RESEARCH PAPER

Agreement between invasive and oscillometric arterial blood pressure measurement using a high-definition oscillometric device in normotensive New Zealand White rabbits using two different anaesthetic protocols

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Abstract

Objective To use American College of Veterinary Internal Medicine (ACVIM) criteria to evaluate a high-definition oscillometric (HDO) blood pressure monitoring device *versus* invasive blood pressure (IBP) measurement in normotensive rabbits anaesthetized with two different anaesthetic protocols.

Study design Prospective experimental study.

Animals A group of 20 healthy adult New Zealand White rabbits weighing 4.36 ± 0.37 kg (mean ± standard deviation).

Materials and methods Rabbits were premedicated with butorphanol 0.5 mg kg^{-1} and midazolam 0.5 mg kg^{-1} subcutaneously (SC, group BMA) or ketamine 25 mg kg^{-1} and medetomidine 0.4 mg kg^{-1} SC (group KM). Anaesthesia was induced with alfaxalone administered intravenously (group BMA) or isoflurane by face mask (group KM) and maintained with isoflurane in oxygen. IBP was measured from the central auricular artery. The cuff for the HDO monitor was placed distal to the left elbow and distal to the left tarsus. Agreement between invasive and HDO measurements was evaluated using Bland–Altman method.

Results In group KM there was better agreement between the HDO device and IBP when the cuff was placed on the thoracic limb, with 100% and 91% of the readings for mean (MAP) and diastolic arterial pressure (DAP), respectively, within 10 mmHg of the IBP measurements. The agreement, although worse, also met the ACVIM criteria for systolic arterial pressure (SAP; 53% of the readings within 10 mmHg). In group BMA, the device met the criteria with the cuff on the thoracic limb only, and only for MAP and DAP (73% and 75% of the measurements within 10 mmHg of the IBP, respectively) but not for SAP (12%).

Conclusion and clinical relevance The HDO device met most of the ACVIM criteria for noninvasive blood pressure measurement in anaesthetized rabbits, specifically when the cuff was placed distal to the elbow and the anaesthetic protocol included ketamine and medetomidine.

Keywords anaesthesia, blood pressure, high-definition oscillometry, rabbits.

Introduction

According to a large epidemiologic study (Brodbelt et al. 2008) and several more recent investigations (Matthews et al. 2017; Lee et al. 2018), anaesthesia-related mortality is greater in rabbits than in dogs and cats (1.39–4.8% *versus* 0.05–0.17% and 0.11–0.24%, respectively). To help reduce possible complications and mortality, accurate perianaesthetic monitoring is vital.

Monitoring blood pressure is considered part of standard of care for animals during general anaesthesia (Bednarski et al. 2011). Invasive blood pressure (IBP) monitoring, which is considered the 'gold standard' for blood pressure measurement, requires insertion of a catheter into the lumen of a peripheral artery. This method is the most accurate and provides additional advantages such as continuous measurement, pressure wave display and access to arterial blood sampling. Important disadvantages include the technical skill needed for arterial cannulation and specialized equipment, as well as risks of infection, embolism, thrombosis, haemorrhage or inadvertent intra-arterial injections (Love & Harvey 2006). In rabbits, auricular haematoma and necrosis of the ear are other possible

complications of this technique (Washington & van Hooiser 2012). Noninvasive techniques have been developed to overcome some of the aforementioned disadvantages of IBP measurement, but the main disadvantage is that these techniques tend to be less accurate. The Doppler technique has shown good agreement with systolic arterial pressure (SAP) in isoflurane-anaesthetized rabbits (Harvey et al. 2012), but cannot provide information about mean (MAP) and diastolic blood pressure (DAP). Oscillometric devices, which measure blood pressure through detection of vessel wall oscillations caused by blood flow, are generally easy to use and can provide information about MAP and DAP. However, they can become inaccurate at high heart rates or at reduced pulse pressure (Alpert et al. 2014).

High-definition oscillometric (HDO) devices have been developed to improve some of the characteristics of the classic devices. Arguably, they feature a higher sensitivity at low pulse amplitudes and a better signal recognition and fewer artefacts at higher heart rates (Egner 2006). Several HDO devices have been tested previously in veterinary species. The American College of Veterinary Internal Medicine (ACVIM) requirements are outlined in the Guidelines for the Identification, Evaluation and Management of Systemic Hypertension in Dogs and Cats (Brown et al. 2007). In healthy anaesthetized dogs (Seliškar et al. 2013), one HDO device met most of these guidelines for MAP and DAP but not for SAP. While satisfactory precision was found for MAP in anaesthetized cats (Petrič et al. 2010). To date, no reports describe the performance of an HDO during rabbit anaesthesia.

