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COMPARISON OF HIGH-DEFINITION OSCILLOMETRIC AND DIRECT ARTERIAL BLOOD PRESSURE MEASUREMENT IN ANESTHETIZED CHEETAHS (*ACINONYX JUBATUS*)

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?1 *Abstract:* Blood pressure measurement reveals important insights into the health of conscious and anesthetized individuals. This is of particular interest in cheetahs (*Acinonyx jubatus*), which in captivity are known to suffer from chronic diseases that may be associated with hypertension and which often require immobilization for transport or veterinary treatment. Invasive testing methods are considered the gold standard but are not practical in many settings. Consequently, it is important to evaluate the use of noninvasive methods in this species. Measurements for systolic, diastolic, and mean arterial pressure obtained using high-definition oscillometry (HDO) at the coccygeal artery were compared to simultaneous direct measurements obtained via catheterization of the femoral or dorsal pedal artery in eight anesthetized captive cheetahs during nine anesthetic events. Overall, HDO and direct measurements agreed most closely for mean arterial pressure, and the poorest agreement was observed for systolic pressure. There was a tendency for low diastolic pressures to be underestimated and for high diastolic pressures to be overestimated. Across all three parameters, HDO measurements from the tail overestimated directly measured pressures in the femoral artery and underestimated those in the dorsal pedal artery. HDO agreed most closely with directly measured dorsal pedal pressures. Mean arterial pressure showed the greatest precision (standard deviation of 10.2 mm Hg) and lowest bias (–1.2 mm Hg), with 75.9% of readings within 10 mm Hg of the direct dorsal pedal pressure. Agreement with systolic pressure was hindered by a high bias (–10.4 mm Hg), but if a correction factor of +10 mm Hg was applied to all systolic measurements, agreement was improved and 65.7% of readings were within 10 mm Hg of the direct pressure. When compared to criteria defined by the American College of Veterinary Internal Medicine for validation of blood pressure devices, results were favorable, but a limited sample size prevented formal validation.

Key words: *Acinonyx jubatus*, blood pressure, cheetah, felid, oscillometry.

INTRODUCTION

Under anesthesia, the monitoring of blood pressure is important, as it provides an indirect estimate of cardiac output and tissue perfusion.[11] Chemical immobilization is often necessary for the transport and veterinary care of both wild and captive cheetahs (*Acinonyx jubatus*). The various agents employed in immobilization can have profound effects on cardiovascular function,[33] and monitoring of blood pressure allows corrective action to be taken if severe hypo- or hypertension develops.

Cheetahs in captivity frequently suffer from chronic diseases, including glomerulosclerosis and renal amyloidosis,[6,22,23] which may be associated with systemic hypertension. Hypertension may occur as a consequence of renal disease, as commonly occurs in domestic cats, but it may also contribute toward progressive renal injury.[15] It has also been suggested that cheetahs in captivity suffer from chronic stress,[34] which may, as it does in humans, produce hypertension.[12,19] No physiologic range has been established against which to diagnose hypertension, and little is known about how hypertension may contribute toward, or be a consequence of, chronic disease in this species.

The gold standard method of blood pressure measurement is via the use of an intra-arterial catheter, linked to a transducer and monitor, which directly measures arterial pressure.[38] However, the technique is cumbersome and invasive and therefore impractical in many field or zoo situations. As a result, indirect methods are often used, commonly Doppler ultrasound or oscillometric techniques.

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High-definition oscillometry (HDO) is a recent innovation that offers many potential advantages over Doppler and conventional oscillometry. HDO is fully automated after application of the cuff, requiring no particular training or expertise. It therefore should not suffer from interobserver variations, which can be a problem associated with the use of Doppler,[9] or from errors associated with inexperience, which are considered to be a leading cause of inaccurate readings.[8] Conventional oscillometry only estimates the mean arterial pressure (MAP) and then calculates the systolic and diastolic pressures using proprietary algorithms,[1] while Doppler is an insensitive tool for diastolic pressure measurement.[13] In contrast, HDO performs real-time analysis of arterial oscillations to obtain pulse amplitudes and an estimate of systolic, mean, and diastolic pressures.[29] The cuff deflates in a linear manner, unlike the step-wise deflation of conventional oscillometric devices, and readings can purportedly be obtained in as few as 10 sec, which has clear advantages, especially in conscious animals. Additionally, the HDO device is small and portable, which is convenient for use in field situations, but can be connected to a computer for more detailed evaluation of the data.

HDO is untested in cheetahs, and previous studies[18,20,36,40] in other species have reported disparate results. Therefore, the aim of this study was to evaluate the agreement of the HDO device with the gold standard direct intra-arterial blood pressure measurement in order to validate it for use in this species,[8] the ultimate goal being to find an accurate device suitable for clinical use both in zoos and in the field, as well as for ongoing research into the diseases of cheetahs.

