Invasive blood pressure measurement in
anaesthetised horses: a clinical and an experimental study.

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This thesis is presented for the degree of Research Masters with Training (RMT) of
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Declaration

I declare that this thesis is my own account of my research and contains as its main content, work which has not previously been submitted for a degree at any tertiary education institution.

Chapter three and four are articles published in peer-reviewed scientific journals. I am the primary author of these manuscripts, although they were written under the guidance of my principle supervisor and co-authors. The study design, experimental research and data analysis was primarily undertaken by myself with assistance from my principle supervisor and other co-authors.

Chapter three and four have been published in Veterinary Anaesthesia and Analgesia. As a result, formatting was performed according to the publication guidelines for this Journal and may differ from remaining thesis.

Ethical approval for the research outlined in chapters three and four of this thesis was granted by Murdoch University Animal Ethics Committee with Permit numbers R2798/15 and R2861/16 respectively.

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Statement of contribution

Paper 1

Agreement between invasive blood pressure measured in three peripheral arteries in anaesthetized horses under clinical conditions.

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## Agreement between invasive blood pressure measured centrally and peripherally in anaesthetized horses.

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Abstract

General anaesthesia of horses is associated with an increase in mortality and morbidity in comparison to other species. The association between the development of hypotension and major anaesthetic complications is well documented. Thus, the recommendation to monitor and treat hypotension is based on measuring pressure directly from a catheter inserted in a peripheral artery.

Although invasive blood pressure (IBP) is considered the gold standard in blood pressure measurement, it is unknown whether pressure measured in different peripheral arteries is uniform across the various sites. It is also unknown whether pressure at these peripheral sites are indicative of the central pressures, which govern perfusion to the vital organs.

Objectives

1. To determine agreement between invasive blood pressure measured in three peripheral arteries in anaesthetized horses undergoing elective surgery.
2. To determine the agreement between invasive blood pressure measured in the facial and the metatarsal artery with the carotid artery and to evaluate the effects of two haemodynamic conditions on this agreement in anaesthetised horses.

Methods

The first objective was achieved using clinical cases undergoing anaesthesia for elective surgery. Invasive blood pressure was measured simultaneously in one of the
following three combinations: i) transverse facial and facial artery; ii) transverse facial and metatarsal artery and iii) facial and metatarsal artery. The agreement in blood pressure measured for each combination was performed in six horses, three positioned in dorsal recumbency and three positioned in lateral recumbency as determined by a balanced incomplete block design. At each sample time, systolic (SAP), mean (MAP) and diastolic (DAP) arterial pressures were measured concurrently in each artery and the mean of three consecutive measurements was recorded. Position of horse, heart rate and the use of dobutamine were also recorded. Bland Altman analysis was used to assess agreement between sites.

The second objective was achieved using a non-recovery experimental model. Horses were anaesthetised and positioned in dorsal recumbency. Invasive blood pressure was measured simultaneously via catheters placed in the facial, metatarsal and carotid artery. Cardiovascular function and agreement between arteries was assessed before and during administration of phenylephrine and sodium nitroprusside. Phenylephrine and sodium nitroprusside were administered until carotid mean pressure (MAPc) increased or decreased from baseline (65 ± 5 mmHg) to > 90 mmHg or < 50 mmHg, respectively. The order of phenylephrine and sodium nitroprusside was balanced and allocated randomly by selecting the protocol from sealed envelopes on the day of the study. Data recorded at each sample time included systolic, mean and diastolic pressure for carotid (c), facial (f) and metatarsal (m) artery as well as cardiac output (Qt) and systemic vascular resistance (SVR). Bland-Altman analysis was used to assess agreement between peripheral and central sites and regression analysis was used to determine influence of Qt and SVR.
Results

In the clinical study, a total of 54 paired measurements were obtained, with 18 paired measurements from each combination. All paired measurements showed poor and haphazard (non-systematic) agreement. The widest limit of agreement (LOA) was 51 mmHg for SAP measured in the facial artery and metatarsal artery with a bias of -11 mmHg. The smallest limit of agreement was 16 mmHg for MAP measured in the transverse facial and the metatarsal artery with a bias of 1 mmHg.

In the experimental study, a total of 96 paired measurements were obtained between peripheral arteries and the carotid artery. The largest difference was observed in the SAP of the carotid and the metatarsal arteries with a bias (LOA) of 2 (-15 to 19) mmHg. The bias (LOA) for MAP between the carotid and the facial arteries was 2 (-4 to 9) mmHg and for MAP between the carotid and metatarsal arteries was 5 (-4 to 14) mmHg. The best agreement for DAP was seen between the carotid and the facial arteries with a bias (LOA) of 1 (-3 to 5) mmHg. Regression analysis indicated marginal influence of Qt on agreement between MAPc and MAPf and little influence of systemic vascular resistance.

Conclusion and clinical relevance

There was poor and haphazard agreement for SAP, MAP and DAP measured in each pair of peripheral arteries in the clinical study. This was supported by the results of the experimental study. These results show that blood pressure measured in different peripheral arteries cannot be used interchangeably. This has implications for studies that use IBP as an outcome variable and studies determining agreement
between non-invasive blood pressure and IBP measurements in horses under general anaesthesia.

In the experimental study MAP and DAP of the carotid was generally higher compared to the peripheral arteries. Thus, measurement of blood pressure in peripheral arteries may lead to overzealous treatment of hypotension, albeit maintaining central pressures. The best agreement observed with the carotid artery was the facial artery. Cardiac output and systemic vascular resistance did not largely influence the difference between sites.
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Chapter One

Literature review

1.1 Introduction

The importance of monitoring blood pressure in anaesthetized horses is well established (Martinez et al. 2005). Hypotension may be associated with tissue hypoperfusion and hypoxia, which can result in post-anaesthetic myopathy (PAM). When severe, PAM can prevent the horse from standing, warranting euthanasia. In less severe cases, the resultant uncoordinated attempts by the horse to stand can increase the risk of fractures in the recovery period and due to the presence of myoglobinaemia, can predispose the animal to acute kidney injury (Grandy et al. 1987; Johnston et al. 2002).

To ensure adequate blood pressure and thus perfusion of vital organs and skeletal muscles, monitoring is vital, and the measurements gained must be accurate. Invasive blood pressure (IBP) is the current reference technique when measuring blood pressure. However, there are many technical factors that could interfere with the accuracy of values obtained using this method. In particular, there is evidence that the site used for IBP measurement affects the measurements obtained.

The following literature review will provide an overview of the physical principles of blood pressure and how it is measured. It will detail the components of the invasive arterial blood pressure measurement system and the technical factors that can affect accuracy of such systems. Physiological phenomena that can affect readings
will also be discussed. A brief review on the literature investigating invasive blood pressure measured at different sites between the species will conclude the review.

1.2 Principles of arterial blood pressure measurement

Invasive blood pressure can be measured in horses directly via an arterial catheter placed in various peripheral arteries including the facial, transverse facial artery or the metatarsal artery. In horses, catheterization of a peripheral artery is relatively easy to perform due to the thin skin and superficial nature of the vessels. The catheter is connected via fluid filled tubing to a pressure transducer. The pressure transducer converts the mechanical energy of the blood pressure in the artery to an electrical signal which then undergoes processing to produce a waveform that is displayed on a monitor. The waveform that is generated is a representation of the multiple pulse waves within the artery and the measured values associated with this waveform are the systolic, mean and diastolic arterial pressures (Fig. 1.1). Mean arterial pressure is considered to be the driving pressure that determines perfusion of vital organs and major muscle groups. Hence it is seen as the most important of the three values and is used to guide therapeutics. Monitoring invasive blood pressure allows beat by beat measurements, pulse contour analysis and arterial blood sampling and blood gas analysis (Jones & Pratt 2009; Romangnoli et al. 2011). To have a deeper understanding of the generation of the arterial pressure waveform and associated measurements, we first need to understand how pressure is generated in the body.
1.2.1 What is blood pressure?

Pressure is the force (N) exerted per unit area (m²) which is expressed with the derived Le Système International (SI) unit: Pascal (Pa). Blood pressure is the force exerted by blood over the arterial wall area. The non-SI unit, millimetre of mercury (mmHg), remains the universal unit for blood pressure. Arterial blood pressure is influenced by cardiac output, the compliance of the vessel and resistance (or impedance) to flow of blood to the periphery. Another, more clinically useful way to conceptualise blood pressure is as the product of cardiac output multiplied by the systemic vascular resistance (which encompasses both compliance and resistance).

This is a modification of Ohm’s Law, which describes the flow of fluids (Q) through non-distensible tubes. According to Ohm’s law, Q is determined by the driving pressure (P) and resistance to flow (R) and is calculated by the following formula:

\[ Q = \frac{P}{R} \]

**Cardiac output**

Cardiac output (Qt) is defined as the volume of blood moving through either side of the heart in one minute and is usually measured in litres per minute (L min⁻¹). It is calculated from the following formula:

\[ Qt (L \text{ min}^{-1}) = \text{stroke volume (SV)} \times \text{heart rate (HR)} \]

Stroke volume is the volume of blood ejected by the heart during one heart beat and is calculated as end diastolic volume - end systolic volume within the left ventricle.
Any factor that alters the heart rate or stroke volume of the horse will affect cardiac output and thus blood pressure.

**Heart rate**

The rate at which the heart beats per minute can influence the cardiac output in a linear fashion. However, although increasing the rate can increase the cardiac output at supramaximal heart rates cardiac output can be reduced, as the time for filling of the heart during diastole is reduced and thus stroke volume and cardiac output is reduced. The autonomic nervous system regulates the heart rate, with predominance of the sympathetic nervous system resulting in an increase in heart rate and predominance of the parasympathetic nervous system resulting in a decrease in heart rate. The heart rate of a horse is inherently low due to parasympathetic dominance. Under anaesthesia this low heart rate persists, and unlike small animal patients, heart rate rarely changes unless certain disease processes (hypovolaemia, electrolyte abnormalities etc.) or administration of certain drugs (vasopressors, inotropes, anticholinergics etc.) cause deviations either side of this normal heart rate.