The main objective of the present study was to evaluate the accuracy of an HDO device for arterial blood pressure measurement (VET HDO; S + B medVet GmbH, Germany) in normotensive isoflurane-anaesthetized rabbits. The accuracy was evaluated following the guidelines provided by the ACVIM. As a second assessment of accuracy, the device was evaluated using the standards laid down by the Association for the Advancement of Medical Instrumentation (AAMI; O'Brien et al. 2002). Furthermore, we investigated the effect of two different anaesthetic protocols in addition to cuff site on accuracy. Our hypothesis was that the HDO device would provide accurate readings when compared with IBP measurements independently of the anaesthetic protocol or cuff site used.

Material and methods

A total of 20 adult New Zealand White Rabbits were anaesthetized for a nonrelated terminal study investigating a new design of a supraglottic airway device (unpublished study). The sample size was powered according to the aforementioned terminal study. However, the authors considered it to be sufficient based on the ACVIM recommendation that a database of no fewer than eight animals should be used for the evaluation of blood pressure monitoring devices when compared with invasive arterial pressure (Brown et al. 2007). Ethical approval was obtained (AVD108002016767, protocol number: WP8B2, date of approval: 15 March 2018) from the national Central Authority for Scientific Procedures on Animals. The rabbits were considered healthy according to physical examination. Rabbits were housed in pairs in cages with a 12 hour light and 12 hour night cycle. Commercial food and hay were provided daily to the rabbits and water was available *ad libitum*.

Rabbits were randomly assigned to one of two groups and subsequently anaesthetized using one of two standardized anaesthetic protocols, using an online random group generator (randomlist.com). In the first group, rabbits ($n = 10$) were premedicated with 0.5 mg kg^{-1} butorphanol (Morphasol, 4 mg mL^{-1}; aniMedica GmbH, Germany) and 0.5 mg kg^{-1} midazolam (Midazolam Actavis, 5 mg mL^{-1}; Actavis, Ireland) administered subcutaneously (SC; group BMA). In the second group, rabbits ($n = 10$) were premedicated with 25 mg kg^{-1} ketamine and 0.4 mg kg^{-1} medetomidine (Sedastart, 1 mg mL^{-1}; ASTfarma, the Netherlands) SC (group KM). Rabbits were placed in sternal recumbency over a padded surface, 10 minutes after premedication, and pre-oxygenation was started with a tightly fitted homemade face mask (half a plastic bottle with a latex glove as a diaphragm) connected to a Mapleson D non-rebreathing system (Intersurgical Ltd., UK) delivering 2 L $minutes^{-1}$ of oxygen. A 24 gauge catheter (Vasofix; Braun, Germany) was inserted in the caudal auricular vein of one of the ears. In group BMA, anaesthesia was induced with alfaxalone (Alfaxan, 10 mg mL^{-1}; Jurox Limited, UK) administered intravenously to effect (2−6 mg kg^{-1}), whereas in group KM, anaesthetic induction was achieved using isoflurane (Isoflo; Abbot Logistics, the Netherlands) in oxygen delivered by face mask attached to a Mapleson D non-rebreathing system (vaporizer dial set at 5% and flow rate of 3 L $minute^{-1}$). Once the anaesthetic plane was considered sufficient to allow intubation (i.e., no voluntary movement, no response to a toe pinch of the pelvic limb, relaxation of the jaw muscle tone, and exteriorization of the tongue performed with relative ease), a supraglottic airway device (prototype V-gel ADVANCED size 4-6; DocsInnovent Ltd., UK) was placed. The animals were subsequently connected via the airway device to a Mapleson D non-rebreathing system and isoflurane in oxygen was administered to maintain anaesthesia, with the vaporiser dial set at 1% and a flow rate of 3 L $minute^{-1}$. If the rabbits developed apnoea after the supraglottic airway device was in place, they were manually ventilated until return of spontaneous ventilation. After induction, rabbits in both groups were given 0.02 mg kg^{-1} buprenorphine SC (Vetergesic, 0.3 mg mL^{-1}; Ecuphar, the Netherlands).

For IBP monitoring, a 22 gauge or 24 gauge catheter (Vasofix; Braun, Germany) was placed in the central auricular artery of the contralateral ear and connected to a pressure transducer (Meritrans DTXPlus; Meritmedical, the

Netherlands) via its noncompliant tubing and a pressurized bag (300 mmHg) filled with heparinized saline. Heparinized saline was made by adding 1 mL heparin 5000 IU mL^{-1} (Heparine Leo; Leo Pharma, the Netherlands) to 500 mL of sodium chloride 0.9% (NaCl 0.9% Ecobag; Braun, Germany). The transducer was placed and zeroed at the level of the sternum of the rabbit and was connected to a multiparameter monitor (BeneView T5; Mindray, Guangdong, China). A dynamic response test (fast flush) was performed at the beginning of each procedure and evaluated visually. The transducer was calibrated every day of the study with a standard aneroid manometer. During the procedure, attention was paid to avoid kinking of the arterial catheter by maintaining the ears parallel to the table. For noninvasive arterial blood pressure (NIBP) monitoring, the smallest available cuff (cuff 'C1') of the HDO device (VET HDO; S + B medVet GmbH, Germany) was placed distal to the left elbow and a second cuff was placed distal to the left tarsus. Before cuff placement, the circumference of both limbs was measured to calculate cuff width − circumference of the limb ratio, for each limb and each rabbit. The HDO device was set up in 'automatic' measurement mode as per manufacturer's instructions.