MATERIALS AND METHODS

Eight captive cheetahs (three males and five females) were recruited from animals requiring anesthesia for reasons unrelated to the study in July 2014 at the AfriCat Foundation, Otjiwarongo, Namibia. A total of nine anesthetic events resulted from one individual requiring two procedures. Animals were selected on the basis of estimated length of anesthesia and therefore greatest clinical benefit from invasive blood pressure monitoring. This study was approved by the Zoological Society of London Ethics Committee.

Food was withheld for 24 hr before immobilization, and cheetahs were contained in smaller management camps within their large enclosures. Immobilization was achieved by intramuscular (IM) remote injection (darting) using a Dan-Inject JM Special rifle (Dan-Inject ApS, Sellerup Skovvej 116, Borkop, DK7080, Denmark), with a combination of medetomidine (Medetomidine, Kyron Laboratories, Johannesburg, Gauteng Province, 2094, South Africa) and tiletamine-zolazepam (Zoletil, Virbac RSA [Pty] Ltd., Centurion, Gauteng Province, 0157, South Africa). The intended doses were based on body weights determined at the previous annual health check and modified if body condition had noticeably changed. The doses administered per cheetah were 1.2–1.6 mg medetomidine (equating to 0.033–0.046 mg/kg based on last known weights) and 35–50 mg tiletamine/zolazepam (equating to 0.97–1.45 mg/kg).

Animals were typically safe to handle 10 to 20 min after darting. Three individuals required an additional dose of 30–50 mg of ketamine administered by IM or intravenous injection to ensure adequate anesthesia. Once fully anesthetized, the cheetahs were transported to the AfriCat clinic (a drive of between 2 and 10 min), where they were weighed and intubated for maintenance of anesthesia with isoflurane (0.5–2%) and oxygen.

Procedures performed during anesthesia included blood and urine sampling, abdominal ultrasound, vaccination, laparoscopic sterilization, and dental procedures. Any animals undergoing surgery received morphine (0.2 mg/kg; Morphine Sulphate, Fresenius, Fresnius Kabi [Pty] Ltd., Halfway House, Gauteng Province, 1685, South Africa) and meloxicam (0.3 mg/kg; Metacam, Boehringer Ingelheim Vetmedica, Randburg, Gauteng Province, 2125, South Africa). Intravenous fluids (Sabax Ringer Lactate, Adcock Ingram Critical Care [Pty] Ltd., Midrand, Gauteng Province, 1865, South Africa) were administered at 10 ml/kg per hour via an 18-ga catheter (Jelco, Johnson & Johnson, Johannesburg, Gauteng Province, 1600, South Africa) into the cephalic vein.

In order to facilitate recording, an area overlying the coccygeal artery on the ventral surface of the tail base was clipped on each animal. The cuff supplied with the Vet HDO MD Equine (S+B medVET GmbH, Neuer Weg 4, Babenhausen, 64832, Germany) unit was fitted (by either ESC or AT) at the base of the tail, according to the manufacturer's instructions, such that a little finger could just fit underneath. The equine unit was used under advice from the manufacturers as a result of the need for a more powerful pump to repeatedly inflate the cuff to 300 mm Hg. The device was connected to a laptop via a USB cable

Figure 1. The Vet HDO MD Equine, which has a numerical display, is connected to a laptop that allows visualization of the pressure waveform.

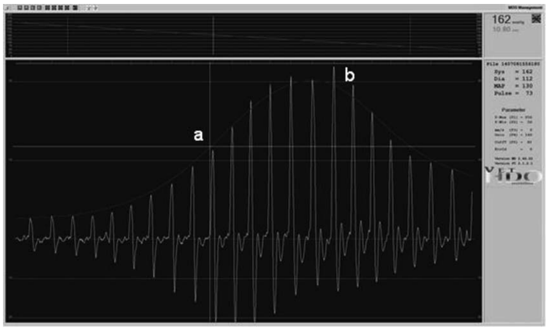

Figure 2. An example of an excellent trace, displaying linear deflation (upper section) and a complete bell-shaped curve devoid of strong movement artefacts in the key period (lower section). The key period is between systolic (**a**) and diastolic measurements (**b**).

to allow visualization of the waveform and easier control of the settings (Fig. 1).

Direct blood pressure measurement was achieved via aseptic placement of an intra-arterial catheter in either the femoral artery ($n = 4$; 22G Arrow SAC-00522, Teleflex Medical [Pty] Ltd., Sandton, Gauteng Province, 2191, South Africa) using the Seldinger technique or in the dorsal pedal artery ($n = 5$; 21G Jelco, Johnson & Johnson) following a standard technique described in the literature.[38] The catheter was connected via low-compliance tubing primed with heparinized saline to a pressure transducer located at the level of the right atrium (the level of the sternum in lateral recumbency or the level of the scapulohumeral joint in dorsal recumbency). The transducer was connected to a SurgiVet Advisor Vital Signs Monitor V9203 (Smiths Medical, Dublin, Ohio 43017, USA) and zeroed to atmospheric pressure. Facilities did not permit calibration or dynamic function testing. A bag of heparinized saline, pressurized to 300 mm Hg, enabled intermittent flushing of the catheter to maintain patency, remove air bubbles, and correct for overdamping.