**Stroke volume**

Stroke volume is influenced by myocardial contractility, preload and afterload. Myocardial contractility describes the inherent ability of the cardiac muscle to contract and eject a stroke volume at a given afterload and preload. The ultimate determinant of contractility is the shortening capability of the myosin cross bridges of the sarcomeres which is determined by the rate and extent of calcium activation,
the cross-bridge turnover and the relative calcium responsiveness of the sarcomeres (Solaro 2011). Under general anaesthesia, there is direct myocardial depression from both injectable and inhalation agents, all reducing contractility of the heart causing a decrease in cardiac output.

Preload is defined as the initial stretching of the myocardium prior to ejection and is affected by factors that alter the volume of blood in the ventricle at end of diastole (end-diastolic volume) and the compliance of the myocardium. Factors that influence end diastolic volume include blood remaining after previous systole (and thus contractility and afterload), volume of blood entering ventricle during diastole, which in turn is affected by venous return, atrial contraction and time available for filling (heart rate). An intrinsic property of myocardial cells is that the force of their contraction depends on the length to which they are stretched: the greater the stretch, the greater the force of contraction (Frank-Starlings Law of the heart). Increased stretch will cause an increase in the distension of the ventricle and will therefore result in an increase in the force of contraction and thus cardiac output. However, excessive distension reduces contractility due to insufficient overlapping of actin and myosin (Vincent 2008). During anaesthesia, reduction in preload is most commonly due to decrease in venous return. This can be caused by pre-existing disease states such as sepsis or endotoxaemia, surgical blood loss, mechanical ventilation and the effects of anaesthetic drugs on venous tone. Certain positions under anaesthesia, for instance the reverse Trendelenburg utilised during dystocia, can also severely reduce venous return to the heart causing a decrease in cardiac output.
Afterload is the load that the heart must eject blood against and is closely related to the aortic pressure and the thickness of the heart muscle wall. Afterload increases when aortic pressure and systemic vascular resistance (or impedance) are increased, causing an increase in end systolic volume and decrease in stroke volume.

**Systemic vascular resistance**

As mentioned previously, blood pressure is the product of cardiac output and systemic vascular resistance. Systemic vascular resistance (SVR) is the sum of all the resistance in the circulatory system.

The resistance to blood flow is determined by blood vessel geometry (radius, length, elasticity) and characteristics of the fluid, especially blood viscosity ($\eta$) and can expressed by Hagan-Poiseuille’s Law which states:

$$ R \propto \frac{\eta L}{r^4} $$

Where, vessel resistance ($R$) is directly proportional to the length ($L$) of the vessel and the viscosity ($\eta$) of the blood, and inversely proportional to the radius to the fourth power ($r^4$). Viscosity is a direct function of the forces acting horizontally on the flow of blood (sheer stress) and inversely related to the varying velocities of the blood flowing downstream (shear rate or velocity gradient of the red blood cell) and can be described according to:

$$ \eta = \text{shear stress (dyn cm}^{-2})/\text{shear rate (s}^{-1}) $$
Shear rate is determined by the diameter of vessels. A high shear rate is present when flow is fast and the vessel diameter small, and low shear rate is present when flow is slow and the vessel has a large diameter. Furthermore, when shear rate is high, the erythrocytes are deformed to optimally adapt to flow conditions. In normal circumstances, in capillaries, high shear rates occur and blood viscosity is low.

Viscosity of the blood is determined by the shear rate as well as temperature, and the elements found in plasma i.e. white blood cells, red blood cells and platelets. However, the biggest determinant of blood viscosity is the concentration of red blood cells, or the haematocrit. Increased blood viscosity occurs during times of haemoconcentration (dehydration, splenic contraction etc.), while decreased blood viscosity occurs when dilution of red blood cells occurs in anaemic states or following fluid administration.

As the radius of the vessel has a large impact on resistance, systemic vascular resistance is affected by the predominant vessel tone. Thus, states of vasoconstriction or vasodilation will affect SVR and in turn systemic blood pressure.

The arterioles are muscular and of small diameter so contribute the most to SVR.

General anaesthesia using inhalational anaesthetic agents can produce vasodilation which decreases SVR. This, in conjunction with the decrease in contractility due to the depressant effects of the anaesthetic agents, cause the majority of the decrease in cardiac output and subsequently hypotension seen under anaesthesia in horses.

As it is not possible to measure resistance directly, systemic vascular resistance can be calculated using the modification of Ohm’s law:

\[
\frac{Aortic - Right\ atrial\ mean\ pressure}{cardiac\ output} = \frac{\text{dynes}^{-1}\ \text{sec}^{-1}\ \text{cm}^{-5}}
\]
However as it is difficult to measure right atrial and aortic pressure clinically, systemic vascular resistance can be estimated by measuring cardiac output (Qt), mean arterial pressure and central venous pressure (CVP)

$$SVR \text{ (dynes second cm}^5) = 80 \left( \frac{\text{MAP} - \text{CVP}}{\text{Qt}} \right)$$

**Compliance of the vessel**

The compliance of the arterial blood vessel wall is determined by the elasticity or stiffness and thickness of the wall and can be described as

Compliance = change in volume/change in pressure

The change of the elastic properties along the aorta in the horse has been recently described, with a decrease in compliance as the age of the horse increased (Endoch et al. 2017). However these changes have not been investigated in the peripheral arteries. Vessels that have less elasticity would result in higher pressures due to the decreased in compliance.

The relationship between vessel pressure, vessel diameter and wall thickness vs tension in the vessel wall can be described by Laplace law which states:

$$P = 2HT/r$$

Where P is transmural pressure, H is the stress on the membrane wall, T is the wall thickness and r is the radius of the vessel.
**Impedance**

It is important to note, that the laws and equations described above are only relevant to non-pulsatile, laminar fluid flow. In reality, blood flow and the associated blood pressure are much more complex (see section 1.2.2 below). As such, impedance is the more appropriate concept for defining the opposition to blood flow. However, the measurement of resistance is simpler and therefore still remains the most common measure used to represent the forces opposing blood flow in clinical and experimental veterinary studies.

1.2.2 The blood pressure waveform

The physical principles that govern the fundamentals of blood pressure and flow are usually classified according to a Windkessel model in which resistance and compliance are fixed, or binary along the length of the arterial tree (Nichols & O’Rourke 1998). This is a simplistic way of looking at a complex biological system.

A distributive system in which variations in pressure, flow and vessel geometry occur along the circulatory system is more appropriate when understanding the mechanics of the circulation and generation of the pressure waveform. Accurate representation of this pressure waveform is essential in any blood pressure measurement system.

**Generation of the pressure waveform**

The systemic arterial waveform results from the ejection of blood from the left ventricle into the aorta during systole, followed by peripheral arterial runoff of this
stroke volume during diastole. The intrinsic nature of the cardiovascular system allows the even distribution of the ejected blood along the length of the whole arterial tree. Wave reflection at each branching artery causes a fraction of the forward traveling pulse wave to be reflected back towards the heart, where is summated with the forward traveling waves (Dart et al. 2001). The steep upstroke on the pressure waveform (Figure 1.1) coincides with the period of ventricular ejection (systole). The downstroke represents the peripheral run off and occurs during period of ventricular relaxation and filling (diastole). The downstroke can be interrupted by reflected pulse waves particularly in the pressure waveforms generated close to the heart.

The pressure waveform can be used to obtain a variety of different information. Systolic arterial blood pressure (SAP) represents the maximum pressure of the waveform and diastolic arterial blood pressure (DAP) represents the minimum. The mean arterial pressure (MAP) is calculated either by the area under the arterial pressure waveform or use the equation \( \text{MAP} = \text{DAP} + \frac{\text{SAP} - \text{DAP}}{3} \). The shape and area under the pressure waveform can be used to measure or calculate other cardiovascular parameters using mathematical algorithms. This forms the basis of pulse waveform analysis.
When interpreting the measured arterial pulse wave and associated pressure readings of this complex system, it is important to understand that the blood pressure waveform generated at an exact point is a summation of the forward and reflected waves at that point. Thus, the resulting waveform will differ along the arterial tree producing waveforms represented in the Figure 1.2. These differences can result in different measurements of pressure, particularly SAP and DAP, along the arterial tree.
Components of the pressure waveform

As discussed earlier, the pressure wave is a summation of forward moving waves in combination with reflected waves. As a result, the arterial pressure waveform is a periodic complex wave, which may be considered to be the sum of a series of overlapping sine waves of different frequencies, amplitudes, and phase relationships (Thomas & Duffin Jones 2015).

Fourier analysis within the microprocessor of the arterial blood pressure monitor converts a complex waveform into its component sine waves (see Figure 1.3).
Figure 1.3

Arterial blood pressure waveform produced by summation of sine waves. The fundamental wave (top) added to the second harmonic wave (middle) resulting in the pressure wave (bottom) that resemble an arterial blood pressure waveform. (Source: Mark JB: Atlas of Cardiovascular Monitoring Fig. 9-1)

The fundamental frequency (f) is the most basic sine wave component common to the invasive blood pressure measurement system and blood flow itself and is equal to the heart rate. The second harmonic has a frequency twice that of the fundamental harmonic. As the frequency of the harmonics increase, their amplitude decreases. Thus, higher order harmonics contribute least to the shape of the arterial pressure wave, and the pressure wave can be reliably reconstructed from the first ten harmonics (Thomas & Duffin-Jones 2015). The fundamental frequency of the pressure waveform is one factor that determines the accuracy of pressure measurement system.
1.2.3. Components of direct measurement system

The fluid filled haemodynamic monitoring system is the most common and clinically used technique for measuring invasive blood pressure. The components of an intra-arterial monitor using a pressure transducer are as follows:

(Source: https://www.slideshare.net/drurehman/invasive-blood-pressuremonitoring)

**Catheter**

A catheter or cannula is made of Teflon or polyurethane and is inserted into an artery. Ideally the catheter should have parallel sides and be short in length to ensure accurate transmission of pressure waveform. The risk of thrombus formation is directly proportional to the diameter of the cannula, so occupation of no more
than 10% of vessel lumen is recommended. The use of small gauge catheters can increase damping, which will be discussed later.

**Fluid filled tubing**

The catheter is directly connected to fluid filled tubing which provides a column of non-compressible, bubble free fluid between the arterial blood and the pressure transducer. The tubing should be non-compliant and as short as possible. The fluid filled tubing is then connected to an aneroid manometer or a pressure transducer.