An intravenous infusion of isotonic electrolyte solution (Sterofundin ISO; Braun, Germany) was provided at 10 mL kg^{-1} $hour^{-1}$ via a syringe driver (Syramed SP6000; Arcomed, Switzerland). The electrocardiogram, heart and respiratory rates (HR and f_R respectively), temperature, haemoglobin oxygen saturation, end-tidal carbon dioxide and end-tidal isoflurane were monitored continuously and recorded every 5 minutes (BeneView T5; Mindray, Guangdong, China). An electric warming device (Hotdog; Augustine Temperature Management, MN, USA) was used during the anaesthesia. For the purpose of this study, normotension was arbitrarily defined as an IBP MAP between 60 and 90 mmHg. Blood pressure readings with the HDO device were taken every minute, and simultaneously with the appearance of the HDO values, values displayed by direct IBP measurement were recorded. If the graph displayed by the software of the HDO device did not show the appropriate bell shape, or the measurement result read 'error' (in the HDO device screen), the measurement was discarded. Readings were taken from the pelvic and thoracic limbs alternatingly every four recorded readings, by switching the tubing connected to the monitor while both cuffs were left in place. Between 10 and 12 paired IBP and HDO readings were recorded in each rabbit for each limb in the previously defined normotensive range over the duration of the anaesthetic procedure (1 hour). After 1 hour of anaesthesia, blood pressure monitoring was discontinued and recumbency was changed for purposes of the main research study; finally, rabbits were euthanized during anaesthesia with an intravenous injection of 1 mL of T61 (200 mg embutramide, 50 mg mebezonium iodide and 5 mg tetracaine hydrochloride per 1 mL of T61 solution; MSD, the Netherlands).

Statistics

For further statistical analysis, one out of every three paired IBP and NIBP measurements in each limb was randomly selected, to avoid pseudo-replication (Hartnack 2014). Student's paired *t* test was performed for the bias of SAP, MAP and DAP for the two different cuff positions in groups BMA and KM. Student's paired *t* test was also performed to compare HR, f_R, weight and temperature between groups. For differences in sex distribution between groups, a chi-square test was performed.

Agreement between IBP and HDO readings for SAP, DAP and MAP was assessed with the method suggested by Bland and Altman for multiple observations per individual (Bland & Altman 2007). Bias was calculated as the mean of the difference between paired IBP and HDO measurements for SAP, DAP and MAP separately. A positive bias indicates a systematic underestimation and a negative bias indicates an overestimation of the arterial blood pressure by the HDO device.

Statistical analysis was performed using MedCalc Version 19.4.1 (Medcalc Software Ltd, Belgium). Values for bias and cuff width to limb circumference ratio are presented as mean ± standard deviation (SD). Values for HR, f_R and temperature are presented as a range. Statistical significance was accepted if $p < 0.05$.

Agreement between the two methods was assessed according to the criteria outlined by the ACVIM consensus statement (Brown et al. 2007) for dogs and cats. These guidelines state that for acceptable agreement, the bias must be less than 10 mmHg and the precision (as indicated by the SD) less than 15 mmHg. Also, more than 50% and 80% of the NIBP measurements must lie within 10 and 20 mmHg from the IBP measurements, respectively. A third criterion stipulates that the correlation coefficient for SAP and DAP between the invasive method and the noninvasive device should be higher than 0.9. In the present study, neither correlation coefficients nor linear regressions were calculated since these analyses are not appropriate methods for comparative studies (Bland & Altman 1986).

The agreement between methods was also evaluated based on the standards laid down by the AAMI (O'Brien et al. 2002), which requires a mean bias of less than 5 mmHg and SD of less than 10 mmHg. Although the recommendations only evaluate bias for SAP and DAP, this study also evaluated MAP to the same criteria.

