







Comparison of invasive and non-invasive blood pressure monitoring in *Cuniculus paca* (Spotted paca)

Comparação da monitorização invasiva e não invasiva da pressão arterial em *Cuniculus paca* (Paca)

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ABSTRACT: *Cuniculus paca*, a South American wild rodent with zootechnical potential, requires anesthesia for management procedures. However, limited information is available regarding safe monitoring of this animal under anesthesia. This study aimed to compare with gold standard invasive method and validate non-invasive blood pressure measurements using an oscillometric monitor in *Cuniculus paca*. Eight healthy adult females undergoing general anesthesia for follicular aspiration were included. Systolic, diastolic, and mean arterial pressures were measured simultaneously using oscillometric non-invasive monitor with its cuff placed on the radial artery and an invasive catheter placed in the dorsal metatarsal artery. Measurements were compared using the t-test, correlated by Pearson test, and analyzed using the Bland-Altman concordance test. The results indicated that only systolic pressure measured by non-invasive oscillometric method was similar to the pressure measurement by invasive method ($P=0.6372$, $r=0.5969$, bias 0.59 ± 20.9 mmHg); while mean and diastolic pressures were underestimated by the non-invasive method. In conclusion, non-invasive oscillometric monitor provides a valid and reliable method for systolic blood pressure measurement in *Cuniculus paca* under general anesthesia.

KEYWORDS: general anesthesia; invasive monitoring; neotropical rodent; oscillometric sphygmomanometer; wild animals.

RESUMO: *Cuniculus paca* é um roedor selvagem da América do Sul com potencial zootécnico. Este animal requer anestesia para diversos procedimentos, no entanto, há limitada informação disponível sobre o monitoramento seguro deste animal para anestesia. Este estudo objetivou comparar o método invasivo (padrão ouro) com o método não invasivo usando um monitor oscilométrico para a monitorização da pressão arterial em *Cuniculus paca*. Oito fêmeas adultas saudáveis submetidas a anestesia geral para aspiração folicular foram incluídas no estudo. As pressões arteriais sistólica, diastólica e média foram mensuradas simultaneamente pelo método invasivo mediante cateter inserido na artéria metatarsiana dorsal e usando um monitor oscilométrico com seu manguito colocado sobre a artéria radial. As medidas foram comparadas usando o teste-T, correlacionadas pelo teste de Pearson e analisadas para validação usando o teste de concordância de Bland-Altman. Os resultados indicaram que, apenas a pressão sistólica medida pelo método oscilométrico foi semelhante à medida pelo método invasivo ($P = 0,6372$, $r = 0,5969$, viés de $0,59 \pm 20,9$ mmHg); já as pressões média e diastólica foram subestimadas pelo método oscilométrico. Em conclusão, o monitor oscilométrico não invasivo fornece um método válido e confiável para medição da pressão arterial sistólica em *Cuniculus paca* sob anestesia geral.

PALAVRAS-CHAVE: anestesia geral; monitorização invasiva; roedor neotropical; esfigomanómetro oscilométrico; animais selvagens.

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INTRODUCTION

Cuniculus paca is indeed the second most common neotropical rodent in South America. It belongs to the Kingdom *Animalia*, Phylum *Chordata*, Class *Mammalia*, Order *Rodentia*, Suborder *Stricognatha*, Family *Cuniculidae*, and Genus *Cuniculus* (Bonilla-Morales *et al.* 2013; IUCN, 2016). According to the International Union for Conservation of Nature, it is not considered an endangered species. However, it has experienced population declines and local extinctions in certain regions of South America due to uncontrolled hunting and habitat destruction (IUCN, 2016).

The species holds significant zotechnical potential, primarily attributed to the high quality of its meat. Consequently, captive breeding is being considered as an economically and conservational sustainable alternative. To support such initiatives, it is essential to conduct research and conservation studies to gather valuable information that can contribute to zotechnical and clinical approaches (Bonilla-Morales *et al.*, 2013; Lourenco *et al.*, 2008).

Approaching and managing *Cuniculus paca* can be challenging due to their aggressive behavior, necessitating the use of pharmacological means for restraint (Uscategui *et al.*, 2021). In such cases, a comprehensive monitoring system is crucial to ensure the animals' vital functions are closely attended to (Uscategui *et al.*, 2021; Uscategui *et al.*, 2019; Uscategui *et al.*, 2016; Almeida *et al.*, 2019). Among the physiological variables, blood pressure is of utmost importance as it provides valuable insights into hemodynamic function, allowing for the early detection and management of hypotension, a common anesthesia complication that can have adverse effects on the animal's health (Gaynor *et al.*, 1999; Grandy *et al.*, 1987; Bijker *et al.*, 2007).