**Pressure transducer**

The arterial pressure transducer is the interface allowing conversion of mechanical energy from the arterial pulse wave to electrical energy. Fluid in the tubing is in direct contact with a flexible diaphragm that is distorted in response to pressure changes. This in turn moves strain gauges in the pressure transducer and is incorporated into the four-resistor arrangement of a Wheatstone bridge containing a null deflection galvanometer. Pressure on the diaphragm causes gauges on one side of the bridge to be compressed, reducing their resistance, whilst on the other side the gauges are stretched, increasing resistance. The bridge becomes unbalanced and the potential difference generated is proportional to the pressure applied and this is measured by the galvometer and is illustrated below.
Figure 1.4

Wheatstone bridge. When \( R_1/R_2 = R_4/R_3 \) there is no potential difference and the bridge is balanced. When \( R_3 \) changes due to applied pressure from the diaphragm, the two sides of the bridge become unbalanced and resulting potential difference is measured by \( V \) (galvometer). (Source: www.instrumentationtoday.com)

Typically, the transducer and fluid filled tubing is also connected to a bag of saline pressurized to 300mmHg allowing continuous flow of 2-4 mL hr\(^{-1}\) to maintain catheter patency. This system allows the performance of a high-pressure flush to check the damping and natural frequency of the system (see later).

**Electrical cable and monitor**

The pressure transducer relays its converted electrical energy signal via an electrical cable to a microprocessor where it is filtered, amplified, analysed and displayed on a screen as a waveform. The waveform graphically depicts the pressure within the artery over time.
1.2.4. Technical factors that affect accuracy of invasive blood pressure measurement

There are certain technical factors that can occur in invasive blood pressure measurement systems. These are due to a certain set of physical laws that governs the behaviour these measurement systems. Theoretically the invasive blood pressure measurement system is a distributed system like the circulatory arterial blood pressure system itself. However, in the clinical setting and for simplicity, it can be approximated by a simple second order system. A second-order system can be characterized by three mechanical factors; elasticity, mass and friction. In a standard invasive blood pressure measurement system, the elasticity is the stiffness of a system produced by the flexibility of the transducer diaphragm and distensibility of the tubing. The elasticity can be altered by the presence of air bubbles and use of compliant tubing. However, too much elasticity, for example using intravenous fluid administration lines, can impact the readings from the system (see section on damping). Mass is produced by the form of fluid, usually in the catheter and interconnecting tubing. The mass of the system can be altered by altering the length of the tubing. Lastly, friction is exerted on the fluid moving within the measurement system with each pulsatile beat, by the catheter and tubing and can be disturbed by the presence of clots (Gardner 1981). The major factors that affect invasive blood pressure readings are damping and resonance.

**Natural frequency and resonance**

Every material has a frequency at which it oscillates freely. This is called the natural frequency. For example, when mass (inertial force) at the end of a spring (elastic
force) is pulled and then is released in a medium (friction force), a series of oscillations are observed from the movement of the spring. The natural frequency (Fn) is the frequency that a material oscillates in the absence of frictional forces.

If the fundamental frequency in the pressure waveform is similar to the natural frequency of the invasive blood pressure measurement system, the signal becomes exaggerated and distorted and will oscillate at its maximum amplitude. This phenomenon is called resonance and will result in erroneously wide pulse pressure and elevated systolic pressures and lower diastolic pressures. Thus, the natural frequency of the measuring system must exceed the natural frequency of the arterial pulse (or the pulse rate) to avoid this. Hence, it is important that an invasive arterial blood pressure system (IABP) has a very high natural frequency. Most measurement systems are designed to have a natural frequency that is 8 times the fundamental frequency of the arterial waveform. For example, if the heart rate of a patient can be up to 180 bpm then the natural frequency is \((180 \times 8)/60\) secs = 240 Hz. For conventional IBP systems a sufficiently high natural frequency cannot be achieved with most systems having a natural frequency of approximately 200Hz. As invasive blood pressure measuring devices are designed for human patients, the natural frequency far exceeds that needed to measure IBP in horses, due to the low heart rates.

Natural frequency of the measurement system can be increased by reducing the dynamic response of the system. This can be achieved by reducing the length of catheter or tubing, reducing the compliance of the catheter or diaphragm, reducing the density of fluid in the tubing and increasing the diameter of the catheter or
tubing. Natural frequency is also increased by the addition of three-way taps, bubbles and clots.

The rapid flush test is a method used to evaluate the dynamic response of a measurement system and determine the natural frequency of the system. This is comparable to standard laboratory square wave testing and will be discussed below. Due to the fundamental frequency being inherently low for measuring blood pressure in horses, the presence of three-way taps, bubbles and clots will greatly influence readings.

**Damping**

Damping is anything that reduces energy in an oscillating system. Damping reduces the amplitude of the oscillations and the natural frequency of a system (Fn), allowing resonance and distortion of the signal. Most damping is caused by friction and viscosity in the fluid pathway. The damping coefficient of a monitoring system is a measure of how quickly the oscillations of a shock-excited system dampen and eventually come to rest. Damping factors between 0.64 and 0.77 are considered optimal for blood pressure monitoring systems. However, this is based on human heart rates (60-100bpm). Optimal damping factors for horses which have a normal heart rate under anaesthesia of 24-48bpm, is not known.
Figure 1.5

The effect of over or underdamping is represented:

Optimally damped: The system responds rapidly to a change in signal by allowing a small amount of overshoot (Damping factor 0.7).

Over-damped: This may be due to soft tubing, a bubble, or a constriction. The signal takes a long time to reach equilibrium but will not overshoot. It may not reach equilibrium in time for a true reading to be given (Damping factor >1.0). Falsely low SAP and high DAP but MAP is preserved.

Under-damped: Resonance occurs causing the signal to oscillate and overshoot (Damping factor <0.7). Falsely high SAP, falsely low DAP and again MAP is preserved.

(Source: https://www.aic.cuhk.edu.hk/web8/haemodynamic%20monitoring%20intro.htm)
1.2.5. Assessment of natural frequency and damping

**Square wave test**

Generation of a square wave by an impulse at the catheter tip is one of the in vitro laboratory verification “gold” standards for the overall determination of dynamic response of a pressure monitoring system. The square waves are generated at the distal catheter orifice and detected by the transducer. The signals generated are recorded on a strip chart recorder from which the natural frequency and damping coefficient are calculated. This method however, cannot be used clinically (Kleinman et al. 1992).

**Fast flush test**

The fast-flush test is the only test that allows clinicians to determine in vivo the natural frequency and damping coefficient of any invasive blood pressure monitoring system from proximal extension tubing to catheter tip. Under most conditions, this method yields results that are essentially identical to those from the standard laboratory square-wave testing. By exposing the system to a sudden pressure change, the signal recorded at the transducer will be a sinusoidal pressure wave of a given frequency and progressively decreasing amplitude (Kleinman et al. 1992).

Briefly, it is performed by rapidly administering saline pressurised to 300mmHg via the flush system of the transducer. This generates an undershoot and overshoot of waves that will decay exponentially in accordance with the damping coefficient. The natural frequency can be measured by dividing the paper speed by the wavelength.
or period generated by the flush. The damping coefficient (B) can be derived from the amplitude ratio (AR) of the two consecutive resonant waves. Amplitude ratio is calculated by dividing the second smaller wave with the first higher wave. Once AR is measured the corresponding B is then determined from a chart (Figure 1.6). Finally, the natural frequency and the AR or the corresponding B can be plotted in a specific graph that shows three areas: adequate dynamic response, overdamping, underdamping (Jones & Pratt 2009; Romagnoli et al. 2014).

**Figure 1.6**

In the catheter-transducer system, the operation and release of the fast flush device produce a square pressure wave followed by a small number of oscillations at the system’s natural frequency. The ratio of adjacent oscillation amplitudes, A₁ and A₂, can be used to calculate damping coefficient by this equation: (Source: Jones A & Pratt O (2009))

\[
\zeta = -\ln\frac{A_2/A_1}{\sqrt{\pi^2 + \ln(A_2/A_1)^2}}
\]
Zeroing and levelling

According to Bernoulli’s principle regarding conservation of energy, the measured pressure (pressure energy) is influenced by the hydrostatic pressure (potential energy), which is produced by gravitational forces and velocity of fluid flow (kinetic energy). According to this principle a change in one energy must be offset by the opposite change in one or both of the other energy components. Thus, an increase in potential energy must be offset by either a decrease in the kinetic energy or a decrease in pressure energy or both. Potential energy within the pressure measurement system is altered by height of the transducer relative to the site of
pressure measurement.

Thus, for a transducer to provide an accurate measure of the pressure in a certain artery, the transducer must be level with that artery. As the pressure within the central conducting vessels is of greater importance to organ perfusion than pressure within a peripheral artery, it is common clinical practice to position the transducer at the level of the right atrium. This is also known as the phlebostatic axis and is accepted as the ideal reference level as it is the point in which blood returns to the heart. This will reduce the effects of gravity and establishes the interface level as the hydrostatic zero reference point. In horses in dorsal recumbancy, this corresponds to the level of the thoracic inlet, and in lateral recumbancy it corresponds to the point of the shoulder. Due to the effect of hydrostatic pressure, changing the transducer 10cm up or down will impart a change of 7.4mmHg, higher if below the heart, and lower if above the heart. To remove the effect of hydrostatic pressure on pressure measurement, the pressure transducer is exposed to atmospheric pressure once it is appropriately positioned and the baseline set to zero.

1.2.6. Physiological factors that affect invasive blood pressure readings

Although the invasive arterial system can be correctly set up, with minimal factors contributing to errors, physiological factors can influence invasive pressure readings leading to discrepancies between actual and measured blood pressure.

**Haemodynamics and shape of the waveform**

Pressure recorded anywhere in the arterial system is the sum of the forward wave and the reflected wave (see Figure 1.8) and is dependent on three factors: the
amplitude and duration of ventricular ejection, the amplitude of the reflected wave and the velocity of the reflected wave from the periphery.