Results

There was no significant difference between groups in relation to the sex ($p = 0.07$) or body weight ($p = 0.58$) of rabbits

Table 1 Sex distribution, weight (mean ± standard deviation), heart and respiratory rates (range), temperature (range) and ratio between cuff width and circumference of the limb (mean ± standard deviation) in rabbits anaesthetized with isoflurane after premedication with butorphanol 0.5 mg kg^{-1} and 0.5 mg kg^{-1} midazolam subcutaneously (SC) and induction with alfaxalone 2–6 mg kg^{-1} intravenously (group BMA; $n = 10$) or after premedication with 25 mg kg^{-1} ketamine and 0.4 mg kg^{-1} medetomidine SC and induction with isoflurane (group KM; $n = 10$)

	Group BMA	Group KM
Sex (female/male)	8/2	4/6
Weight (kg)	4.48 ± 0.33	4.24 ± 0.39
Heart rate (beats $minute^{-1}$)*	166–275	105–175
Respiratory rate (breaths $minute^{-1}$)	8–57	8–70
Temperature (°C)	36.7–39.8	37.5–40.6
Ratio cuff width (in mm) and circumference of thoracic limb (in mm) (%)	75.9 ± 4.8	69.4 ± 5.9
Ratio cuff width (in mm) and circumference of pelvic limb (in mm) (%)	72.7 ± 7.7	63.8 ± 6.9

*$p < 0.05$ between groups.

included (Table 1). The HR, f_R, and temperature during anaesthesia and the ratio between the cuff width and the circumference of the limb for both groups are presented in Table 1. There were no significant differences between groups BMA and KM for temperature ($p = 0.08$), f_R ($p = 0.75$) and cuff width and circumference of the limb ratio ($p = 0.07$). A significant difference was found in HR between the groups ($p = 0.001$). There were no complications during anaesthesia, and all the animals completed the study.

During anaesthesia, mainly at the beginning, some of the measurements were performed when the MAP was less than 60 mmHg or greater than 90 mmHg. A total of 30 measurements in group BMA had a MAP less than 60 mmHg and 43 measurements in group KM had a MAP greater than 90 mmHg. These values were not included in the statistical analysis.

A total of 15 measurements (3% of the total) were considered as 'error' by the device and were discarded. A total of 222 valid readings for group BMA and 228 valid readings for group KM were recorded. A total of 88 and 82 paired measurements for group BMA and group KM, respectively, were statistically analysed and used as the definitive data set.

Bland–Altman plots for SAP, DAP and MAP for the thoracic and pelvic limbs in groups BMA and KM are presented in Fig. 1 and Fig. 2, respectively. Since we found a significant difference in bias between the two different premedication groups ($p < 0.001$, $p < 0.001$ and $p = 0.007$ for SAP, MAP and DAP, respectively) and also between the two cuff sites (thoracic and pelvic limb) ($p < 0.001$, $p < 0.001$ and $p = 0.003$ for SAP, MAP and DAP, respectively) for all blood pressure readings (SAP, MAP and DAP), the results are presented separately for each group and each cuff position. The bias and SD for SAP, DAP and MAP of each group and cuff site are presented in Table 2. The percentage of measurements that lay within 10 and 20 mmHg of the reference method for SAP, MAP and DAP for groups BMA and KM are presented in Table 3 and Table 4, respectively.

According to the ACVIM recommendation, the mean difference of paired measurements for SAP and DAP should be < 10 mmHg with an SD of < 15 mmHg. The HDO device met these criteria for MAP and DAP in both protocols regardless of the cuff site, but not for SAP in either group. When the results were analysed by cuff location, SAP in group KM also met this first recommendation but only when the cuff was placed on the thoracic limb.

The second ACVIM criterion (50% of measurements should lie within 10 mmHg of invasive measurement, and 80% within 20 mmHg) was met for DAP in both groups and at both cuff sites. Again, for SAP, only when the cuff of the device was on the thoracic limb and only in group KM, the recommended percentages were achieved. Although the second ACVIM recommendation does not mention MAP, these same criteria were met for MAP in both the groups when the cuff was placed on the thoracic limb, but only in group KM when the cuff was on the pelvic limb.

Overall, agreement between IBP and HDO readings was better (i.e., the bias was smaller) in group KM than in group BMA, and with the cuff positioned on the thoracic limb rather than the pelvic limb.

The current guidelines for blood pressure monitoring devices for use in humans, set out by the AAMI (O'Brien et al. 2002), are even more restrictive than the ACVIM guidelines (bias less than 5 mmHg and SD of less than 10 mmHg). The device tested in the present study would meet these requirements only for MAP and DAP in group KM, and for DAP in group BMA.