There are two main methods for measuring blood pressure: invasive and non-invasive. The invasive method involves catheterization of a peripheral artery to directly measure systolic and diastolic pressures and accurately estimate mean arterial pressure. However, this method can carry complications such as infections, thromboembolism, and necrosis, and it requires preparation and experience from the operator. On the other hand, the non-invasive method utilizes electronic devices such as vascular Doppler or electronic oscillometric devices. The oscillometric method is an easily applicable and automatic non-invasive alternative that is properly used in humans and has been studied in multiple animal species, although the results regarding its accuracy have been controversial (Binns *et al.*, 1995; Aarnes *et al.*, 2012; Aarnes *et al.*, 2014; Vachon *et al.*, 2014).

To date, no studies have reported whether blood pressure measured using non-invasive techniques is reliable in any neotropical rodent. Therefore, there is scientific and clinical interest in determining the validity of oscillometric non-invasive blood pressure measurements in *Cuniculus paca* under general anesthesia.

MATERIAL AND METHODS

Animals and ethical aspects

Ethical approval for this study was obtained from the institutional ethics committee (CEUA) of FCAV-Unesp, under protocol number 027420/11. Eight healthy adult female *Cuniculus paca*, aged over seven months with an average weight of 9.3 ± 0.9 kg, were selected based on their health records, general inspection, behavior analysis, and weight measurement. These animals are housed in the Sector of Wild Animals of the Animal Science Department at FCAV-Unesp and are registered with IBAMA as breeders of Brazilian wildlife specimens for scientific purposes, with registration number 482508.

Experimental protocol

The animals were kept in specialized enclosures designed to accommodate their natural habits and were individually identified using a microchip inserted into the subcutaneous tissue of the scapula. These animals were already adapted to captivity and provided with ad libitum access to food (rodent food, fruits, and vegetables) and water. Each animal underwent the experimental protocol on three different occasions, with a 15-day interval between sessions. They received one of three intraoperative analgesic treatments, tramadol, methadone, or a control treatment, randomly assigned as described in a previous anesthetic study (Uscategui *et al.*, 2021).

The animals were not fasted due to the anatomical and metabolic rodents' characteristics. On the day of the experimental procedure, animals were captured and physically restrained using a net appropriate for their size. Immediately, were administered a combination of 0.5 mg/kg of midazolam and 25 mg/kg of ketamine intramuscularly (IM). Once lost postural reaction and motor response to manipulation, were transported in boxes to the research center and positioned in a supine position on a surgical table covered with absorbent cloth and thermal insulation to prevent humidity and hypothermia.

At this point, hair removal and aseptis of the skin were performed for the insertion of two 22G catheters. One catheter placed in the "dorsal metatarsal artery", located on the cranial face of the pelvic limb at the height of the tarsus, and the other in the "cephalic vein". The arterial catheter was connected to a calibrated pressure transducer and positioned at the height of the heart (Modulo IBP Plus® Dixtal Biomédica, Brazil), which was coupled to the multiparameter monitor (Monitor DX2023®, Dixtal Biomédica, Brazil) for invasive measurement of systolic (iPAS), mean (iPAM) and diastolic blood pressure (iPAD) in mmHg. Additionally, a constrictor bracelet, with a width of 40 to 50% of the limb's circumference and an appropriate length, was placed around the right

anterior limb between the elbow and the carpus. The oscillometric sphygmomanometer of the multiparameter monitor was connected to this bracelet for the non-invasive measurement of systolic, mean, and diastolic blood pressure (NiPA) in mmHg (Figure 1).

The oscillometric monitor was programmed to automatically measure blood pressures every 5 minutes, emitting an audible warning to indicate that made a successful measurement. At that moment, the evaluator recorded both the invasive and non-invasive blood pressures, from the first successful measurement until the end of the surgical procedure. After the placement of monitoring sensors, induction of general anesthesia was performed, and anesthesia was maintained using inhalation of isoflurane diluted in 0.2 L/kg/min of oxygen through a face mask connected to a circular circuit, adjusting the concentration as needed to maintain the desired anesthetic plane. Once the anesthetic plane was achieved, the animals received opioid analgesia, and laparoscopic follicular aspiration was initiated after a 10-minute waiting period (Barros *et al.*, 2016).