The direct pressure system produced a continuous trace, whereas the HDO device utilizes a deflating cuff and typically took between 20 and 40 sec from inflation to generate a reading. Systolic (SYS), diastolic (DIA), and mean arterial (MAP) pressures were obtained from each device every 3 to 5 min. The HDO device was set on a loop function to facilitate this. For consistency, the instant the HDO device displayed a reading, the direct measurements were written down. All measurements were recorded by a single investigator, and blinding was considered unnecessary, as both devices produced readings without intervention from an operator.

No direct reading was recorded if the HDO device generated an error message. However, provided a reading was produced by the HDO unit, all readings were initially accepted and recorded.

At the end of the procedure, the animal was placed in a crate, extubated, and the medetomidine reversed with a combination of atipamezole (Antisedan, Novartis Animal Health, Johannesburg, Gauteng Province, 1600, South Africa) at 2.5 mg per 1 mg of medetomidine and yohimbine (Antagonil, Wildlife Pharmaceuticals [Pty] Ltd., White River, Mpumalanga, 1240, South Africa) at 3.125 mg per 1 mg of medetomidine, injected IM. Once fully recovered the cheetahs were released into their management camps and then into the wider enclosures.

Data analysis

The waveforms generated by the HDO device were analyzed post hoc to detect readings that may be unreliable, and these were then earmarked for rejection. Strict criteria were applied as advised by the manufacturers and while researchers were blinded to the direct measurements. Thus, an acceptable reading displayed linear cuff deflation and a complete bell-shaped curve devoid of strong movement artefacts in the key period (between systolic and diastolic measurements; Fig. 2), and the violation of any of these features resulted in the rejection of that whole reading (i.e., SYS, DIA, and MAP; Fig. 3).

The agreement between direct and indirect (HDO) blood pressure measurements for the SYS, DIA, and MAP readings was evaluated

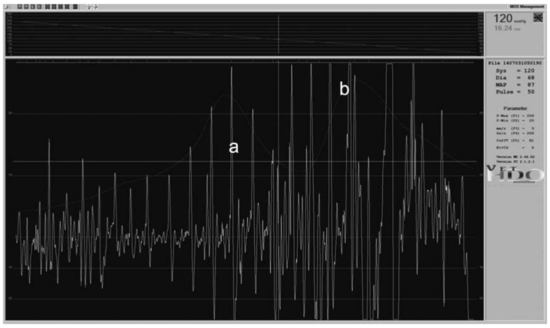

Figure 3. An example of an unacceptable reading, displaying strong movement artefacts in the key period, between systolic (**a**) and diastolic measurements (**b**), leading to the rejection of all parameters.

using Bland–Altman plots, in which the difference between two simultaneous readings (HDO minus direct, such that a positive number indicates an overestimate and a negative indicates an underestimate) was plotted against the mean of the two readings.[4,5]

Bias was assessed by calculation of the mean difference (HDO – direct) from the direct blood pressure reading. Precision was assessed by calculation of the SD of the differences, taking into account that multiple measurements of a changing quantity were taken from each individual.[5] Ninety-five percent limits of agreement (mean $\pm$ 1.96 SD) were also calculated.[5]

The percentages of HDO readings that fell within 5, 10, and 20 mm Hg of the direct pressure were calculated for each parameter.

Analysis was initially performed on the data set as a whole and again once rejected readings were removed. Subsequently the data set was divided according to the anatomic location of the intra-arterial catheter. One individual was anesthetized twice and data were collected on both occasions, but the intra-arterial catheters were placed in different arteries. Data analysis showed high variability between these two occasions, and they were therefore treated as two different animals.

Results were compared with the validation criteria outlined by the American College of Veterinary Internal Medicine (ACVIM), based on the those of the Association for the Advancement of Medical Instrumentation (AAMI).[2,8] The ACVIM criteria require that the mean difference of paired measurements for systolic and diastolic pressures treated separately is $\pm$10 mm Hg or less, with a SD of 15 mm Hg or less; the correlation between paired measures for systolic and diastolic pressures treated separately is $\geq$0.9 across the range of measured values of blood pressure; 50% of all measurements for systolic and diastolic pressures treated separately lie within 10 mm Hg of the reference method, and 80% lie within 20 mm Hg of the reference method.[8] While no provision is made for MAP, the same criteria were applied. Although correlation is not considered an appropriate measure of agreement,[4] it was included in the analysis to facilitate comparison with ACVIM criteria and other studies.

Analyses were performed using R, version 3.1.1.[25]

RESULTS

Cheetahs ranged in age from 4 to 13 yr (median, 7 yr), as determined on arrival at the center, typically as cubs, and weights ranged from 31.2 to 46.7 kg (median, 34.8 kg). Actual doses of medetomidine and tiletamine-zolazepam received by the cheetahs ranged from 0.034 to 0.046 mg/kg (median, 0.037 mg/kg) and 1.04 and 1.44 mg/kg (median, 1.07 mg/kg), respectively.