Discussion

This study investigated an HDO device for NIBP monitoring in healthy normotensive rabbits during isoflurane anaesthesia

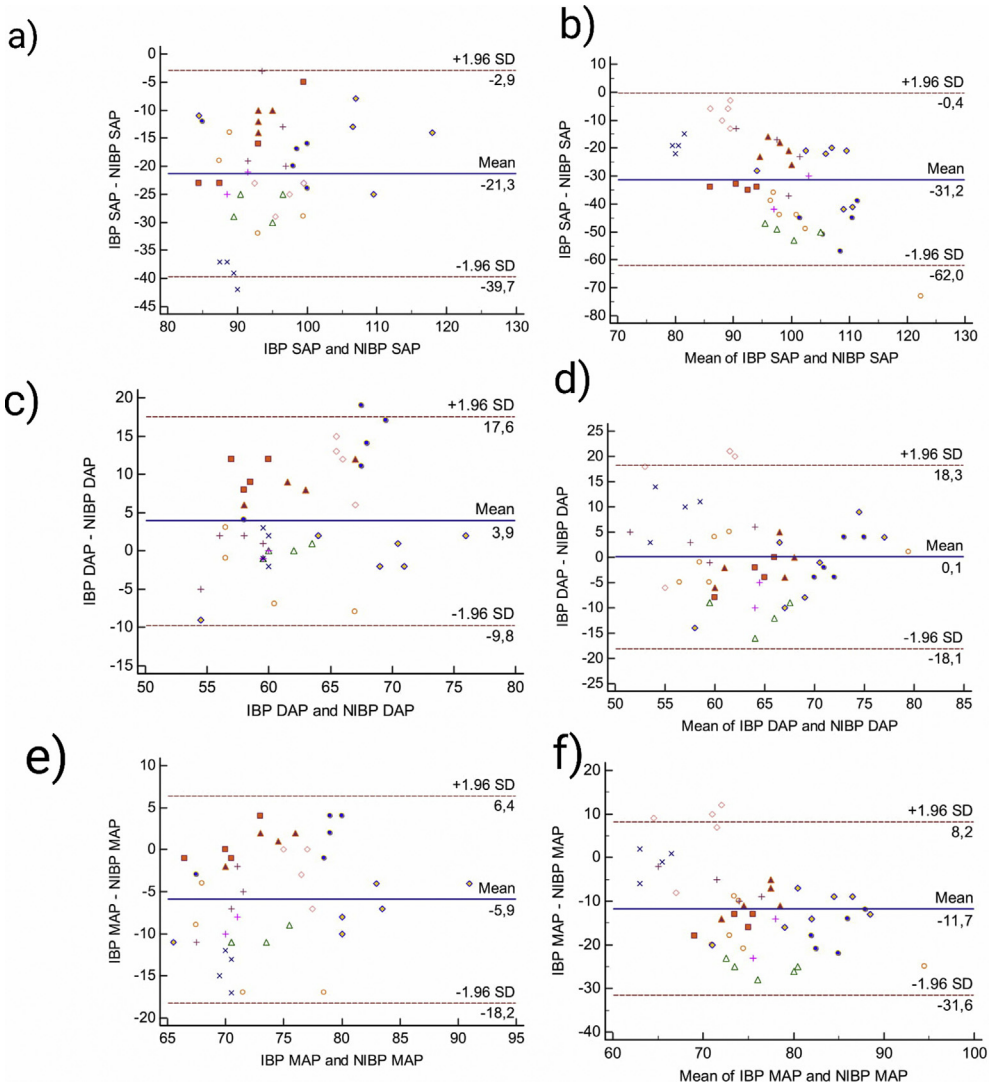

Figure 1 Bland–Altman plots of systolic arterial pressure (SAP; graphs a and b), diastolic arterial pressure (DAP; graphs c and d) and mean arterial pressure (MAP; graphs e and f) measured in 10 isoflurane-anaesthetized New Zealand White rabbits following premedication with butorphanol and midazolam and induction with alfaxalone (group BMA). The blood pressure cuff was placed on the thoracic limb (graphs a, c, and e) and pelvic limb (graphs b, e, and f). For detailed information of drug doses, see Table 1 legend. IBP, invasive blood pressure; NIBP, noninvasive blood pressure; SD, standard deviation. Different coloured symbols represent individual animals.

after two different premedication and induction protocols. We also evaluated two different locations for the placement of the cuff of the HDO device. Performance of the device was evaluated using the previously established ACVIM criteria for blood pressure measurements in dogs and cats (Brown et al. 2007). As a secondary evaluation tool, the device was evaluated following the guidelines of the AAMI.