**Figure 1.8**

Arterial pressure waveform showing summation of waves (Source: https://hindawi.com/journals/ijvm/2012/903107/fig1/)

Duration of ventricular ejection is altered by changes in heart rate. A slower heart rate leads to a longer ejection time, increasing the likelihood that the reflected wave will return earlier during the cardiac cycle, thereby augmenting SAP. Conversely an elevated heart rate has a faster ejection period and the reflected wave returns later in the cardiac cycle and thus does not cause elevations in SAP.

Augmentation of the central pressure can be quantified as the amount of pressure added to the systolic pressure peak based on the reflected wave. This pressure is referred to as augmentation pressure, the ratio of augmentation to the central pulse pressure is referred to as the augmentation index and is expressed as a percentage (Nelson et al. 2010). Degree of augmentation will depend on the amplitude and velocity of the reflected wave. Amplitude of the reflected wave is related to the
impedance to pulsatile blood flow by the narrowing and bifurcation of the arterial vessels. Increasing impedance leads to greater backward or retrograde reflection of the pressure wave and thus greater augmentation of the SAP. The velocity of the reflected wave is influenced by the tone in the conducting vessel walls. The faster the velocity, the greater the chance the reflected wave will return earlier in the cardiac cycle and thus the greater the augmentation.

There are varying opinions on what produces the dicrotic notch. Some believe it is due to difference in overlap of the different waveforms produced and this is altered by impedance, others believe the location of the dicrotic notch varies according to the timing of aortic closure in the cardiac cycle (O’Rourke et al 1968; Nichols & O’Rourke 1998). Figure 1.9 illustrates the difference in the shape of the arterial waveforms as the catheter is moved down the length of the arterial tree. This demonstrates the different shape and timing of the dicrotic notch as the distance from the heart increases.
Figure 1.9
The difference in arterial waveforms along the vascular tree.
(Source: http://www.derangedphysiology.com/main/cicum-primary-exam/required-reading/cardiovascular-system/Chapter%207.6.0/normal-arterial-line-waveforms)

Respiratory variation

Beat by beat variation in the pulse waveform occurs with the respiratory cycle.

During normal respiration inspiration causes a negative intrathoracic pressure, pooling blood in the pulmonary circulation and reducing left ventricular preload. This produces a lower stroke volume; hence systolic pressure is reduced during inspiration. Normal fluctuations are between 5-10mmHg. During positive pressure ventilation, increasing alveolar pressure compresses and displaces the pulmonary venous reservoir into the left side of the heart, increasing preload. Simultaneously,
the increase in intrathoracic pressure reduces left ventricular afterload and decreases right ventricular preload by a reduction in venous return from the increase pressure on the caudal vena cava. The initial increase in left ventricular preload (and decreased afterload) produces an increase in left ventricular stroke volume and increase in systemic arterial pressure. Due to reduction in right ventricular preload, the subsequent left ventricular stroke volume falls and systemic arterial pressure decreases, this is called cyclic pressure variation. Normal systolic pressure amplitude can increase by 2–4 mmHg and decrease by 5–6mmHg. Marked depression of systolic pressure associated with mechanical ventilation occurs in hypovolaemic patients. Clinically if respiratory variation is seen, once hypovolaemia is ruled out, an average of pressure readings over several cardiac cycles should be taken. Experimentally invasive pressure readings should be taken during expiratory pauses, to minimize the respiratory effects on the cardiovascular system.

Figure 1.10

Respiratory variation. (Source: https://www.aic.cuhk.edu.hk/web8/haemodynamic_monitoring.htm)
1.2.7. Other artefacts that affect accuracy

**Distance of vessel from the heart/distal pulse wave amplification**

Amplification of blood pressure from the aorta to the periphery occurs as a result of blood travelling from more elastic central arteries to the less elastic narrower peripheral arteries. The combination of the forward and reflected wave increasingly augments the SAP further down the blood pressure is measured in the arterial circuit. Hence peripheral systolic pressures do not accurately represent central pressures in the aorta (McGhee & Bridges 2002; Nelson et al. 2010). The DAP and MAP remain unchanged as illustrated in Figure 1.11.

**Figure 1.11**

Pulse wave amplification (Source: McEniery et al. 2014).
**Movement artefacts**

Motion of the tubing system enhances the fluid oscillations of the system. Although the clinical significance of movement artifact is not known, it is recommended that extrinsic movement of the tubing system be kept at an absolute minimum. In anaesthetised patients this is less of a concern (McGhee & Bridges 2002).

**End hole artefact/position of catheter in vessel**

The arterial catheter of the IBP monitoring system is generally placed so that the catheter is positioned retrograde to the blood flow in the artery with the tip against the blood flow. This is due to the assumption that this pressure is the same as that exerted on the vessel wall. The forward-flowing blood contains kinetic energy and when the flowing blood is suddenly stopped by the tip of the catheter, the kinetic energy of the blood is partially converted into pressure. This converted pressure may add 2 to 10 mm Hg to the systolic pressure measured by an intra-arterial monitoring system. The artificial augmentation of directly monitored systolic pressure by converted kinetic energy is referred to as the end-hole artifact (McGhee and Bridges 2002).

**Attenuation**

Attenuation is not well described in the human literature and is absent in the veterinary literature. The phenomenon of attenuation has been simulated in an electric model of the vascular system with the addition of proximal impedance to the
site of IABP measurement. Investigation of the presence of attenuation has been prompted by the presence of suboptimal readings seen in bubble free, short IBP systems. Ercole (2006) hypothesized that due to attenuation, the IBP waveform may appear similar to that observed with overdamping but differs from overdamping in that the measured SAP and DAP will both be erroneously low.

It is postulated that attenuation is caused by a disturbance or resistance to laminar flow proximal to the catheter that leads to turbulent flow. The physical principles underlying IBP monitoring are based on laminar flow so when turbulent flow is present these principles no longer apply. Disturbance of the laminar flow could be caused by vessel narrowing, for example an arterial spasm, the catheter itself, thrombus secondary to endothelial trauma or any change in vessel geometry due to decreasing systemic vascular resistance.

The distinction between damping and attenuation is of practical importance as the SAP, DAP and thus MAP are underestimated, and this error varies inversely with the peripheral vascular resistance of the tissues distal to the measurement point, therefore apparently magnifying the effect of vasodilation (resulting in decreased SVR) on blood pressure (Ercole 2006). This could lead to overdiagnosis of low blood pressure and inappropriate treatment with vasopressors or inotropes, particularly when low blood pressure is associated with low SVR.

1.2.8. Summary

The invasive blood pressure measurement system is a complex system that relies on microprocessors to produce a waveform and associated values that the clinician can
monitor. The system has to be correctly set up to avoid inaccuracies or errors that might cause erroneous readings. However, physiological phenomena can also cause errors or changes to invasive pressure readings, so the clinician has to be aware of these. In particular, as described above site of measurement can affect the pressure waveform and thus has potential to cause differences in measured pressure when different sites are used.

1.3. Statistical assessment of agreement in blood pressure measurements

Bland-Altman is a method of assessing agreement that uses a visual inspection in conjunction with measurement of bias across measurements. It is commonly used to compare measurements made by two different methods. It is the method most commonly used to compare different methods of measuring BP or for comparing measurements obtained from different arteries. A scatter plot is constructed in which the difference between the two measurements is plotted on the y axis and the average of the two measurements on the x axis. The mean difference in values of the two measurements is referred to as the bias and is represented by a horizontal line on the plot. The standard deviation (SD) of differences between the paired measurements is then used to construct horizontal lines above and below the bias to represent 95% limits of agreement (mean bias ± 1.96 SD) and these are referred to as the upper and lower limits of agreement (LOA) (Chapola et al. 2014; Abu-Arafeh et al. 2015). See Figure 1.11.

Bland Altman analysis requires several statistical assumptions to be met. Normality of the data should be assumed or transformation of the data to account for the variance in the differences is required. The repeatability of the measurements
should be calculated. If poor repeatability is observed, poor agreement will follow. The range of the mean values should also be sufficient as a narrow range of original values will result in agreement being inevitable (Abu-Arafeh et al. 2015).

Interpretation of the Bland Altman plot has several aspects to it.

1) Visual inspection. Bland Altman plots allows any pattern or trends of agreement to be observed. Points distributed in both positive and negative areas of the plot indicate haphazard, or non-systematic agreement. Points can also be distributed to cause a positive or a negative trend to be observed. Distribution of points can also indicate over which ranges of measurement agreement is better. This can then be quantified by separating these measurements and comparing two Bland Altman analyses. Due to the information taken from visual assessment of the plots, it is preferable to assess agreement over a wide range values, so that patterns of agreement can be fully assessed (Giavarina 2015).

2) Bias

When observing the bias, a positive bias indicates that generally the site that is compared against, is being over-estimated by the second site and vice-versa for a negative bias. Bias can also be described as changing when systematic patterns of agreement have been observed. A small bias does not necessarily depict good agreement, as it must be used in conjunction with the LOA.

3) LOA and confidence intervals (CI) of the upper and lower LOA.
Limits of agreement should be established a priori based on clinical necessity, biological considerations or other goals. A marginal bias with small LOA would indicate good agreement between both sites, whilst a marginal bias with wide LOA would indicate poor, non-systematic agreement, as wide LOA indicate poor agreement observed. Perfect agreement is seen when points are plotted on the x axis and would result in a small bias and small limits of agreement (Abu-Arafeh et al. 2015; Giavarina 2015).

In contrast to correlation, which should not be used for assessing method comparability, Bland Altman estimates bias and LOA, hence precision calculation (confidence intervals) of bias and LOA are needed. The CI limits represent the range within which a single, new observation would lie if taken from the same population. The greater the number of samples used for the evaluation of the difference between the methods, the narrower the CI’s will be, both for the mean difference and for the LOAs (Chhapola et al. 2014; Giavarina 2015).

