an acceptable method for measuring MAP in foals. Blood pressure does not correlate well with cardiac output in anesthetized foals.

Key words: Cardell; Cardiac output; Dinamap; Lithium dilution; Monitoring.

Bacterial sepsis and hypoxic-ischemic encephalopathy are the leading causes of morbidity and mortality in neonatal foals. Foals affected with these diseases commonly have a compromised cardiovascular system and require intensive monitoring. Arterial blood pressure monitoring is routine practice in equine neonatal intensive care units, allowing recognition of some cardiovascular derangements and titration of therapy with IV fluids, vasopressors, and inotropic agents.

Arterial blood pressure can be measured by direct and indirect methods. Direct monitoring via cannulation of a peripheral artery is accurate and provides a continuous display of blood pressure results. However, the difficulty in maintaining an arterial catheter in nonanesthetized foals makes direct blood pressure measurement less practical for routine monitoring. Indirect approaches of measuring blood pressure include auscultatory, Doppler, and oscillometric methods. Oscillometric techniques offer the advantage of providing systolic, diastolic, and mean arterial pressures, whereas other indirect methods do not provide mean arterial pressure (MAP). Several automated oscillometric blood pressure devices are currently available for use in human or veterinary medicine. Studies in people and small animals have underscored considerable differences in accuracies between various monitors. In 1 report, indirect oscillometry with a cuff placed over the coccygeal artery was found to be an acceptable method for measuring MAP in both anesthetized and conscious neonatal foals. Other sites of cuff placement that have been recommended for indirect blood pressure measurement in foals include the dorsal metatarsal or median arteries. However, the effects of the type of monitor and site of cuff placement on the accuracy of indirect oscillometric blood pressure measurements have never been critically investigated in neonatal foals.

Blood flow and blood pressure are distinct physical entities. Global blood flow (ie, cardiac output) rather than blood pressure is a critical determinant of tissue perfusion and its measurement is required for calculation of global oxygen delivery and consumption. Because measurement of cardiac output is currently considered impractical for routine use in foals, arterial blood pressure is commonly used as an indication for potential blood flow. MAP is the product of cardiac output and systemic vascular resistance. Thus, when systemic vascular resistance is altered, the arterial pressure may not be a reliable index of arterial flow. To the authors’ knowledge, the strength of the relationship between cardiac output and arterial pressure has never been established in anesthetized neonatal foals.

The objectives of this study were to assess and compare the accuracies of 2 automated indirect oscillometric monitors commonly used for measurement of MAP in foals, to determine the optimal site of cuff placement for each monitor, and to determine the relationship between arterial blood pressure and cardiac output in healthy anesthetized foals.

Materials and Methods

Animals

Six female and 4 male Thoroughbred or Thoroughbred-cross foals, 2–6 days old and weighing 32.5–61.0 kg, were used in this study. All foals were delivered uneventfully at term. The foals were considered healthy based on complete physical examination and echocardiography. Transfer of passive immunity was confirmed before initiation of the study by measurement of plasma immunoglobulin G concentration with a commercial immunoassay. The study was approved by the University of Florida Institutional Animal Care and Use Committee.

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Anesthesia and Instrumentation

Foals were sedated by IV injection of xylazine\textsuperscript{e} (1.0 mg/kg) before placement of a 16-gauge, 2-inch catheter in the right jugular vein. Anesthesia was induced by IV administration of ketamine\textsuperscript{e} (2.0 mg/kg). Foals were placed in left lateral recumbency and an orotracheal tube was placed. Thereafter, anesthesia was maintained with isoflurane in oxygen by using a rebreathing circuit system with an oxygen flow of 2–3 L/min. End-tidal isoflurane concentration was monitored by using an infrared gas analyzer\textsuperscript{e} calibrated before each experiment with a standardized calibration gas mixture\textsuperscript{e} designed for the analyzer. Heart rate was monitored from an ECG and rectal temperature was monitored throughout the study. Mechanical ventilation was used at a rate of 8–10 breaths/min and a tidal volume of 10–15 mL/kg adjusted to maintain the end-tidal CO\textsubscript{2} concentration between 40 and 50 mm Hg. Plasma lactate 148\textsuperscript{a} with 5% dextrose was administered intravenously at a rate of 5 mL/kg/h during anesthesia to prevent hypoglycemia and maintain volemia.