During the time of direct monitoring, error messages were generated on 13 occasions (7.5% of attempted HDO readings). A total of 160 simultaneous pairs of successful measurements (direct and HDO) were obtained for each blood pressure parameter (SYS, DIA, and MAP). Post hoc analysis of the HDO readings resulted in 12 sets (7.5%) being rejected. Ten were rejected as a result of the presence of artefact and two as a result of the selection of inappropriate settings that resulted in an incomplete curve. All other readings were considered acceptable. The rejected readings were not necessarily those which showed the greatest discrepancies, and their removal resulted in only slight revisions in bias (mean differences went from –3.5, –0.2, and 0.9 to –3.2, –0.04, and 1.1 for SYS, DIA, and MAP, respectively) and precision (SD of differences reduced from 18.4, 15.1, and 12.6 to 18.2, 14.6, and 12.4 for SYS, DIA, and MAP, respectively).

Direct pressures ranged from 91 to 243 mm Hg SYS, from 59 to 155 mm Hg DIA, and from 72 to 203 mm Hg MAP, representing the range over which the HDO device was tested. Average direct systolic pressures were measured at 141.2 and 170.1 mm Hg in the femoral and dorsal pedal arteries, yielding average pulse pressures of 45.0 and 62.8 mm Hg, respectively. In contrast, average systolic pressure as recorded by the HDO device at the tail base was 159.1 mm Hg, resulting in an average pulse pressure of 54.9 mm Hg.

Table 1. Agreement of systolic (SYS), diastolic (DIA), and mean arterial (MAP) blood pressures measured using high-definition oscillometry (HDO) with those measured directly, in either the femoral or dorsal pedal artery.

Statistical parameter	ACVIM criteria[a]	Overall, $n = 148$[b] SYS	Overall DIA	Overall MAP	Femoral, $n = 40$[b] SYS	Femoral DIA	Femoral MAP	Dorsal pedal, $n = 108$[b] SYS/+10[c]	Dorsal pedal DIA	Dorsal pedal MAP
Mean difference (mm Hg)	≤±10	**−3.2**[d]	**−0.04**	**1.1**	16.3	**4.6**	**7.4**	−10.4/**−0.4**	**−1.8**	**−1.2**
SD[a] of differences (mm Hg)	≤15	18.2	**14.6**	**12.4**	**11.7**	18.5	**14.8**	**13.8**	**13.4**	**11.1**
Correlation coefficient[e]	≥0.9	0.88	0.88	**0.92**	**0.93**	0.80	0.89	**0.93**	**0.91**	**0.95**
≤5 mm Hg (%)[f]		18.9	27.0	37.8	5.0	0	12.5	24.1/27.8	37.0	47.2
≤10 mm Hg (%)[f]	≥50	33.8	**55.4**	**66.9**	20.0	42.5	42.5	38.9/**65.7**	**60.2**	**75.9**
≤20 mm Hg (%)[f]	≥80	73.0	**89.9**	**95.3**	60.0	**82.5**	**92.5**	77.8/**96.3**	**92.6**	**96.3**
95% limits of agreement		−38.9 to 32.6	−28.7 to 28.6	−23.1 to 25.4	−6.6 to 39.1	−31.7 to 40.9	−21.7 to 36.5	−37.4 to 16.7/ −27.4 to 26.7	−28.1 to 24.5	−23.0 to 20.6

[a] ACVIM, American College of Veterinary Internal Medicine; SD, standard deviation.
[b] n = number of readings.
[c] Systolic pressure + correction factor of +10 mm Hg.
[d] Bold, results meet ACVIM criteria.
[e] All significant to $P < 0.001$.
[f] Percentage of HDO readings within 5, 10, and 20 mm Hg of the direct value.

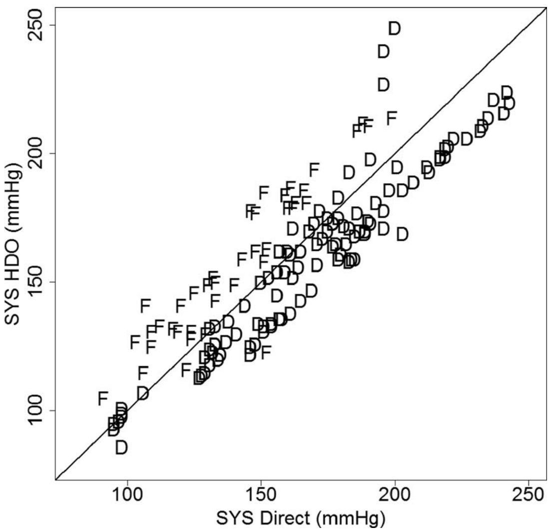

Figure 4. Plot of systolic blood pressure (SYS) as measured by high-definition oscillometry (HDO), against SYS measured directly, with a line of equality drawn. Each point corresponds to one measurement pair, with "F" and "D" denoting that the direct measurement was taken in the femoral or dorsal pedal artery, respectively.