Figure 1.12 is an example of two Bland Altman plots. Plot (a) is an assessment of agreement between the systolic arterial pressure of the carotid artery and the facial artery. The bias is marginal, and the LOA are wide, due to the presence of points both in the positive and negative area of the plot. This results in poor agreement being observed between these two sites. Plot (b) is an assessment of agreement between the mean arterial pressures between the carotid and metatarsal artery. A positive bias indicates, that generally the metatarsal overestimated pressures in the carotid. There is also a changing bias as pressures increase, in contrast to the plot (a)
Figure 1.12

Bland Altman plots of invasive arterial blood pressure

(a) Bland Altman plot of systolic arterial pressure (SAP) between the carotid and facial arteries
(b) Bland Altman plot of systolic arterial pressure (MAP) between the carotid and metatarsal arteries
1.4. Review of studies investigating pressure measured at different arterial sites

Due to the extensive use of invasive cardiovascular measurement techniques in human medicine, there is a large body of research investigating the agreement between blood pressure measured at different peripheral sites and between these sites and central sites. Less information is available in other species.

1.4.1. Human literature

There is conflicting evidence in the human literature as to the agreement between central and peripheral sites with some studies showing good agreement and others poor agreement. Early experimental studies (Nichols & O’Rourke 1998) have observed systolic pressure increasing, with mean and diastolic pressures decreasing along the arterial tree. This phenomenon of systolic amplification has been documented clinically in children with the effects of increasing age decreasing its presence (O Rourke et al. 1968; O’Rourke et al. 2000; Wojciechowska et al. 2012). This is confirmed in a study in adults in which systolic pressures were significantly higher when measured from the femoral vs. radial site (p < .005) (Dorman et al. 1998). Another study also observed poor agreement between these two sites with overall mean bias between radial and femoral for MAP of 4.27 mmHg (LOA: -3.41 to 11.94) (Galluccio et al 2009). However, in another study where agreement was assessed over a wide range of pressures in critically ill patients, the authors claimed there was no difference between the femoral and radial artery across systolic, mean or diastolic pressures even when vasoactive agents were used. Assessment of agreement between radial and femoral for mean arterial pressures produced a bias (precision) of 3 (4) mmHg, which, in light of a calculated LOA, could be interpreted as
poor agreement being observed (Mignini et al. 2006). Due to the inconsistency between studies, there is a lack of consensus as to which peripheral artery reflects central pressure and whether central pressures should be monitored instead of peripheral pressures in humans, particularly if critically ill.

1.4.2. Veterinary literature

The assessment of agreement between IBP measured at different sites is limited to a few veterinary species. One study, in client owned anaesthetised dogs, compared arterial blood pressure measured invasively from one of two pairs of arteries i) the superficial palmar arch and the contralateral dorsal pedal and ii) the superficial palmar arch and sacral artery (Acierno et al 2014). This study also investigated the effect of different body position on agreement between measurements from the different sites. The results demonstrated poor agreement for SAP, DAP and MAP for each pair of arteries, with the worse agreement observed for being measurements from the superficial palmar arch and the contralateral dorsal pedal. The bias (LOA) for systolic arterial pressures obtained when the dogs were in dorsal and lateral recumbency were -16.2 (-43.17 to 11.16) mmHg -14.7 (-43.28 to 13.88) mmHg respectively, illustrating agreement was not significantly altered by changes in body position.

Another study performed in anaesthetised dogs compared blood pressure measured invasively from the carotid, femoral and dorsal pedal arteries (Monteiro et al 2013). In this study 8 different haemodynamic conditions were produced by administration of different pharmacological agents. Fentanyl (infusion or bolus) administration was used to induce bradycardia, noradrenalin (infusion or bolus) was used to cause
hypertension and tachycardia and increasing isoflurane concentrations were used to
induce hypotension. This resulted in a range of alterations in HR and blood pressure.
Cardiac output and SVR was not measured. This study found that in hypotensive
conditions SAP was lower in the peripheries compared to centrally, whereas in
normotensive and hypertensive states SAP was higher in the peripheral arteries
compared to central arteries. Mean and diastolic pressures were lower in peripheral
sites than the carotid during most haemodynamic conditions with the authors
hypothesising that the mean and diastolic pressures are less affected by wave
reflection.

Another study in anaesthetised piglets, compared blood pressure measured in
femoral and carotid arteries when the abdomen was insufflated to 24 mmHg with
carbon dioxide (Aksasal et al 2012). There were no changes associated with
increasing intra-abdominal pressure and their findings were more in line with the
studies in humans describing distal pulse wave amplification with femoral systolic
readings being higher than carotid, with poor agreement between DAP and MAP.

There is limited research investigating agreement between invasive blood pressure
measured both peripherally and centrally in equids, albeit one study in ponies (Gent
et al 2015). In this study, agreement between various peripheral invasive and non-
invasive sites were compared with blood pressure measured invasively from the
central carotid artery, which had been surgically translocated to a more superficial
position. The study was part of a parallel investigation looking at the effects of
dexmedetomidine on MAC of sevoflurane in these ponies. This experimental study
had many limitations including; assessing agreement over a very narrow range of
blood pressure and no assessment of cardiovascular function such as cardiac output and systemic vascular resistance. This study characterised the left metatarsal, left carotid and left facial artery, thus the catheter placed in the carotid artery on the same side as the facial catheter could have affected flow and thus pressure measured from the facial artery. Furthermore, the result published in this paper did not follow the standard Bland Altman reporting hence, their data interpretation may have been incorrect. Bland Altman analysis should be reported in a standardised manner including an a priori decision of acceptable limits of agreement and an estimate of the precision of the limits of agreement including confidence intervals around those limits (Abu-Arafeh et al 2016). In fact, the wide limits of agreement present when comparing the MAP between carotid and facial artery are reported as follows. Saline group bias (LOA) 0.7 (-10.9 to 19) mmHg and dexmedetomidine group 3.3 (-0.5 to 10.2) mmHg with the MAP between carotid and metatarsal artery in the saline group 2.9 (-10 to 15) mmHg and the dexmedetomidine group 4.9 (-0.3 to 10) mmHg. The administration of dexmedetomidine caused improved agreement with the carotid in comparison to saline administration. The authors hypothesised that these observations were as a result of vasoconstriction by dexmedetomidine, increasing the damping of the pressure waves in a smaller vessel further away from the heart. This could also be explained by the phenomena described by Ercole (2006) with less attenuation of the peripheral blood pressure during vasoconstriction

1.5. Conclusion

There is a large gap in knowledge in the area of the assessment of agreement of IBP measured between peripheral sites and between central and peripheral sites, with
only a handful of studies in veterinary species. Moreover, only one study investigated the effect of different haemodynamic states and none of the studies specifically investigated changes in vascular resistance. It is important not to extrapolate research and theories from humans and small animals to horses, due to the large difference in size of the vascular tree.

The effect of site of measurement on measured blood pressure in horses and how it alters in different physiological states has not been studied. Despite this, many clinical and experimental studies have used measurements from different sites interchangeably and many studies have used these different arteries to validate non-invasive blood pressure devices. Furthermore, it is not known whether these peripheral sites reflect pressures in the central circulation.

Understanding the factors that affect the measured blood pressure at different sites will assist with interpretation of blood pressure changes and ultimately improve the management of these changes in equine patients under anaesthesia and help in the development of more accurate non-invasive blood pressure devices.
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Chapter two

Objectives and hypotheses

2.1. Objectives

- To assess agreement between measurements of arterial blood pressure recorded from the facial artery, the transverse facial artery and the metatarsal artery in anaesthetised horses undergoing routine surgery
- To assess the influence of dobutamine and the effect of recumbency on agreement
- To assess agreement between measurements of arterial blood pressure obtained from the peripheral arteries (facial and metatarsal artery) and the carotid artery and between measurements obtained from the facial and metatarsal arteries across a wide range of blood pressure in anaesthetised horses by manipulating systemic vascular resistance using vasoactive agents.
- To determine the effect of cardiac output and systemic vascular resistance on agreement

2.2. Hypothesis

- We hypothesised that agreement between systolic (SAP), diastolic (DAP) and mean (MAP) arterial pressure measured in the transverse facial, the facial and the metatarsal arteries would be poor in the clinical study.
• We hypothesised that position of the horse and the use of dobutamine
  would not influence agreement

• In the experimental study, we hypothesised that agreement would be poor
  between central and peripheral sites

• We hypothesised that changes to systemic vascular resistance and cardiac
  output would influence agreement.
Chapter Three

Agreement between invasive blood pressures measured in three peripheral arteries in anaesthetized horses under clinical conditions

3.1. Abstract

Objective

To determine agreement between invasive blood pressure measured in three peripheral arteries in anaesthetized horses undergoing elective surgery.

Study design

Prospective balanced incomplete block design.

Animals

A total of 18 client owned horses

Methods

Invasive blood pressure (IBP) was measured simultaneously in one of the following three combinations: i) transverse facial and facial artery; ii) transverse facial and metatarsal artery and iii) facial and metatarsal artery. The agreement in blood pressure measured for each combination was performed in six horses, three positioned in dorsal recumbency and three positioned in lateral recumbency. At each
sample time, systolic (SAP), mean (MAP) and diastolic (DAP) arterial pressures were measured concurrently in each artery and the mean of three consecutive measurements was recorded. Position of horse, heart rate and the use of dobutamine were also recorded. Bland Altman analysis was used to assess agreement between sites.

**Results**

A total of 54 paired measurements were obtained, with 18 paired measurements from each combination. All paired measurements showed poor and haphazard (non-systematic) agreement. The widest limit of agreement was 51 mmHg for SAP measured in the facial artery and metatarsal artery with a bias of -11 mmHg. The smallest limit of agreement was 16 mmHg for MAP measured in the transverse facial and the metatarsal artery with a bias of 1 mmHg.

**Conclusion and clinical relevance**

There was poor and haphazard agreement for SAP, MAP and DAP measured in each pair of peripheral arteries in this study. These results show that blood pressure measured in different peripheral arteries cannot be used interchangeably. This has implications for studies that use IBP as an outcome variable and studies determining agreement between non-invasive blood pressure and IBP measurements in horses under general anaesthesia.
3.2. Introduction

The importance of monitoring blood pressure in anaesthetized horses is well established (Martinez et al. 2005). Hypotension may be associated with tissue hypoperfusion and hypoxia which can result in postanaesthetic myopathy. The resultant uncoordinated attempts by the horse to stand can increase the risk of fractures in the recovery period (Grandy et al. 1987; Johnston et al. 2002).