Direct Blood Pressure Measurement

A 20-gauge, 1.88-inch catheter was placed in the right dorsal metatarsal artery. An electronic pressure transducer\textsuperscript{e} was positioned and zeroed at the level of the sternal manubrium and systolic, diastolic, and mean arterial pressures as well as heart rate were monitored continuously and displayed on a monitor.\textsuperscript{d} The monitor was calibrated by using a mercury manometer before initiation of the experiments.

Indirect Blood Pressure Measurement

Systolic, diastolic, and mean indirect arterial pressures were obtained with Cardell\textsuperscript{d} and Dinamap\textsuperscript{d} oscillometric monitors. For each monitor, indirect blood pressure was obtained from cuffs placed at the base of the tail (middle coccyeal artery), at the proximal aspect of the left metatarsus (dorsal metatarsal artery), and around the right forearm, midway between the carpus and the elbow (median artery). The circumference of each appendage was measured to determine the correct size cuff to be used according to the manufacturer’s instructions. The cuffs were repositioned as needed to acquire data acceptable to the internal sensor of the monitor. Because the foals were in lateral recumbency on a soft mattress, cuffs were approximately at the level of the sternal manubrium.

Cardiac Output Measurement

A LiDCO lithium dilution cardiac computer was used to determine cardiac output according to the manufacturer’s instructions. Lithium dilution cardiac output has previously been shown to compare closely to thermodilution cardiac output in anesthetized foals.\textsuperscript{10} The hemoglobin concentration and sodium concentration required for cardiac output measurement were determined immediately before obtaining cardiac output measurement with a blood gas analyzer.\textsuperscript{e} The sensor for the lithium chloride measurements was attached to the side port of a 3-way valve connected to the arterial catheter. Extension tubing attached the sensor to a blood collection bag and blood passed through a peristaltic pump that produced a blood flow of 4 mL/min across the sensor. The dose attached of lithium chloride\textsuperscript{d} (0.16–0.28 mmol) was parked into an extension set attached to the jugular vein catheter and flushed with 8 mL of saline 8 seconds after starting the LiDCO computer.

Experimental Design

For collection of the 2nd set of data, depth of anesthesia was decreased to 0.9–1.4% end-tidal isoflurane concentration and therapy with dobutamine\textsuperscript{e} (1–3 \(\mu\)g/min) was initiated. The 3rd set of data was obtained by further decreasing depth of anesthesia to 0.8–1.0% end-tidal isoflurane concentration and increasing the rate of dobutamine (3–6 \(\mu\)g/min). In 4 foals, a 4th set of data was collected after the highest level of blood pressure during IV administration of intermittent boluses of phenylephrine\textsuperscript{e} (total cumulative dose of 1.1–1.7 mg) over a 5- to 10-minute period to further increase blood pressure and increase systemic vascular resistance. Direct blood pressure was measured and displayed continuously. For each monitor, indirect blood pressure was measured twice from each site at each level of blood pressure by using a randomization scheme for both monitors and sites. The concurrent direct arterial pressure was recorded each time an indirect measurement was obtained. Cardiac output was measured at least twice at each level of blood pressure, allowing at least 3 minutes between measurements. Concurrent heart rate and end-tidal isoflurane concentration as well as systolic, diastolic, and mean direct arterial blood pressure obtained immediately after cardiac output measurement were recorded. Cardiac index was obtained by dividing cardiac output by body weight. Systemic vascular resistance was calculated as direct MAP/cardiac output. At least 6 pairs of indirect-direct blood pressure or direct blood pressure–cardiac output readings were obtained from each foal. Total duration of anesthesia ranged between 75 and 90 minutes.