Our results are similar to those of other veterinary studies performed with HDO devices for blood pressure monitoring. In the study by Wernick et al. (2010), an HDO blood pressure monitor device did not fulfil the ACVIM requirements in anaesthetized dogs. As in our study, the greatest bias and worst precision was obtained for SAP, although the percentage of values within 10 mmHg of the IBP measurement was less than in the present study (58.7% and 52.4% for SAP and DAP, respectively). Seliškar et al. (2013) also evaluated an HDO device in anaesthetized dogs. The ACVIM requirements were met for MAP and DAP but not for SAP, as seen in the present study. In another study in anaesthetized dogs (Rysnik et al. 2013), an HDO device provided reduced bias compared with

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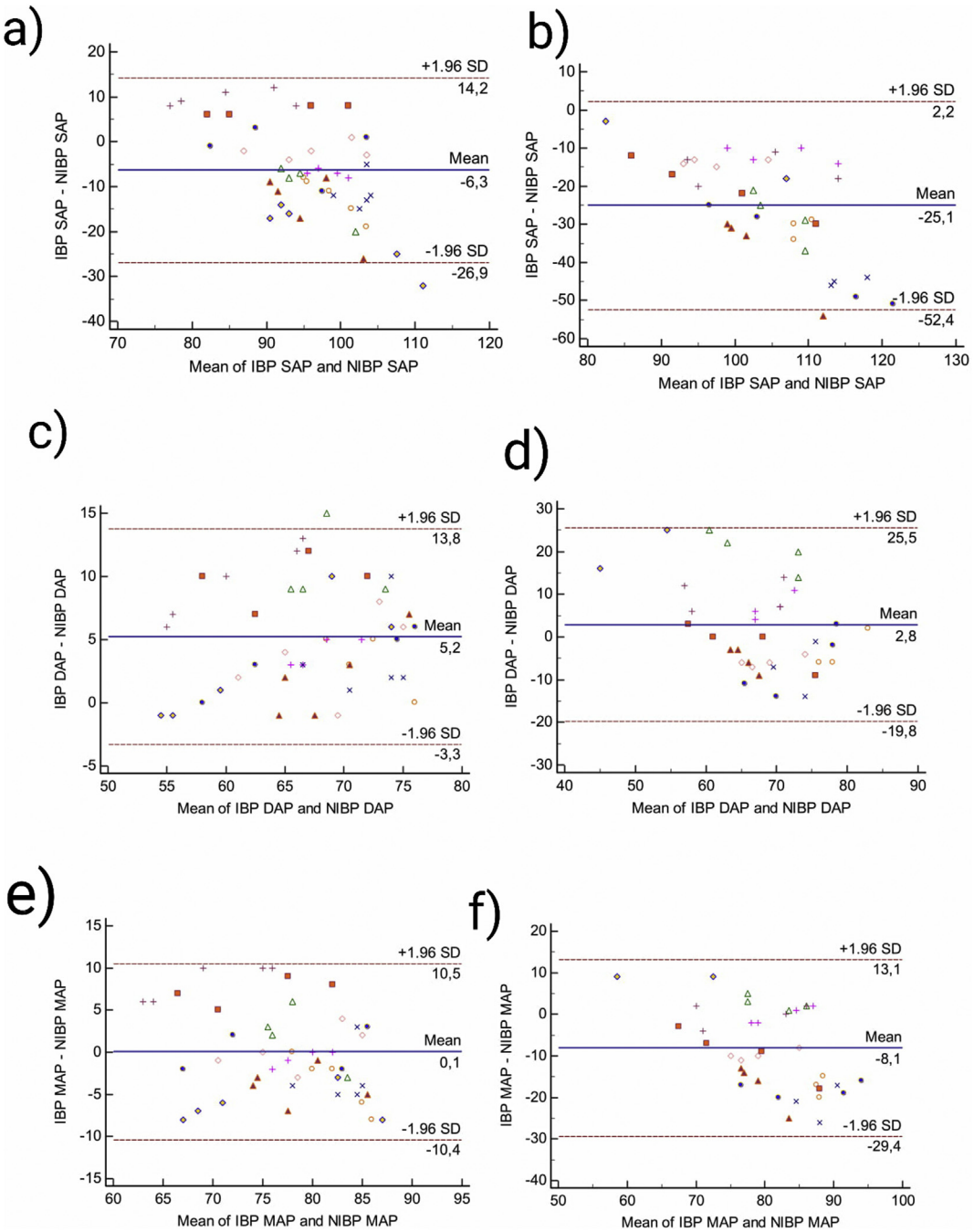

Figure 2 Bland–Altman plots of systolic arterial pressure (SAP; graphs a and b), diastolic arterial pressure (DAP; graphs c and d) and mean arterial pressure (MAP; graphs e and f) measured in 10 isoflurane-anaesthetized New Zealand White rabbits after premedication with ketamine and medetomidine and induction with isoflurane (group KM). The blood pressure cuff was placed on the thoracic limb (graphs a, c, and e) and pelvic limb (graphs b, e, and f). For detailed information of drug doses, see Table 1 legend. IBP, invasive blood pressure; NIBP, noninvasive blood pressure; SD, standard deviation. Different coloured symbols each represent an individual animal.