Considering the data set as a whole (148 readings; Table 1), the mean differences for SYS, DIA, and MAP were all under ±5 mm Hg, with that for SYS being the highest. SDs indicate that the precision was poor for SYS but acceptable for DIA and MAP. Bland–Altman plots revealed a tendency for the DIA to be underestimated at low pressures and overestimated at high pressures, although similar patterns were not observed for the other parameters. MAP was the parameter most accurately measured by the HDO device, with all key statistics passing the ACVIM criteria. SYS was the poorest parameter, with only the mean difference (–3.2 mm Hg) being acceptable.

When blood pressure measured by the HDO device was plotted against that measured directly, distinct groupings emerged based on the anatomic location of the intra-arterial catheter (e.g., SYS in Fig. 4). With the data then divided into these two groups (femoral [40 readings] and dorsal pedal [108 readings]), significant differences were observed (Table 1; Figs. 5, 6), and a t-test comparing the means of the two groups confirmed this ($t = 12.3$, $P < 0.001$, with 79.6 degrees of freedom). The HDO device overestimated the direct pressures measured in the femoral artery and underestimated those measured in the dorsal pedal artery across all parameters, with the difference being most pronounced in the SYS

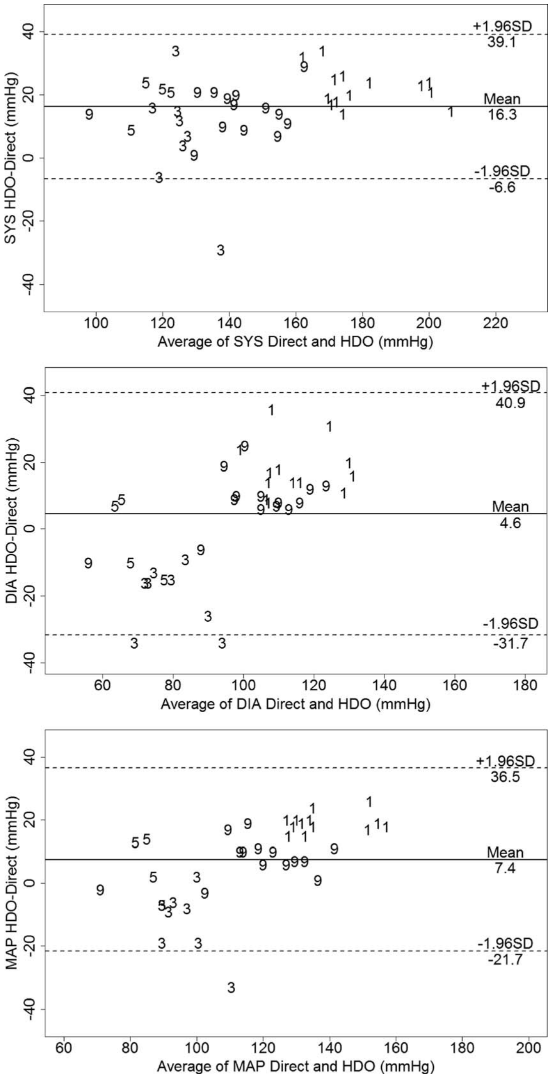

Figure 5. Bland–Altman plots showing agreement between systolic (SYS), diastolic (DIA), and mean arterial pressure (MAP) measured using high-definition oscillometry (HDO) with those measured directly in the femoral artery. Each point corresponds to one measurement pair, with the number denoting the individual cheetah from which the measurements were taken. The difference between the HDO and direct measurements is plotted against the mean of the HDO and direct measurement. Horizontal lines indicate the mean difference (bias; solid line) and 95% limits of agreement (dashed line).