Statistical Analysis

For each monitor and site of cuff placement, agreement between indirect and direct MAP measurement was determined by using the method for repeated measurements reported by Bland and Altman.\textsuperscript{11} The bias was calculated as the mean difference between direct and indirect MAPs. A positive bias reflected underestimation of direct MAP by a given oscillometric monitor, whereas a negative value indicated overestimation of direct MAP. The limits of agreement were reported as bias ± (1.96 \times \text{ standard deviation [SD]} of the bias). A mixed-model analysis of a split-unit experiment with repeated observations was conducted to compare the bias for MAP < 65 mm Hg to that for MAP > 65 mm Hg. Foal was the blocking factor. MAP and type of monitor (Dinamap or Cardell) in a 2 × 3 factorial arrangement were the main unit treatments. Site of placement (coccyeal, dorsal metatarsal, or median artery) was the subunit treatment. Repeated observations were taken for each MAP monitor, and site combination.

A mixed-model analysis of a split-unit experiment with repeated observations was conducted to assess the effect of type of monitor (Dinamap or Cardell) and site of cuff placement (coccyeal, dorsal metatarsal, or median artery) on the absolute value of the bias. Foal was the blocking factor. Blood pressure and type of monitor (Dinamap or Cardell) in a 4 × 3 factorial arrangement were the main unit treatments. Site of placement (coccyeal, dorsal metatarsal, or median artery) was the subunit treatment. Repeated observations were taken for each blood pressure, monitor, and site combination. In preliminary analysis, the effect of cuff bladder diameter to tail or limb circumference ratio was not significant and was therefore removed from the final model. For effects found to be significant by an overall F-test, pairwise comparisons were made by using Fisher’s protected least significant difference.

Calculation of coefficients of correlation for repeated measurements was used to examine the linear relationship between cardiac index and heart rate, end-tidal isoflurane concentration, systolic blood pressure, diastolic blood pressure, MAP, and systemic vascular resistance. To estimate the correlation of A and B, the variances of A and B and the covariance between A and B were estimated based on the following model:

\[
\text{response} = \text{foal} + \text{treatment} + \text{foal} \times \text{treatment} + \text{error}
\]

Tests of significance used a t-test, and tests for equality were con-
Table 1. Summary statistics of the differences between direct mean arterial pressure and indirect mean arterial pressure (mm Hg) obtained with 2 monitors at 3 sites of cuff placement.

<table>
<thead>
<tr>
<th>Monitor</th>
<th>Site (n)</th>
<th>Mean Bias (± SD)</th>
<th>Least-Squares Limits of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dinamap</td>
<td>Coccygeal (62)</td>
<td>4.5 ± 8.8</td>
<td>−12.7 to 21.2</td>
</tr>
<tr>
<td></td>
<td>Median (54)</td>
<td>−5.3 ± 9.0</td>
<td>−22.9 to 12.3</td>
</tr>
<tr>
<td></td>
<td>Metatarsal (60)</td>
<td>−1.4 ± 8.8</td>
<td>−18.6 to 15.8</td>
</tr>
<tr>
<td>Cardell</td>
<td>Coccygeal (62)</td>
<td>−0.5 ± 8.8</td>
<td>−17.7 to 16.7</td>
</tr>
<tr>
<td></td>
<td>Median (62)</td>
<td>−10.8 ± 8.8</td>
<td>−28.0 to 6.4</td>
</tr>
<tr>
<td></td>
<td>Metatarsal (62)</td>
<td>−4.1 ± 8.8</td>
<td>−21.3 to 13.1</td>
</tr>
</tbody>
</table>

[]Different letters between sites within a given monitor indicate a statistically significant difference in the absolute value of the bias (P ≤ .01). Different numbers between monitors within a given site indicate a statistically significant difference in the absolute value of the bias (P ≤ .0010).