Arterial blood pressure can be measured directly from a catheter placed in various peripheral arteries. The artery used for invasive blood pressure (IBP) measurement in clinical cases is largely dictated by accessibility to the site during the surgery. It is generally assumed that the blood pressure in different arteries is similar. However, poor agreement between IBP measured in different peripheral arteries has been demonstrated in anaesthetized dogs (Monteiro et al. 2013; Acierno et al. 2015). Poor agreement has also been reported between IBP measured in the carotid artery and IBP measured in the facial and metatarsal arteries in anaesthetized ponies; however, agreement between facial and metatarsal arteries was not assessed (Gent et al. 2015).

Inconsistency in blood pressure measured in different peripheral arteries would prohibit interchanging the results of these measurements. This is an important consideration for studies investigating agreement between non-invasive blood pressure (NIBP) and IBP measurement techniques. It is also relevant to the design of studies that use IBP as an outcome variable. To date, no studies assessing agreement of IBP recorded simultaneously in different peripheral arteries in anaesthetized adult horses have been reported. The aim of this study was to quantify agreement
between IBP measured in different peripheral arteries in anaesthetized horses. Based on the studies in ponies and dogs, we hypothesized that agreement between systolic (SAP), diastolic (DAP) and mean (MAP) measured in the transverse facial, the facial and the metatarsal arteries would be poor (Monteiro et al. 2013; Acierno et al. 2015; Gent et al. 2015).

3.3. Materials and Methods

Animals

Eighteen client-owned adult horses with ASA (American Society of Anaesthesiologists) physical status I and II undergoing general anaesthesia for routine procedures at Murdoch University Teaching Hospital were included in the study after obtaining written client consent. A sample size of 18 horses, based on a conservative estimate of only one measurement per horse, was determined to give a 95% confidence interval for the estimation of the limits of agreement (LOA) within ± 0.8mmHg standard deviation (www.users.york.ac.uk/~mb55/meas/sizemeth). The study was approved by The Institutional Animal Ethics Committee (Permit number R2798/15) and was performed in accordance with the Animal Welfare Act of Western Australia.

Study design

A balanced, incomplete block design was used to evenly pair three peripheral sites. Only two sites were measured simultaneously in each horse due to limited access to relevant arteries during some surgical procedures. Thus, three possible pairs (blocks) were created containing six horses: 1) transverse facial (TF) and facial (F); 2) TF and
metatarsal (MT); and 3) F and MT. Within each block, three horses in lateral recumbency and three horses in dorsal recumbency were included, since the position of the horse varied with the surgical procedure. Horses were designated to an appropriate block upon presentation after their positioning was known.

**Anaesthesia**

The horses were fasted for at least 12 hours before induction of anaesthesia with water available *ad libitum*. A catheter was placed in a jugular vein after disinfection and desensitization of the site with lidocaine 2% (1 mL; Ilium; NSW, Australia). Each horse was sedated with xylazine (0.08–1.1 mg kg\(^{-1}\); Ilium, NSW, Australia) intravenously (IV) and five minutes later, anaesthesia was induced with ketamine (2.2–3.0 mg kg\(^{-1}\); Ilium, NSW, Australia) and diazepam or midazolam (0.06–0.1 mg kg\(^{-1}\); Ilium, NSW, Australia) IV administered in the same syringe. Following orotracheal intubation, the horses were hoisted onto a padded surgery table and positioned in either lateral or dorsal recumbency, depending on the surgical procedure. The horses were then connected to a large animal anaesthetic machine using a circle breathing system (Tafonius Junior, Vetronics, UK; Dräger, DRE veterinary, KY). Anaesthesia was maintained with isoflurane (VCA, NSW, Australia) delivered in 95-98% oxygen. All horses were mechanically ventilated to maintain an end-tidal carbon dioxide tension of 40-55 mmHg (5.33-7.33 kPa). Pulse oximetry, electrocardiography (ECG) and IBP measurement was performed using the Surgivet V9203 multiparameter monitor (Surgivet, Sound Medical, Australia). Sidestream capnography and inspiratory and end-expiratory concentration of agent were monitored using the Vamos plus (Dräger, DRE medical, KY). Compound sodium...
lactate solution (Baxter, NSW, Australia) was administered at approximately 10 mL kg$^{-1}$ hour$^{-1}$ by gravity using a giving set that delivered 1 mL in 20 drops. Dobutamine (Hospira, Australia) was also administered at 0.2-2 µg kg$^{-1}$ minute$^{-1}$ via infusion pump to maintain MAP above 60 mmHg, according to blood pressure measured in the most centrally located peripheral artery.

**Instrumentation**

Each artery was catheterized with a 20-gauge 2.9 cm catheter (BD Instyle; Becton, Dickenson and Company NJ, USA) after clipping and disinfection of site with chlorhexidine and alcohol. The catheters were connected to an electronic pressure transducer via a 127 cm non-compliant fluid-filled extension line (DTX Plus; Argon, Singapore). Before each anaesthetic, the accuracy of each transducer was assessed using a water manometer, as described by Drynan et al. (2016). After placement of the catheters, pressure transducers were positioned at the level of the right atrium and zeroed to atmospheric pressure. The right atrium was considered to be at the level of the sternal manubrium in lateral recumbency and the scapulohumeral joint in dorsal recumbency. At the start of each study, a rapid flush test was performed and the waveform assessed subjectively to ensure that the damping was similar between the arterial pairs. A screen capture of the waveforms was also recorded during the rapid flush test for subsequent calculation of the damping coefficient.

Measurements of SAP, MAP and DAP were displayed continuously on one multiparameter monitor (Surgivet V9203). Repeated visual evaluation of the rapid flush test was performed at 10 minute intervals to ensure changes in damping did
not occur over time due to development of clots, or presence of air bubbles in the fluid line.

The SAP, MAP, DAP and heart rate (HR) were measured concurrently in the two arteries immediately after instrumentation and then every 20-40 minutes for two subsequent readings. This enabled three measurements from each horse, regardless of the variable duration of anaesthesia. At each sample time, three consecutive readings were recorded at 20 second intervals and the average of the readings was subsequently used for analysis.

Statistical analysis

All data were examined for normality using the Shapiro-Wilk test. Normally distributed data was summarized as mean and standard deviation (SD). Non-normal data was summarized as median and range. Repeatability of the three consecutive measurements was described by the coefficient of variation and the mean coefficient was reported for each artery. Agreement for SAP, MAP and DAP measured in the different arteries was determined using the Bland-Altman method for single paired measurements. The difference in paired measurements was plotted against the mean of the two measurements, with the most centrally located artery used as the reference (Bland & Altman 2007). The bias was calculated as the mean difference between arteries, the precision as the standard deviation (SD) of the bias and the limits of agreement (LOA) were calculated as the bias ± 1.96 (SD) (Bland & Altman 2007). The pattern of agreement was visually assessed. We considered liberal LOA of ± 5 mmHg as acceptable. This allowed a difference in magnitude of up 10 mmHg between arteries, which was considered the most that
could be accepted without compromising patient management. All statistical analysis was performed using GraphPad Prism Version 6.00 for Mac OS X (GraphPad Software, Inc., CA, USA).

### 3.4. Results

All horses completed the study and recovered uneventfully. The 18 horses included 5 stallions, 4 mares and 9 geldings, with a median (range) age of 4 (1-21) years and a mean ± SD body weight of 490 ± 67 kg. Horses underwent 7 orthopaedic and 11 soft tissue procedures. Duration of anaesthesia was 112 ± 37 minutes. The range of pressures over which agreement was evaluated were SAP of 81-162 mmHg, MAP of 59-136 mmHg and DAP of 45-119 mmHg. The HR was 35 ± 6 beats per minute. The mean coefficient of variation of the consecutive measurements for the transverse facial, facial and metatarsal artery were 0.02, 0.03 and 0.03 respectively. Due to poor image quality, damping coefficients were only calculated from 9 horses. The damping co-efficient was 0.18 ± 0.05 and was identical between each pair of arteries. A total of 15 horses required dobutamine (0.1-0.5 µg kg minute⁻¹) for a duration of 31 ± 24 minutes. The three blocks (or arterial pairs) contained 6 horses, with three paired measurements for SAP, MAP and DAP obtained from each horse yielding 54 measurements in total.

Bland-Altman plots for SAP, MAP and DAP measured in each combination of arteries are presented in Figure 3.1. Bias, precision and LOA with their 95% confidence intervals for SAP, MAP and DAP measured in each pair of arteries are presented in Table 3.1. The LOA were greater than ± 5 mmHg, for each pair of arteries for SAP, MAP and DAP. Visual assessment of the plots showed a haphazard
(non-systematic) pattern of agreement with both under and overestimation of the reference blood pressure across the spectrum of pressures evaluated. The largest bias and widest LOA was for SAP measured in F and MT (Fig. 3.1d), followed by SAP measured in the TF and MT (Fig 3.1f). In addition, the majority of the measurements of SAP from the MT overestimated the measurements from the F and TF. The best agreement was observed for MAP measured in all pairs with smaller LOA than SAP and DAP (Fig. 3.1a, 3.1b and 1c and Table 3.1). The smallest LOA was observed for MAP measured in the TF and MT (Fig. 3.1c). Visual assessment of the plots revealed no obvious pattern of agreement for different body positions or use of dobutamine (Fig. 3.1).