Table 2 Mean values (± standard deviation) of bias in systolic arterial blood pressure (SAP), mean arterial blood pressure (MAP) and diastolic arterial blood pressure (DAP) measurements made in isoflurane anaesthetized rabbits after premedication with butorphanol and midazolam and induction with alfaxalone (group BMA; 10 rabbits) or after premedication with ketamine and medetomidine and induction with isoflurane (group KM; 10 rabbits). For detailed information, see Table 1 legend. n = number of measurements: PL, pelvic limb; TL, thoracic limb. Bold numbers are in agreement with the American College of Veterinary Internal Medicine recommendations

	Group BMA		**Group KM**	
	TL ($n = 41$)	**PL ($n = 47$)**	**TL ($n = 46$)**	**PL ($n = 36$)**
SAP	−21 ± 9.2	−32 ± 15.63	**−7 ± 10.27**	−25 ± 13.27
MAP	**−6 ± 6.11**	−12 ± 9.82	**0 ± 5.22**	**−8 ± 9.84**
DAP	**4 ± 6.91**	**0 ± 8.96**	**5 ± 4.24**	**2 ± 10.76**

IBP but low precision with wide limits of agreement; again, SAP showed poor agreement with the invasive method, as seen in our study. In cats during anaesthesia (Petrič et al. 2010), an HDO device showed lower precision than a Doppler device. The authors concluded that the HDO device with the cuff placed on the tail was not a reliable blood pressure monitor for use in anaesthetized cats.

Other authors have compared several NIBP monitoring devices with IBP in rabbits. Doppler and oscillometric measurements were compared with auricular and carotid artery blood pressure in anaesthetized rabbits (Barter and Epstein, 2014). The authors considered both noninvasive techniques tested to be of poor performance and not good substitutes for carotid blood pressure measurements. Limits of agreement were wider for SAP than for MAP and DAP, as in the present study. In the current study, we used the same peripheral artery for cannulation in all rabbits to reduce the variability between measurements. Although the central auricular artery provides lower absolute IBP values than the carotid artery pressure, it is considered to be a good substitute for clinical use where a carotid artery cannot be routinely catheterized (Barter and Epstein, 2014). A non-HDO device (PetTrust Blood Pressure Monitor; Aster Electrical, Taiwan) was tested in anaesthetized rabbits by Bellini et al. (2018). As in our study, the device met the ACVIM recommendations for MAP and DAP but not for SAP, but the recommendations of the AAMI were only met for MAP, while the HDO device evaluated in our study met the AAMI requirements for both MAP and DAP. Classic oscillometric devices estimate MAP, and through specific algorithms, calculate SAP and DAP. By contrast, the HDO device is able to estimate all three variables, and this may be part of the reason for the differences between studies. This may represent an advantage of the HDO technique over classic oscillometric devices (Skelding & Valverde 2020).

Our results showed an effect of anaesthetic protocol and cuff site on the level of agreement between the HDO and IBP readings. The protocol in group BMA was chosen for the minimal cardiovascular effects of butorphanol and midazolam for sedation in dogs (Kojima et al. 1999). The protocol used in group KM was chosen to reflect more closely the protocols commonly used in general practice. Therefore, it was considered to be more representative of the cardiovascular status of healthy rabbits during general anaesthesia in various clinical settings. The reason for the overall better agreement in group KM than in group BMA is unknown. Speculatively, it might result from anaesthesia-related differences in vascular wall tone affecting reverberations of the vessel wall and thereby HDO device performance. The vasoconstrictive effect of α_2-adrenoceptor agonists such as medetomidine and the indirect effect of ketamine on the cardiovascular system could influence the vessel tone and pulse quality, and therefore the measurements of the NIBP monitoring device (Hynson et al. 1994). Notably, both bias and SD were lower in group KM than in group BMA for SAP, DAP and MAP, suggesting an effect of cardiovascular tone on the ability to determine blood pressure accurately and precisely by the HDO device.

Of the two cuff locations we tested, our data suggest that the thoracic limb would be a better site when using this HDO device for blood pressure monitoring in anaesthetized rabbits. The bias and SD for all measurements were smaller with the cuff placed on the thoracic limb, and the percentage of measurements within 10 or 20 mmHg of the corresponding IBP measurements were greater. This agrees with other published reports about NIBP monitoring in rabbits (Ypsilantis et al. 2005) and dogs (Gains et al. 1995; Fujiyama et al. 2017). The anatomical conformation of the limbs and the use of an inappropriate cuff size for either limb could be factors leading to this difference.