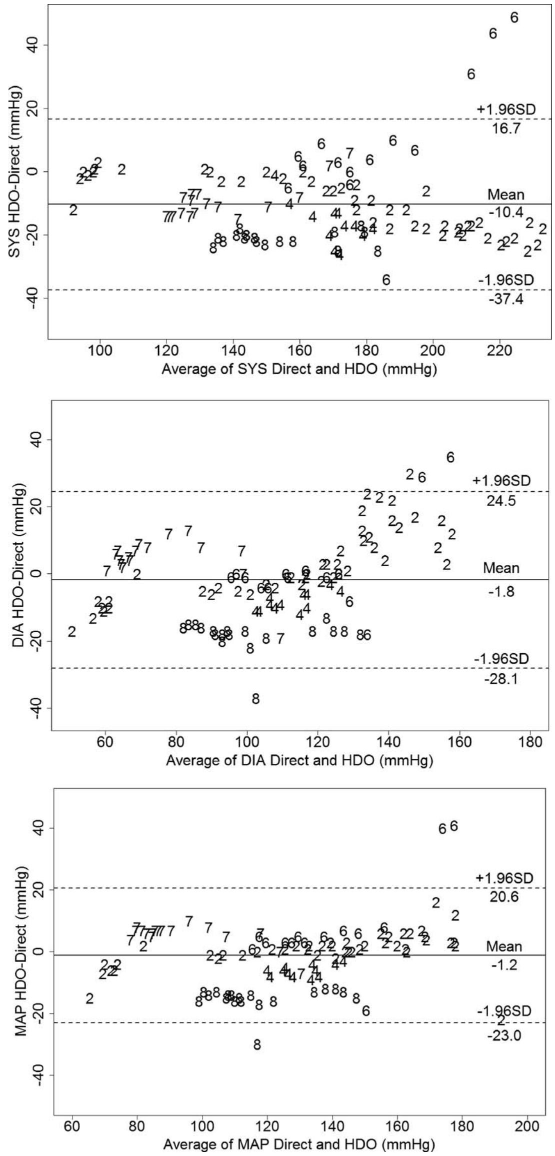

Figure 6. Bland–Altman plots showing agreement between systolic (SYS), diastolic (DIA), and mean arterial pressure (MAP) measured using high-definition oscillometry (HDO) with those measured directly in the dorsal pedal artery. Each point corresponds to one measurement pair, with the number denoting the individual cheetah from which the measurements were taken. The difference between the HDO and direct measurements is plotted against the mean of the HDO and direct measurement. Horizontal lines indicate the mean difference (bias; solid line) and 95% limits of agreement (dashed line).

measurements. Overall, there was better agreement with pressures measured in the dorsal pedal artery, as demonstrated by lower mean differences, lower SDs, and a greater percentage of readings within 10 and 20 mm Hg of the direct pressures. SYS estimation performed poorly whether compared to femoral or dorsal pedal pressures, but agreement with femoral pressures was especially poor, achieving a mere 20% and 60% of readings within 10 and 20 mm Hg, respectively, of the femoral pressure, despite a high correlation coefficient of 0.93 ($P < 0.001$) and relatively narrow limits of agreement. Bland–Altman plots again reveal a tendency to underestimate low and overestimate high DIA (and, to a lesser extent, MAP) pressures obtained in either artery (Figs. 5, 6). Compared to direct pressure in the dorsal pedal artery, both DIA and MAP were estimated with acceptable accuracy and precision, with MAP being the most reliable parameter.

The main weakness with the SYS agreement was an excessive bias of –10.4 mm Hg. If a correction factor of +10 mm Hg is applied to the HDO SYS measurements, then agreement with direct dorsal pedal pressure is improved (Table 1). While SD and correlation remain the same, bias improves to –0.4 mm Hg, and the percentage of readings within 10 and 20 mm Hg of the direct pressure improves to 65.7% and 96.3%, respectively, although the limits of agreement remain quite wide.

DISCUSSION

In this study blood pressure parameters (SYS, DIA, and MAP) measured by HDO at the tail base were compared to direct pressures measured using an intra-arterial catheter in either the femoral or dorsal pedal artery. While pressures were not deliberately manipulated pharmaceutically, as has been done in other studies,[18,20] anesthesia did create circumstances in which the device was tested across a wide range of pressures (e.g., SYS of 91–243 mm Hg).

Depending on whether the direct pressures were measured in the femoral or dorsal pedal artery, significant differences were observed in the agreement found. Femoral pressures were overestimated by HDO at the tail base (coccygeal artery), and dorsal pedal pressures underestimated, across all three parameters (SYS, DIA, and MAP). This would suggest a disparity among the pressures in these three different arteries, with the dorsal pedal being the highest, the femoral the lowest, and, if the HDO device was accurate, the coccygeal occupying an intermediate position. This finding is consistent with the phenomenon, described in humans, dogs, and rats, of distal pulse amplification caused by reflections and changes in impedance as the pulse wave propagates along the arterial tree under normal physiologic conditions.[17,21,28,35] The result is that systolic blood pressure is markedly higher, and diastolic slightly lower, in peripheral than in central arteries, with a resultant increase in pulse pressure.[17,21,28] In contrast, MAP decreases only slightly, remaining more or less constant.[17,21,28] Human studies[17,28] have demonstrated increases on the order of 10% for systolic pressure and of 18–31% for pulse pressure in arteries such as the femoral or brachial as compared to central arteries such as the aorta or subclavian. Such an effect is augmented by increases in peripheral resistance,[17,41] such as that caused by medetomidine.[32] While results in the present study demonstrate an increase in systolic and pulse pressures from femoral to dorsal pedal arteries (albeit in different individuals), diastolic and MAP increased slightly, on average, counter to the typical pattern of distal pulse amplification. However, the sharp difference in systolic pressure between the femoral artery and the dorsal pedal (dorsal pedal, on average, being 28.9 mm Hg higher than femoral) may explain the consistently poorer agreement between SYS measurements, compared to the DIA and MAP measurements.