Figure 3.1

Bland Altman plots of agreement between invasive blood pressure (IBP) measured between the three pairs of arterial sites including (a) Mean arterial pressure (MAP) of facial and metatarsal arteries; (b) MAP of transverse facial and facial arteries; (c) MAP of transverse facial and metatarsal arteries; (d) Systolic arterial pressure (SAP) of facial and metatarsal arteries; (e) SAP of transverse facial and facial arteries; (f) SAP of transverse facial and metatarsal arteries. (g) Diastolic arterial pressure (DAP) of facial and metatarsal arteries; (h) DAP of transverse facial and facial arteries; (i) DAP of transverse facial and metatarsal arteries. For each arterial pair, agreement was determined from 6 horses. Solid grey lines indicate mean difference (bias) and dotted lines indicate limits of agreement (LOA). Points in black indicate horses in dorsal recumbency, points in grey indicated lateral recumbency. A triangle denotes the use of dobutamine at that time point.
Table 3.1

Mean difference (bias), precision and limits of agreement (LOA) and their 95% confidence intervals (CI) for systolic arterial pressure (SAP), mean arterial pressure (MAP) and diastolic arterial pressure (DAP) measured from three pairs of arteries. The three pairs included i) transverse facial and facial artery, ii) transverse facial and metatarsal artery and iii) facial and metatarsal artery. For each arterial pair, three paired measurements were obtained from 6 horses yielding 54 measurements in total.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Bias (mmHg)</th>
<th>Precision (mmHg)</th>
<th>LOA (mmHg)</th>
<th>95% CI lower LOA (mmHg)</th>
<th>95% CI upper LOA (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse facial vs facial</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP</td>
<td>-3.9</td>
<td>7</td>
<td>-17.8 to 10.0</td>
<td>-23.7 to -11.6</td>
<td>4.0 to 16.3</td>
</tr>
<tr>
<td>MAP</td>
<td>-0.9</td>
<td>4.5</td>
<td>-9.8 to 7.9</td>
<td>-13.6 to -5.9</td>
<td>4.0 to 11.9</td>
</tr>
<tr>
<td>DAP</td>
<td>-1.2</td>
<td>5.2</td>
<td>-11.4 to 9</td>
<td>-15.7 to -6.8</td>
<td>4.6 to 13.5</td>
</tr>
<tr>
<td>Transverse facial vs metatarsal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP</td>
<td>-6.3</td>
<td>9.7</td>
<td>-25.3 to 12.7</td>
<td>-33.4 to -16.7</td>
<td>4.5 to 21.1</td>
</tr>
<tr>
<td>MAP</td>
<td>0.8</td>
<td>4.2</td>
<td>-7.5 to 9.0</td>
<td>-11.1 to -3.9</td>
<td>5.6 to 12.7</td>
</tr>
<tr>
<td>DAP</td>
<td>-0.3</td>
<td>5.1</td>
<td>-10.3 to 9.7</td>
<td>-14.5 to -5.9</td>
<td>5.5 to 14.2</td>
</tr>
<tr>
<td>Facial vs metatarsal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP</td>
<td>-10.7</td>
<td>14.3</td>
<td>-38.7 to 17.4</td>
<td>-50.9 to -26.2</td>
<td>5.5 to 29.9</td>
</tr>
<tr>
<td>MAP</td>
<td>-0.4</td>
<td>5.7</td>
<td>-11.5 to 10.7</td>
<td>-16.2 to -6.5</td>
<td>6.0 to 15.8</td>
</tr>
<tr>
<td>DAP</td>
<td>1.8</td>
<td>6.2</td>
<td>-10.4 to 14.0</td>
<td>-15.7 to -5.0</td>
<td>8.8 to 19.6</td>
</tr>
</tbody>
</table>
3.5. Discussion

The poor and haphazard (non-systematic) agreement in SAP, MAP and DAP observed between measurements obtained from three pairs of arteries in anaesthetized horses supports our hypothesis and indicates that blood pressure measured in these arteries are not interchangeable. The haphazard agreement also precludes use of calculated bias to adjust IBP measured from one artery to that expected in another artery.

The haphazard agreement in SAP, MAP and DAP observed in our study was also evident in other studies (Monteiro et al. 2013, Acierno et al. 2015; Gent et al. 2015). This haphazard agreement between the IBP measurements could be due to alterations in vascular tone or due to errors within the measurement equipment. In the current study, the contribution of equipment errors was minimized by checking accuracy and appropriately zeroing transducers, using identical measurement systems and ensuring damping was similar in each artery and associated measurement system. Damping coefficients available from 9 horses did not demonstrate a difference between each pair of arteries. However, it is unknown if differences in damping were present in the remaining 9 horses. Nevertheless, damping predominantly effects SAP and DAP, thus differences in damping would not explain the poor agreement observed in MAP.

The smallest LOA were observed between MAP in the TF and MT, while the TF and F showed relatively larger LOA. This was surprising as it was expected that arteries in close anatomical proximity such as the F and TF, would have better agreement than arteries further apart, such as the TF and MT. The poor agreement between TF and F
may be explained by the separate origins of these arteries. The facial artery originates from the lingofacial trunk and the transverse facial artery branches directly from the external carotid (Budras et al. 2001). This finding is relevant to studies that used the F and TF interchangeably, such as the study of Heliczer et al. (2016), that compared NIBP measurements to IBP measurements from the F and TF.

Although haphazard agreement was observed, the majority of SAP measured in the MT overestimated SAP measured in the F and the TF. This is similar to results of other studies (Monteiro et al. 2013; Acierno et al. 2015; Gent et al. 2015) and can be attributed to a phenomenon known as pulse wave amplification. Amplification of blood pressure from the aorta to the periphery occurs since blood is travelling from more elastic central arteries to the less elastic peripheral arteries. As a result, SAP increases along the arterial tree, whilst the MAP and DAP remain unchanged. This overestimation could explain the previous reports of poor agreement between IBP and NIBP where the MT and F were used interchangeably to measure IBP (Drynan et al. 2016).

There are several limitations to this study. Ideally, agreement should be assessed over a wide range of measurements so that any change in agreement over the spectrum of measurements can be fully assessed. As this was a clinical study there was a necessity to rapidly treat hypotension. Thus, agreement was not able to be assessed when blood pressure was low (MAP < 60 mmHg). For the same reasons, invasive central cardiovascular monitoring and determination of vascular tone could not be performed. We chose three data collection points that were common to all procedures to accommodate the variability in surgery duration. More data
collection times may have better elucidated any patterns of agreement although they would not extend the spectrum of pressure over which the measurements were taken.

Further investigation in experimental horses, under controlled conditions, is required to determine agreement over a wider range of arterial blood pressure.

3.6. Conclusion and clinical relevance

The poor agreement with wide LOA and a haphazard (non-systematic) pattern of agreement between SAP, MAP and DAP measured in the F, TF and MT arteries demonstrates that measurements from these sites cannot be used interchangeably. This has implications for studies that use IBP as an outcome variable and for studies determining agreement between blood pressure measured using NIBP and IBP devices in horses under general anaesthesia.
References


Chapter Four

Agreement between invasive blood pressure measured centrally and peripherally in anaesthetized horses.

4.1. Abstract

Objective

To determine the agreement of invasive blood pressure measured between the facial and the metatarsal artery with the carotid. Additionally, to evaluate the effects of two haemodynamic conditions on agreement.

Study design

Prospective, randomized experimental cross-over design.

Animals

Eight horses with median (range) age of 7 (4-23) years and a mean (standard deviation) body weight of 493 ± 33 kg.

Methods

Horses were anaesthetized and positioned in dorsal recumbency. Invasive blood pressure was measured simultaneously via catheters placed in the facial, metatarsal and carotid artery. Cardiovascular function and agreement between arteries was assessed before and during administration of phenylephrine and sodium.
nitroprusside. These were administered until carotid mean pressure (MAPc) increased or decreased from baseline (65 ± 5 mmHg) to > 90 mmHg or < 50 mmHg, respectively. Data recorded at each sample time included systolic (SAP), mean (MAP) and diastolic (DAP) for carotid (c), facial (f) and metatarsal (m) artery as well as cardiac output (Qt) and systemic vascular resistance (SVR). Bland-Altman analysis was used to assess agreement between peripheral and central sites and regression analysis was used to determine influence of Qt and SVR.

**Results**

The largest difference was observed in SAPc and SAPm with a bias and limits of agreement (LOA) of 2 (-15 to 19) mmHg. The bias (LOA) for MAPc and MAPf was 2 (-4 to 9) mmHg and for MAPc and MAPm was 5 (-4 to 14) mmHg. The best agreement for DAP was seen between DAPc and DAPf with bias (LOA) of 1 (-3 to 5) mmHg. Regression analysis indicated marginal influence on agreement by Qt on MAPc and MAPf.

**Conclusion and clinical relevance**

Mean arterial pressure and DAP of the carotid was generally higher compared to the peripheral arteries, which may lead to overzealous treatment of hypotension, albeit maintaining central pressures. Cardiac output and systemic vascular resistance did not largely influence the difference between sites.
4.2. Introduction

It is well reported that recognition and management of hypotension will reduce the incidence and severity of post anaesthetic myopathy (Grandy et al. 1987; Johnston et al. 2002). As a result of these studies, it is now commonplace to monitor invasive blood pressure (IBP) in anaesthetised horses directly via a catheter placed in the easily accessible peripheral arteries.

Recent studies in anaesthetised ponies and dogs have demonstrated poor agreement between pressure measured in peripheral arteries compared to the larger conducting artery, the carotid (Monteiro et al. 2013; Gent et al. 2015). In both these studies, other measures of cardiovascular function like systemic vascular resistance (SVR) and cardiac output (Qt) were not assessed. A recent clinical study in anaesthetised horses reported haphazard patterns of agreement between the three peripheral sites commonly used to measure blood pressure; the facial, transverse facial and metatarsal arteries (Wilson et al. 2017). This raises the question as to whether pressure measured in peripheral arteries can provide a meaningful indication of perfusion of the vital organs, especially over a range of hemodynamic states.

In a study using an electrical model of circulation, it was illustrated that a partial obstruction (such as that created by an arterial catheter), or change in vessel shape from decreased SVR, lead to turbulent flow in the peripheral arteries. This could lead to attenuation of the waveform, affecting agreement between central and peripheral sites (Ercole 2006). There are no published studies in anaesthetised horses investigating agreement of IBP measured in the peripheral arteries compared
to the carotid during different haemodynamic states induced by changes to \( Q_t \) and SVR.

The aims of this study were to determine the agreement of IBP between the facial and the metatarsal artery with the carotid and with each other and to evaluate the effects of two haemodynamic conditions (hypotension and hypertension) on agreement. It was hypothesised that agreement would be poor between central and peripheral sites and changes to systemic vascular resistance would influence agreement.