Upon completion of the surgical procedure, analgesic supplementation with tramadol at a dosage of 5 mg/kg was administered. Five minutes later, the administration of isoflurane was discontinued, and the animals were repositioned in the left lateral recumbency while continuing oxygen inhalation. All monitoring instruments and catheters were removed, and the animals received intramuscular administration of 20,000 IU/kg of penicillin, 2 mg/kg of dihydrostreptomycin, and 0.2 mg/kg of meloxicam. Subsequently, the animals were transferred to the recovery room and were continuously monitored until they regained the ability to walk. Once recovered, were placed in individual pens within the enclosures, which were equipped with hay, food, and water. After 24 hours, were released into a collective pen and treated daily with 0.2 mg/kg of meloxicam administered intramuscularly using a remote injection applicator for fifth days. General and behavioral inspections were conducted on each animal for 15 days to assess their health status and ensure satisfactory recovery.

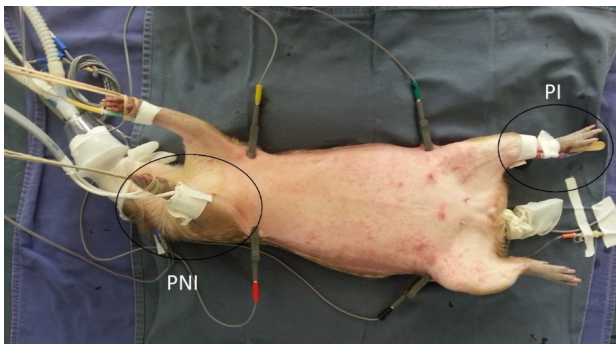


Figure 1. Sensors placements for the monitoring of blood pressures by the invasive (iP = PI) and non-invasive (NiPA = PNI) methods in *Cuniculus pacas* under general anesthesia.

Source: author's collection.

Statistical analysis

The statistical analysis was performed using R software (R® Foundation for Statistical Computing, Austria). The collected variables of invasive and non-invasive blood pressures were initially subjected to distribution validation (Shapiro-Wilk test) and subsequently their compared using the t-Student test and correlated by Pearson test. Additionally, the Bland-Altman analysis was conducted to determine the accuracy and bias of the non-invasive measurements compared to the invasive measurements. A significance level of $P < 0.05$ was considered for all tests.

RESULTS

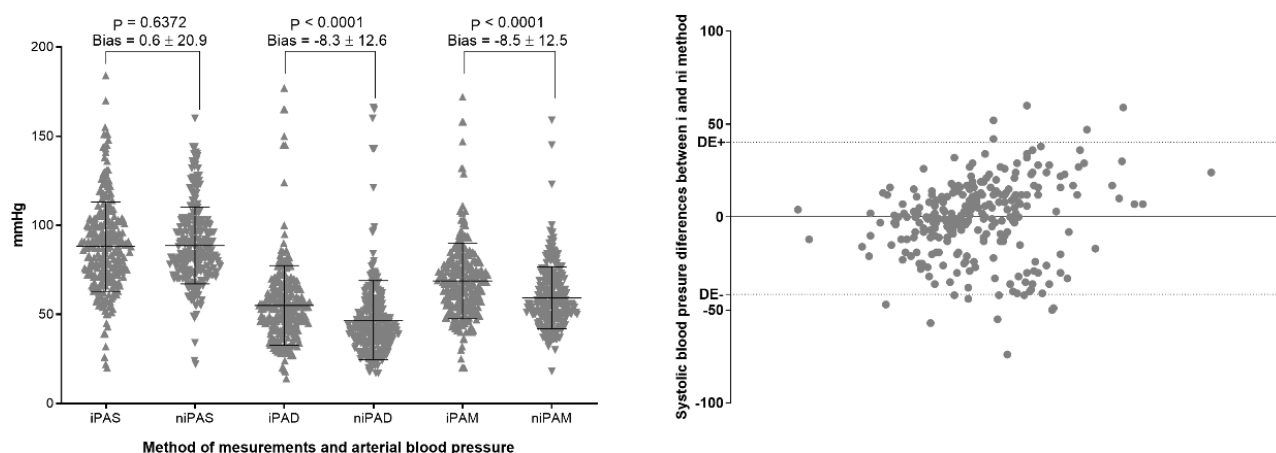
The surgical and anesthetic procedures were successful in all the animals, and there were no complications that posed a risk to their well-being. In the *Cuniculus paca* individuals studied, the systolic arterial blood pressure measured by the oscillometric method yielded similar values to the invasive method ($P = 0.6372$), with a moderate correlation ($r = 0.5969$). This indicates that the non-invasive method provides a reliable measurement of systolic arterial blood pressure, with a low bias (0.59 ± 20.9 mmHg) (Figure 2). The mean and diastolic arterial blood pressures measured by the oscillometric non-invasive method differed significantly from those measured by the invasive method ($P < 0.0001$), resulting in an underestimation of mean and diastolic pressures (-8.25 ± 12.6 mmHg and -8.52 ± 12.47 mmHg, respectively).