This study had several limitations that should be noted. Importantly, we only evaluated HDO performance for measurements taken during normotension (invasive MAP between 60 and 90 mmHg). Evaluation of this blood pressure monitoring device also during hypotension would be beneficial because hypotension is one of the main complications during inhalant anaesthesia (Harvey et al. 2012). In this experiment, we were not free to increase isoflurane delivery to produce vasodilation and hypotension, as it may have interfered with the main experiment (novel airway device performance testing). Hypotension was not seen in group KM at any time. This suggests that hypotension is improbable in healthy rabbits during isoflurane anaesthesia with an end-tidal fraction less than 1% for 1 hour following this premedication. Also, HR values were lower in group KM than in group BMA, probably owing to the cardiovascular effect of medetomidine. The ratio between the width of the cuff and the circumference of the limb was in fact higher than the recommended limit in all rabbits

Table 3 The percentage of high-definition oscillometric measurements of systolic arterial blood pressure (SAP), mean arterial blood pressure (MAP) and diastolic arterial blood pressure (DAP) that lay within 10 or 20 mmHg of the corresponding invasive blood pressure (IBP) measurements in 10 isoflurane-anaesthetized New Zealand White rabbits. For detailed information, see Table 1 legend. BL, both limbs; PL, pelvic limb; TL, thoracic limb. Bold numbers agree with the American College of Veterinary Internal Medicine (ACVIM) recommendations

Difference from IBP	Guidelines of ACVIM	SAP			MAP			DAP		
		BL	TL	PL	BL	TL	PL	BL	TL	PL
± 10 mmHg	>50%	10.2	12.2	8.5	**55.7**	**73.2**	40.4	**78.4**	**75.6**	**80.9**
± 20 mmHg	>80%	37.5	48.8	27.7	**88.6**	**100**	78.7	**98.9**	**100**	**97.9**

Table 4 The percentage of high-definition oscillometric measurements for systolic blood pressure (SAP), mean blood pressure (MAP) and diastolic blood pressure (DAP) that lay within 10 or 20 mmHg of the corresponding invasive blood pressure measurements in 10 New Zealand White rabbits during isoflurane anaesthesia following premedication with ketamine and medetomidine (group KM) and induction with alfaxalone. For detailed information, see Table 1 legend. BL, both limbs; PL, pelvic limb; TL, thoracic limb. Bold numbers are in agreement with American College of Veterinary Internal Medicine (ACVIM) recommendations

Difference from invasive blood pressure	Guidelines of ACVIM	SAP			MAP			DAP		
		BL	TL	PL	BL	TL	PL	BL	TL	PL
± 10 mmHg	> 50%	36.6	**58**	8.3	**80.5**	**100**	**55.6**	**82.9**	**91**	**72.2**
± 20 mmHg	> 80%	72	**93.5**	44.4	**96.3**	**100**	**91.7**	**98.8**	**100**	**97.2**

(40–60%; Brown et al. 2007). We used the smaller cuff size as this was explicitly stated in the manufacturer's instructions. It is also important to note that one HDO measurement takes approximately 10 seconds and during this time IBP may change. We decided to record the measurements simultaneously as displayed in both the HDO device and the IBP monitor. An alternative approach would be to record three IBP readings during the time the HDO device was measuring and then provide an average of them.

Furthermore, the HDO device was set up and used in an 'automatic' mode. A different setting with, for example, a slower cuff deflation rate, may have provided more accurate results, but automatic settings would be a better reflection of conditions in the clinical environment. All the rabbits were anaesthetized in sternal recumbency. The position of the animal, and therefore, of the limbs, could have produced changes in pressure on the limbs, potentially affecting the measurements of the device. The effect of body position on the performance of oscillometric devices has been reported previously in dogs, showing not only different values but also different variability depending on position (Rondeau et al. 2013). Finally, we only used healthy adult animals, so the results we obtained cannot be extrapolated to systemically ill, geriatric or neonatal animals. IBP monitoring is still the gold standard of blood pressure measurement whenever haemodynamic instability is expected and blood pressure should be closely monitored. It is preferred over the noninvasive HDO device tested in the present study.

In conclusion, the HDO device we tested met most of the ACVIM recommendations for the validation of noninvasive devices for blood pressure measurement, in healthy anaesthetized rabbits during normotension. The device fulfilled the criteria for MAP and DAP, but it did not meet those for SAP. According to the present study, placing the cuff on the thoracic limb provides more accurate and precise readings, especially when using an anaesthetic protocol consisting of medetomidine and ketamine premedication. The anaesthetist should note that, even under the aforementioned conditions, the values of MAP and DAP are more accurate than those of SAP. Further studies should be performed to assess this HDO device for accuracy and precision in rabbits under different conditions, especially during hypotension.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Authors' contributions

ACR: anaesthesia management, data collection, data management, statistical analysis, elaboration of drafted and final version of manuscript. YRAvZ: study design, critical review of

manuscript. NJS: study design. JdG: statistical analysis, critical review of manuscript.

Conflict of interest statement

The authors declare no conflict of interest.

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Received 24 October 2020; accepted 31 March 2021.

Available online 12 June 2021