Conducted by using a large sample normal test on the values that have undergone the same transformation. All analyses were done with a statistical software. Statistical significance was set at P < .05.

**Results**

Sixty-two pairs of direct or indirect MAP readings for each monitor at each cuff placement site were taken from the 10 foals. Direct MAP ranged between 23 and 95 mm Hg (mean ± SD: 52.0 ± 15.6 mm Hg). Direct systolic blood pressure ranged between 33 and 145 mm Hg (mean ± SD: 85.7 ± 27.2 mm Hg), and direct diastolic pressure ranged between 17 and 75 mm Hg (mean ± SD: 39.5 ± 11.8 mm Hg). The Cardell monitor displayed blood pressure results for all attempts. With the Dinamap monitor, results could not be obtained despite repeated attempts for 8 (13%) of 62 measurements when the cuff was placed over the median artery and for 2 (3%) of 62 measurements when the cuff was placed over the metatarsal artery. No significant 3-way interaction was found among the type of indirect oscillometric monitor, cuff placement site, and blood pressure. Also, no significant 2-way interaction was found between the blood pressure and cuff placement site and between the blood pressure and the type of monitor. The overall effect of the blood pressure was not significant.

The analysis revealed a statistically significant (P = .025) interaction between type of monitor and cuff placement site. The mean bias and limits of agreement for each monitor at each site of cuff placement are presented in Table 1. With the Cardell monitor, placement of the cuff over the coccygeal artery resulted in a significantly lower bias than placement over the median or dorsal metatarsal artery (P < .0001 and P = .0149, respectively). Placement over the dorsal metatarsal artery resulted in a significantly lower bias than placement over the median artery (P = .0035). No significant difference in bias was found with cuff placement site when using the Dinamap monitor. Cuff placement over the median artery resulted in a significantly lower bias with the Dinamap monitor than with the Cardell monitor (P = .0007). No difference in bias was found between Dinamap and Cardell monitors when the cuff was placed over the metatarsal artery (P = .8448) or over the coccygeal artery (P = .1683). Cuff bladder width to tail or limb circumference ratios ranged between 0.36 and 0.9 (mean ± SD: 0.52 ± 0.13). No correlation was found between cuff bladder width to appendage circumference ratio and mean bias (r = −0.22, P = .13). Similarly, no significant additional effect of cuff bladder width to circumference ratio on mean bias was found after allowing for the effect of cuff placement site (P = .42).

Eighty-two pairs of cardiac output–direct blood pressure measurements were available to evaluate the strength of the relationship between cardiac index and direct arterial pressure. Cardiac output ranged between 3.1 and 14.5 L/min (mean ± SD: 6.4 ± 2.2 L/min), resulting in cardiac indices ranging between 67.7 and 236 mL/kg/min (mean ± SD: 129.6 ± 39.2 mL/kg/min). At constant end-tidal isoflurane concentration, systemic vascular resistance was significantly (P < .0001) higher in foals given phenylephrine (867 ± 49 dynes/cm²) than in the same foals during administration of dobutamine (418 ± 36 dynes/cm²). The correlation between cardiac index and MAP was significantly (P = .025) higher when data collected during phenylephrine administration were excluded (r = .77), compared to that obtained using the complete data set (r = .47; Fig 1). The coefficient of correlation between cardiac index and MAP when no vasopressor or inotropic agents were administered (r = 0.74) was not significantly different from that obtained when data collected during administration of dobutamine were included (P = .783). A slight but statistically significant correlation was found between cardiac index and heart rate, systolic arterial pressure, diastolic arterial pressure, and MAP (Table 2). A negative correlation was found between cardiac index and end-tidal isoflurane concentration and systemic vascular resistance (Table 2).
The present study did not identify statistically significant differences in the performance of the Dinamap and Cardell monitors when data collected from all 3 sites were considered. However, a significant interaction was found between type of monitor and site of cuff placement. With the Cardell monitor, cuff placement over the coccygeal artery resulted in a significantly lower bias than cuff placement over the median and metatarsal artery (Table 1). Although statistically significant, the small difference in mean bias between the coccygeal and metatarsal MAP readings (3.6 mm Hg) is unlikely to be clinically relevant. However, that between the coccygeal and median artery (10.3 mm Hg) could lead to misinterpretation of the patient’s status. The American Association for the Advancement of Medical Instrumentation has recommended a mean difference between the gold standard and a test device of ±5 mm Hg or less, with a standard deviation of 8 mm Hg or less, as acceptable in humans.20 Thus, from a clinical perspective and by standards used in human medicine, both Cardell and Dinamap monitors with cuffs placed over either the coccygeal or dorsal metatarsal arteries would be acceptable for MAP measurement in foals. The present study was conducted in anesthetized foals, eliminating potential inaccuracies due to movement artifacts. However, most critically ill equine neonates for which blood pressure monitoring is likely to affect therapeutic management are recumbent and severely obtunded. In a recent study, the mean bias of indirect MAP measurement was not significantly different between awake foals manually restrained in lateral recumbency and anesthetized foals.6