In 109 (40%) of the 275 paired measurements, hypotension was observed, defined as invasive systolic blood pressure (SAP) < 80 mmHg (Ruffato *et al.*, 2015). On the other hand, hypertension, defined as invasive SAP > 140 mmHg (Acierno *et al.*, 2018), was observed in 12 (4%) of the 275 paired measurements. The pressure measured over time in studied animals can be seen in Table 1.

DISCUSSION

The findings of our study parallel those from research conducted on domestic cats. When comparing arterial blood pressure measured by non-invasive oscillometric and invasive methods, researchers concluded that there is a good correlation in systolic blood pressure regardless of sex. However, there are divergent results for mean and diastolic blood pressures, particularly in small-sized animals, which may be attributed to the strength of pressure on the skin (Binns *et al.*, 1995).

Similarly, in domestic dogs, the oscillometric method is considered reliable for measuring systolic blood pressure in anesthetized animals of medium to large size, but it may not be reliable for small-sized or awake animals, as well as for diastolic and mean pressures. This finding is also associated with the strength of the skin's pulse (Vachon *et al.*, 2014). Although we couldn't compare the



iPAS: Systolic blood pressure using the invasive method; iPAD: Diastolic blood pressure by invasive method; iPAM: Mean blood pressure by the invasive method; niPAS: Systolic blood pressure using the non-invasive method; niPAD: Diastolic blood pressure using the non-invasive method and niPAM: Mean blood pressure using the non-invasive method

Figure 2. Left: Graphic representation of the systolic (S), diastolic (D) and mean (M) arterial blood pressures (PA), measured by the invasive (i) and non-invasive oscillometer (ni) methods in *Cuniculus paca*. Right: Graphic distribution of Bland-Altman from the invasive (i) and non-invasive (ni) systolic arterial blood pressure.

size or weight of our *Cuniculus paca* animals as they were a homogeneous group (9.2 ± 0.9 kg), it is worth noting that the pulse pressure was easily palpable and occasionally visible in these animals.

Another critical factor in non-invasive blood pressure monitoring is the position of the bracelet. For example, in foals, different monitors showed varying reliability depending on whether the bracelet was placed over the coccygeal artery or the dorsal metatarsal artery (Giguère *et al.*, 2005). These foals were larger than our *Cuniculus paca*, with an average weight between 32 and 61 kg. Hence, it can be concluded that oscillometric pressure measurement is reliable, with a correlation coefficient ($r=0.47$) similar to our research findings.

In recent years, high definition oscillometers have been developed, theoretically improving the accuracy of blood pressure measurements in small animals. These devices have shown promising outcomes, including on wild animals such as *Acinonyx jubatus* (Sadler *et al.*, 2013), with respect to mean pressure; however, the bias (-1.2 mmHg) observed in these devices is not less than the bias in our study.

There are only a few studies assessing non-invasive blood pressure monitoring in wild or exotic species. For example, accuracy in measuring systolic pressure using a Doppler device has been reported in anesthetized rabbits (Harvey *et al.*, 2012), and in cheetahs, the accuracy of systolic pressure measurement using an oscillometric device has also been reported (Sadler *et al.*, 2013). However, in other species such as *Boa constrictor*, oscillometric blood pressure monitoring has been found to be unreliable (Chinnadurai *et al.*, 2009). Similar findings have been reported in camels (Aarnes *et al.*, 2012) and domestic ruminants in general (Aarnes *et al.*, 2014), highlighting the species-specific

nature of these techniques and the need for further studies in different animal species.