Given the variation in blood pressure in different parts of the arterial tree, the question, then, is which is the "true" blood pressure? Clearly there is no one uniform value, which highlights the importance of comparing like with like. Ideally, direct and indirect pressures would be measured in the same artery at the same time for the fairest comparison. However, as an inflated cuff will interfere with direct measurement, this is not possible in practice. Under the volatile conditions of anesthesia it seems preferable to obtain measurements at the same time in different places rather than at different times, although the results of the present study show that care must be taken when selecting the location for the comparative method. However, surprisingly, two HDO studies have reported good agreement between HDO-derived measurements from the tail and direct pressures measured by telemetry in the aorta for SYS[18] or MAP.[20]

There are inherent differences between results obtained from direct and indirect blood pressure measuring devices, regardless of the location, because of the method of measurement. Direct techniques measure pressure directly, whereas indirect methods measure flow, and in the case of oscillometry, resulting oscillations in the cuff, as it relates to pressure.[3,7,14] Only under conditions of stable vascular resistance are such inferences legitimate, and vasoactive agents, such as the medetomidine used in this study, may act to destabilize this relationship.[3] It should also be borne in mind that while measurement of blood pressure via an intra-arterial catheter is the accepted gold standard in veterinary medicine,[38] it does not necessarily represent the "true" blood pressure,although it is the closest measurement available.[14]

Even direct measurements are subject to errors. Typical invasive blood pressure systems are described as underdamped, second-order dynamic systems.[10] As such they are characterized by elasticity, friction, and mass, which define the natural frequency and damping coefficient of the system, which in turn affect the accuracy of the measurements derived.[10,30] The natural frequency required is determined by the heart rate of the individual in which the device is to be used, with a higher heart rate necessitating a higher natural frequency.[30] With an inadequate natural frequency, or in an underdamped system, resonance will occur, resulting in an overestimation of the true systolic pressure, while an overdamped system results in a narrowed pulse pressure and an underestimation of systolic pressure.[30] Both the natural frequency and damping coefficient can be assessed by the fast flush test,[16] which, unfortunately, was not performed in this study. While the cheetah's relatively low heart rate lessens the dynamic response demands of the system, and although frequent flushing helps to restore a dynamic response system that can deteriorate overtime,[30] the effect of these two mitigating factors cannot be assessed in this study. Additionally, although it is recommended that tubing and the transducer be replaced after use in each individual, as dynamic response can change over time, financial constraints necessitated the reuse of supplies between cheetahs, although all consumables were new at the beginning of the study. As SYS is the parameter most affected by problems with damping, this offers an additional explanation for the poor agreement observed, although a consistent over- or underestimation, as would be the case with under- or overdamping, was not seen, but rather a bias relative to anatomic location, as previously discussed.

In the present study, MAP consistently showed the best agreement between HDO, and direct measurements and SYS showed the poorest agreement. These observations concur with the findings of two HDO agreement studies[31,39] performed in dogs. A third canine study[20] also found that MAP produced the best agreement with direct measurements. In contrast, in one feline study,[18] SYS showed better agreement with direct pressures than did DIA (MAP was not reported in this study), while in another,[1] agreement was poor across all parameters, evidenced mainly by extremely wide limits of agreement. Conventional oscillometric devices typically estimate only MAP and then calculate the SYS and DIA using an algorithm, and therefore faulty algorithms can be to blame for inaccurate SYS or DIA readings.[1,24] As HDO estimates each individual parameter, these problems should be less likely to occur, and indeed, DIA agreed closely with direct dorsal pedal pressure, and hence the relatively poor SYS performance is perhaps better explained by the amplification in the pulse, as this has a preferentially greater effect on SYS then does DIA or MAP.[17,21,28]

HDO has not previously been tested in cheetahs, but conventional oscillometry and Doppler sphygmomanometry have been investigated in anesthetized cheetahs. The study in question[27] found that the oscillometric device, also placed on the tail, compared well with direct pressures measured at the dorsal pedal artery, with MAP showing the best agreement, followed by SYS and then DIA. In general, precision and limits of agreement were stronger than in the present study, while bias (apart from for SYS) was greater.[27] While ACVIM criteria were not specifically applied to the results in that study, many of the statistical parameters compare favorably with these standards, although, again, calibration and dynamic frequency testing were not reported.

Many HDO studies[1,18,36] have reported an overestimation of low pressures or an underestimation of high pressures, a concerning finding, as this ultimately leads to a lack of recognition of both hypo- and hypertension. However, in the present study the opposite was seen for DIA (and to a lesser degree for MAP), with low pressures being underestimated and high pressures overestimated, as evidenced by the Bland–Altman plots. While this is not optimal, it will at least lead to caution at the more extreme ends of the spectrum.

First- and second-degree atrioventricular (AV) blocks have been reported under medetomidine sedation in the dog.[32] An electrocardiogram was not available, but the waveform produced by the HDO machine was suggestive (although not diagnostic) of occasional AV blocks in one cheetah. The presence of such an irregularity does not present a problem for HDO, which takes its readings as an average over the course of a few beats. However, as direct pressure is measured beat by beat, it is possible that the two readings may differ under these circumstances. The waveforms corresponding to these readings were analyzed for signs of hemodynamic effects (fluctuations in pulse amplitudes), which might cause pressure discrepancies, and direct pressures from that individual were plotted against time in order to identify any outliers. No significant hemodynamic effects and no outliers were identified, so the readings were accepted into the data analysis. It is conceivable, however, that such irregularities did have some more subtle effect on either measurement.