The mean bias and limits of agreements obtained with the Cardell (−0.5; −17.7 to 16.7 mm Hg) and Dinamap (4.5; −12.7 to 21.2 mm Hg) monitors when using cuffs over the coccygeal artery in the present study were similar to that obtained in a recent study evaluating another oscillometric monitor in neonatal foals (−1.1; −9.4 to 7.2 mm Hg).5 In both studies, the oscillometric methods of indirectly measuring blood pressure in neonatal foals agreed more closely with direct measurements than has been reported in adult horses.21,22 In another study involving 1- to 2-month-old foals, cuff placement over the median artery resulted in MAP consistently lower than that obtained by direct measurement.21 In contrast, cuff placement over the median artery in the present study resulted in overestimation of MAP with both Cardell and Dinamap monitors. Likely reasons for inconsistencies between studies include type of oscillometric monitors used as well as site of cuff placement. In addition, the thinner layer of soft tissue surrounding peripheral arteries may allow for more accurate measurements in neonatal foals than in older foals or adult horses. Several studies in humans and small animals have shown that type of oscillometric devices and cuff placement sites affect indirect blood pressure readings.5,24

Another factor reported to affect indirect blood pressure measurements is cuff width to appendage circumference ratio. Cuffs with bladder widths that are too wide result in falsely low indirect blood pressure readings, whereas cuffs with bladders that are too small relative to appendage circumference result in falsely high readings.2 In mature Thoroughbred horses, bladder width to tail girth circumference ratios of 0.34 for systolic pressure and 0.98 for diastolic

Table 2. Correlation between cardiac index measured by lithium dilution and direct mean arterial pressure, direct systolic arterial pressure, direct diastolic arterial pressure, heart rate, end-tidal isoflurane concentration, or systemic vascular resistance.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>0.64 (0.49 to 0.75)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Systolic arterial pressure</td>
<td>0.68 (0.54 to 0.78)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Diastolic arterial pressure</td>
<td>0.37 (−0.17 to 0.55)</td>
<td>.0006</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>0.47 (0.28 to 0.63)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>End-tidal isoflurane concentration</td>
<td>−0.75 (−0.83 to −0.64)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>−0.48 (−0.63 to −0.30)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*Lower and upper 95% confidence limits.*
pressure were found to be optimal for indirect blood pressure measurement when using a Doppler ultrasound technique.\textsuperscript{14} The ideal cuff bladder width to appendage circumference ratio in neonatal foals is unknown. In 1 study, no correlation was found between ratios and bias at ratios ranging between 0.36 and 0.52.\textsuperscript{6} Despite a wider range in cuff bladder to circumference ratios (0.36–0.90), the present study failed to identify a significant correlation between ratio and mean bias.