Information on non-invasive blood pressure monitoring in rodents is even more limited, with one study evaluating and comparing the oscillometric method via telemetry in mice (Whitesall *et al.*, 2004), this study concluded that the non-invasive method is not reliable when measuring pressures above the normal range but is considered reliable within the normal range. In our study, arterial hypotension and hypertension were observed, and these clinical conditions, common in anesthesia, did not appear to alter the accuracy of the oscillometric method.

Based on our analysis, we can conclude that in *Cuniculus paca*, monitoring systolic arterial blood pressure using the non-invasive oscillometric method, with the bracelet placed on the radial artery between the elbow and the carpus of the animal, provides a valid and reliable measure for monitoring this species under general anesthesia.

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Table 1. Paired pressure values of standardized time evaluations measurement in eight adults female *Cuniculus paca* submitted to follicular aspiration under general anaesthesia. iPAS: Systolic blood pressure using the invasive method; iPAD: Diastolic blood pressure by invasive method; iPAM: Mean blood pressure by the invasive method; niPAS: Systolic blood pressure using the non-invasive method; niPAD: Diastolic blood pressure using the non-invasive method and niPAM: Mean blood pressure using the non-invasive method.

Paca	1					2					3					4								
	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD				
15	87	48	64	127	46	73	75	55	65	117	56	76	56	81	36	51	39	18	30	55	18	36		
20	88	61	65	127	46	73	82	54	68	118	56	77	50	47	29	44	45	20	32	55	18	36		
25	81	46	61	121	40	67	88	62	75	123	61	82	39	36	23	35	70	30	45	71	20	37		
30	117	77	94	125	48	74	66	46	56	104	45	65	83	71	54	71	104	58	75	99	53	68		
35	108	72	89	128	74	92	104	82	94	137	77	97	97	86	65	84	91	48	63	91	45	60		
40	122	77	97	139	65	90	100	73	86	126	67	87	87	77	65	80	145	65	96	128	73	91		
45	91	55	70	140	70	93	94	68	83	123	64	84	91	64	55	71	43	37	42	100	48	65		
50	95	56	72	125	34	64	82	61	71	123	64	84	77	53	41	54	71	58	65	100	48	65		
55	91	82	85	132	41	71	87	66	76	119	73	88	83	60	43	56	78	58	68	111	49	70		
60	96	68	80	132	43	72	103	74	88	133	78	96	72	50	37	50	74	53	62	101	40	60		
65	90	79	84	140	53	82	91	66	79	121	72	88	80	57	38	53	75	50	59	99	38	58		
75	62	61	56	136	54	81	90	60	73	126	66	86	66	42	37	50	90	44	63	73	60	64		
Paca	5					6					7					8								
Paca	5					6					7					8								
	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS	niPAD	iPAS	iPAD	iPAM	niPAS
15	90	44	63	73	60	64	84	45	62	86	42	57	118	66	85	102	44	63	59	75	38	50		
20	82	38	56	86	38	54	91	49	67	89	48	61	124	65	87	96	57	70	61	72	35	47		
25	70	32	50	76	32	46	85	48	64	92	46	61	93	46	63	83	38	53	63	81	42	55		
30	86	46	62	83	35	51	91	48	66	91	45	60	62	39	52	70	30	43	57	73	41	52		
35	107	64	85	99	52	68	100	54	73	102	46	65	60	32	47	71	29	43	81	88	55	66		
40	131	79	103	108	68	81	91	45	65	96	48	64	57	49	54	76	33	47	74	91	54	66		
45	126	68	93	110	60	77	76	31	46	77	17	37	78	67	72	69	33	45	75	83	47	59		
50	118	65	87	115	72	86	136	80	101	76	23	41	65	53	61	73	34	47	60	78	40	53		
55	103	57	77	101	51	67	120	69	90	68	29	42	64	57	61	83	57	66	63	81	42	55		
60	96	55	73	98	47	64	107	61	79	100	56	71	63	53	58	89	52	64	66	81	42	55		
65	93	51	68	94	39	57	105	61	76	85	36	53	55	43	49	80	40	53	51	70	28	42		
75	103	58	76	103	60	75	103	54	73	91	47	62	79	31	47	65	25	39	54	74	33	47		

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