An equine HDO unit and cuff were used in this study as a result of a need for the larger pump offered by this unit compared with the small animal unit. While users of conventional indirect blood pressure measurement devices will be accustomed to the importance of cuff selection for the individual animal based on limb (or tail) circumference and cuff width,[13,37] the manufacturers of the HDO device state that cuff size is not a critical determinant of the accuracy of readings derived by this machine, partly because the device makes internal alterations to optimize future readings. As such, measurements of the tail circumference were not necessary, and the only recommendation regarding fit was that a little finger should just fit underneath when the cuff is secured. The use of the equine cuff in these animals is therefore not a likely source of inaccuracy.

The present study has several limitations, in addition to the lack of calibration and dynamic testing. While simultaneous readings were aimed for, this was not practicable. The HDO device took between 30 and 40 sec to generate a reading, during which time it was not possible to determine the points at which SYS, DIA, and MAP were estimated. The protocol was therefore to record the direct parameters at the moment the HDO reading was displayed. By analyzing the HDO waveforms afterwards it could be seen that these "simultaneous" readings were separated by no more than 15 sec, depending on the parameter. While this is only a short delay, an improvement would be to average all of the direct readings over the time window during which the cuff was deflating.

This study was undertaken in a clinical setting, and consequently it was not possible to standardize the entire protocol, nor was this necessarily desirable. While cheetahs received broadly the same anesthetic regime, differences in dose, isoflurane concentration, the use of additional agents, the degree of intervention to which they were subjected, and their positioning may have influenced blood pressures in different parts of the body and, therefore, the agreement seen. It is impossible to quantify the effect of these discrepancies, but it is hoped that the results are thereby more applicable to real-life clinical situations.

Because the investigation was carried out with cheetahs under anesthesia, measurements were taken as they might typically be done for monitoring purposes, with one reading every 3 to 5 min, and pressures were not stable over time. It was therefore not possible to assess repeatability or reproducibility. These would be important features to assess in terms of diagnosis of hypertension in conscious animals. Under these conditions, several measurements are usually taken in quick succession to yield an average.[8] Additionally, agreement in anesthetized animals cannot be extrapolated to agreement in conscious animals,[8] which is a long-term goal, albeit one with more limited applications.

The HDO device appeared to be very sensitive to movement at the time of recording; it can, however, distinguish artefact from genuine arterial oscillations and tune out such disturbances to a degree or generate an error reading if excessive, as happened on a few occasions. Inevitably readings affected by artefacts were produced, and a small number were subsequently rejected on these grounds. In most cases this was not equivocal, and the poor readings were easily distinguished from the acceptable ones. No specific attempt was made to exclude outliers, as such readings may be difficult to detect with the sole use of one device, under the labile conditions of anesthesia and surgery, and their exclusion may have created overly favorable conditions. It was notable that only very few were rejected despite the sensitivity observed during data collection. In a clinical setting it may be that more readings would be rejected on the basis of perceived movement artefact. The accuracy of the device can therefore be improved somewhat by connection to a computer to enable visualization of the pressure waveforms, but at the cost of portability.

Although HDO is a fairly practical technology, especially for use in the field, there were usability issues. While features like the automated loop function were helpful, the device overall could be more user-friendly: for example, it was not possible to change default settings, and the device turned off when it was plugged into the mains after a period on battery power, necessitating reprogramming of the chosen settings.

The results of this study suggest that the blood pressure in the coccygeal artery is more akin to the dorsal pedal than to the femoral artery, and this should be borne in mind for future studies. Despite the shortcomings of the study and the various potential sources of error, good agreement was found with directly measured dorsal pedal pressures for DIA and MAP, meeting and exceeding the ACVIM criteria. The low level of bias also met the more stringent AAMI guidelines, which specify a maximum of ±5 mm Hg; however, the strict maximum SD of 8 mm Hg was exceeded.[2] SYS agreement was poorer, predominantly as the result of a high degree of bias (–10.4 mm Hg), but the application of a +10 mm Hg correction factor brought results in line with the ACVIM criteria. However, the use of two anatomic locations for direct measurements reduced the effective sample size to five cheetahs, which is an insufficient number on which to base validation, and no provision is made within the guidelines for the application of correction factors. Additionally, failure to calibrate the direct blood pressure machine or verify a sufficient natural frequency or damping coefficient prevents true validation and is a common shortcoming of many studies.[26]

However, to the authors' knowledge, no indirect blood pressure device has yet been validated according to the ACVIM criteria, and the results of this study are promising in an atypical species, for which none of these devices were designed. While HDO cannot at this time replace direct blood pressure measuring for either clinical or research purposes, these results are nevertheless encouraging and, taken in conjunction with those of another recent study,[27] suggest that oscillometry may prove to be the technology of choice in this species.

In conclusion, while this study indicates good agreement between the HDO device and directly measured pressures, meeting ACVIM criteria for all parameters after use of a correction factor, the device cannot be said to be fully validated, although the results are encouraging.

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