A minimum MAP of approximately 60–65 mm Hg is vital to adequate cerebral, renal, and coronary blood flow.\textsuperscript{2,12} Increasing the MAP to 75 or 85 mm Hg does not provide additional advantages on systemic oxygen metabolism, skin microcirculatory blood flow, urine output, and splanchnic perfusion compared with 65 mm Hg.\textsuperscript{25} As a result, cardiovascular support with vasopressor drugs in foals is typically initiated when MAP readings fall below this critical level of 60–65 mm Hg.\textsuperscript{1,2}\textsuperscript{12} Therefore, low MAP readings are more likely to have repercussions on patient management than high MAP values. Fortunately, both indirect oscillometric monitors evaluated in the present study performed as well at MAPs < 65 mm Hg as at higher MAPs.

An additional objective of the present study was to evaluate the strength of the relationship between blood pressure and cardiac output in anesthetized newborn foals. A moderate correlation ($r = 0.77$) was found between MAP and cardiac index when data collected during administration of phenylephrine were excluded. Administration of phenylephrine significantly decreased the correlation between MAP and cardiac output. Phenylephrine, an $\alpha$-agonist with no $\beta$-adrenergic activity, decreases cardiac output and increases blood pressure and systemic vascular resistance in neonatal foals and adult horses.\textsuperscript{12,26} Our findings in foals support data in other species showing that arterial pressure is a poor indicator of blood flow when vascular resistance is altered.\textsuperscript{13,15} Systemic vascular resistance is often altered during sepsis.\textsuperscript{12} Studies in children illustrate the advantages of cardiac output measurement during hemodynamic support.\textsuperscript{5,27,28} These findings in humans, combined with the poor correlation between blood pressure and cardiac output obtained in the present study, suggest that cardiac output monitoring may be a valuable monitoring tool in anesthetized and critically ill equine neonates.

In conclusion, the Cardell or Dinamap monitors with cuffs placed over the coccygeal or dorsal metatarsal artery would be acceptable for MAP measurement in foals. Measurement of blood pressure does not correlate well with cardiac output in anesthetized foals, especially when vascular resistance is increased.

### Footnotes

\textsuperscript{a} DVM Stat, Corporation for Advanced Applications, Newburg, WI
\textsuperscript{b} Rompun, Bayer Co, Shawnee Mission, KS
\textsuperscript{c} Ketaset, Fort Dodge Animal Health, Overland Park, KS
\textsuperscript{d} S/5, DATEX-OHMEDA Division, Helsinki, Finland
\textsuperscript{e} DOT-34 NRC 300/375 M1014, DATEX-OHMEDA Division, Helsinki, Finland
\textsuperscript{f} Plasmalyte 148 with 5% dextrose, Baxter Healthcare Corporation, Deerfield, IL
\textsuperscript{g} Logical, Medex Inc, Carlsbad, CA
\textsuperscript{h} Cardell Veterinary Monitor 9402, CAS Medical Systems, Brandford, CT
\textsuperscript{i} Dinamap Pro 100, GE Medical Systems, Milwaukee, WI
\textsuperscript{j} LiDCO cardiac computer CM 31-01, LiDCO Limited, London, UK
\textsuperscript{k} GEM Premier 3000, Instrumentation Laboratory, Lexington, MA
\textsuperscript{l} Lithium chloride, LiDCO Limited, London, UK
\textsuperscript{m} Dobutamine, Bedford Laboratories, Bedford, OH
\textsuperscript{n} Phenylephrine, Baxter Healthcare Corporation, Irvine, CA
\textsuperscript{o} SAS 9.1, SAS Institute, Cary, NC

### Acknowledgment

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### References

18. Parry BW, McCarthy MA, Anderson GA, et al. Correct occlu-