4.3. Materials and methods

Animals

Eight adult horses with ASA (American Society of Anaesthesiologists) physical status I and II were included in the study. A sample size of 8 horses was determined to give a 95% confidence interval for the estimation of the limits of agreement (LOA) within ± 1.2 (SD) (www.users.york.ac.uk/~mb55/meas/sizemeth). Donated horses, that were unable to be rehomed and that the owner had agreed to use in teaching or research prior to humane euthanasia were used for this study. The horses were deemed healthy with no cardiac disease, according to physical, echocardiographic and haematological examinations. The use of these horses in this study was approved by an Institutional Animal Ethics committee (Permit number R2861/16) and was performed in accordance with the Animal Welfare act of Western Australia.
Study design

Each horse was anaesthetised once. Blood pressure was measured throughout anaesthesia and hemodynamic states were altered by administration of phenylephrine (hypertension) or sodium nitroprusside (hypotension). Phenylephrine and sodium nitroprusside were administered until carotid mean pressure (MAPc) increased and decreased from baseline (65 ± 5 mmHg) to > 90 mmHg and < 50 mmHg, respectively. The order for administration of phenylephrine and sodium nitroprusside was balanced (4 nitroprusside/phenylephrine; 4 phenylephrine/nitroprusside) and allocated randomly by selecting the protocol from sealed envelopes on the day of the study.

Anaesthesia

The horses were fasted for at least 12 hours before induction of anaesthesia, but water was available *ad libitum* until premedication. A 14 gauge catheter was placed in the left jugular vein. Each horse was sedated with romifidine (0.08 mg kg⁻¹; Sedivet; Boehringer Ingleheim, MO, USA) intravenously (IV) and five minutes later, anaesthesia was induced with ketamine (2.2 mg kg⁻¹; Ilium, NSW, Australia) and diazepam (0.1 mg kg⁻¹; Ilium, NSW, Australia) IV in the same syringe. Following orotracheal intubation, the horses were hoisted onto a padded surgery table and positioned in dorsal recumbency. The horses were then connected to a large animal anaesthetic machine using a circle breathing system (Tafonius junior, Vetronics, UK). Anaesthesia was maintained with isoflurane (VCA, NSW, Australia) delivered in 95-98% oxygen. Mechanical ventilation was performed in all horses to maintain an end-tidal carbon dioxide tension of 5.33-6.66 kPa (40-50 mmHg). Tidal volume was
adjusted between 10-15 mL kg\(^{-1}\) and respiratory rate between 8-9 breaths minute\(^{-1}\) to achieve this value, which was then confirmed by arterial blood gas analysis [arterial partial pressure of carbon dioxide (PaCO\(_2\)) 45 – 55 mmHg]. Once a value within this range was achieved no adjustment to ventilation parameters were made. Anaesthesia monitoring included pulse oximetry, electrocardiography (ECG) and IBP which were obtained using the Surgivet V9203 multiparameter monitor (Surgivet V9203; Sound Medical, Australia). Sidestream capnography and inspiratory and expiratory agent analyses were performed using the Vamos plus (Dräger; DRE Medical, KY, USA). Supportive care included administration of Hartmanns’s solution (Baxter Healthcare, NSW, Australia) at 5 mL kg\(^{-1}\) hour\(^{-1}\) by infusion pumps. Dobutamine (Hospira, Australia) at 0.5-1.5 µg kg\(^{-1}\) minute\(^{-1}\) was used to maintain MAP > 60 mmHg prior to baseline measurements when required and was stopped at least 10 minutes prior to measurements.

**Instrumentation**

Arterial catheters were placed in the left facial artery (f) at the most ventral part as it traversed the mandible, the right metatarsal artery (m) distal to the head of the lateral splint bone and the right carotid (c) retrograde to the heart. At each site, a 20 gauge 1.88-inch catheter (BD Instyle; Becton, Dickenson and Company, USA) was placed after clipping and disinfection of the site. The carotid catheter was placed after surgical exposure of the proximal third of the artery. This involved an incision over the ventral midline followed by blunt dissection. Following catheterisation, the artery was left in the natural position to prevent interference with blood flow. The catheters were connected to electronic pressure transducers (DTX Plus; Argon,
Singap) via identical non-compliant fluid-filled extension lines (150 cm). The transducers were connected to multiparameter monitors (Surgivet V9203; Sound Medical, Australia). Prior to anaesthesia, the accuracy of each transducer was checked using a water manometer (Drynan et al. 2016) and for linearity at 200 mmHg, 100 mmHg, 50 mmHg and 20 mmHg. After placement of the catheters, all pressure transducers were positioned at the level of the scapulohumeral joint which was confirmed using a laser and spirit level. Each transducer was then zeroed to atmospheric pressure and the difference in height between the transducer and each arterial catheter was recorded. Prior to the first data collection and whenever the waveform changed, a rapid flush test was performed and the amount of damping of the waveform assessed subjectively to ensure that the damping was similar between arteries. Using a screen capture of the waveforms recorded during the rapid flush test, the damping coefficient was calculated subsequently to confirm that differences in damping were not responsible for differences between pressures measured in different arteries.

Central venous pressure was measured from the right atrium via a 90 cm 19 gauge polyurethane equine central venous catheter (Mila International Inc, KY, USA). After clipping and disinfection of the right jugular, the catheter was advanced into the ventricle and then retracted into the right atrium and the location was confirmed by pressure waveform analysis. The catheter was attached to an electronic transducer which was zeroed to atmospheric pressure and positioned at the level of the scapulohumeral joint.

Data collection
Cardiovascular measurements included systolic (SAP), mean and diastolic arterial pressure (DAP), heart rate (HR), Qt and central venous pressure (CVP). All variables were recorded on a separate record sheet. Cardiac index (CI), SVR, systemic vascular resistance index (SVRI) and body surface area (BSA) were subsequently calculated using the following formulae:

\[
\text{SVR (dynes second cm}^{-5}\text{)} = 80(\text{MAP} - \text{CVP})/\text{Qt}
\]

\[
\text{CI (L minute}^{-1}\text{m}^{-2}\text{)} = \text{Qt}/\text{BSA}
\]

\[
\text{SVRI (dynes second cm}^{-5}\text{m}^{-2}\text{)} = 80(\text{MAP} - \text{CVP})/\text{CI}
\]

\[
\text{BSA (m}^2\text{)} = 10.5 \times (\text{body mass in g})^{2/3} \times 10^{-4}
\]

Concurrent measurements of blood pressure from all arteries were recorded at baseline [when carotid mean pressure (MAPc) was 65 ± 5 mmHg], and during administration of phenylephrine or sodium nitroprusside when MAPc had been increased and decreased to maintain a stable pressure of > 90 mmHg or < 50 mmHg, respectively, for at least 5 minutes. At each measurement point, three recordings were taken within 60 seconds and the average calculated for data analysis. In order to prevent variability due to ventilation, data were recorded during transient periods of apnoea where the first IBP recording was started 20 seconds after switching off the ventilator.

Cardiac output was determined following administration of 0.003 mmol of lithium chloride kg\(^{-1}\) (0.15 mmol mL\(^{-1}\)) into the jugular catheter. Duplicate Qt determinations were obtained within a 3-minute period, and the mean Qt was calculated for each
sample time. Prior to each duplicate, [sodium (Na⁺)] and [haemoglobin (Hb)] were measured via arterial blood gas analysis. The sensor was connected to an arterial catheter placed in the right facial artery (opposite side to IBP measurement). The first cardiac output was performed simultaneously with the IBP recording during apnoea, whilst the second was performed three minutes later during another period of apnoea.

All horses were euthanized after completion of further approved investigations using Pentobarbitone 0.1 mL kg⁻¹ (Lethabarb; Virbac, Australia)

**Statistical analysis**

Based on normal distribution being verified, body weight, age, HR, Qt, CVP, SVR and damping coefficients were examined by means of the Shapiro-Wilk test of normality and reported as mean and standard deviation (SD). Other results are given as median (range). Repeatability of the three consecutive IBP measurements were defined by the coefficient of variation and the mean coefficient was reported for each artery. A Wilcoxon ranked sign test was used to compare damping coefficients between the between arterial sites and paired t-tests were used to compare baseline values prior to administration of each drug. $P<0.05$ was considered significant for these analyses.

Agreement of the SAP, MAP and DAP between the carotid and the peripheral sites as well as between the peripheral sites were described using the Bland-Altman method for single paired measurements, plotting the difference in paired measurements against the mean of the two measurements (Bland & Altman 2007). The bias was
calculated as the mean difference between arteries, the precision as the standard deviation of the bias and the limits of agreement (LOA) calculated as the bias ± 1.96 SD (Bland & Altman 2007). The pattern of agreement was visually assessed. We considered acceptable LOA as ± 5 mmHg. This allowed a difference in magnitude of up to 10 mmHg between sites. A leniency of this magnitude was considered acceptable in light of using this information to dictate treatment in clinical cases. Bland Altman and descriptive statistical analyses were performed using GraphPad Prism Version 6.00 for Mac OS X (GraphPad Software, Inc., CA, USA).

For the purpose of exploring whether cardiac output or systemic vascular resistance could explain the disagreement between carotid and facial or metatarsal pressure, regression analysis was performed for SAP, MAP and DAP. The disagreement in measurement was regressed ($R^2$) on $Q_t$ and SVR. The $R^2$ was recorded for addition of first $Q_t$, and then SVR, and used as a description of how much variation in the disagreement the variables could explain. Regression analysis was performed using SAS v 9.4 (SAS Institute, NC, USA).
4.4. Results

Eight horses (two mares and six geldings) were included, with an age of 7 (4-23) years and a body weight of 493 ± 33 kg. Duration of anaesthesia from induction to last measurement was 168 ± 35 minutes. Time to first measurement after induction was 70.5 (60-116) minutes.

Damping coefficients from the IBP(c), IBP(f) and IBP(m) were calculated as 0.2 (0.15-0.35) and were not significantly different (p > 0.99) between all three sites. One set of data from the metatarsal artery was removed from analysis due to significant overdamping being present immediately after measurements. The mean coefficient of variation of the three consecutive IBP measurements was 2% for each individual artery.

Phenylephrine was administered at a range of 0.5 - 2 µg kg⁻¹ minute⁻¹ to increase MAPc and sodium nitroprusside at 0.1-1.5 µg kg⁻¹ minute⁻¹ to decrease MAPc. Dobutamine was administered prior to 7/32 baseline data collection periods. There was no significant difference detected between baseline measurements prior to phenylephrine or sodium nitroprusside administration: SAPc (p = 0.16), MAPc (p = 0.19), DAPc (p = 0.22), HR (p = 0.13) or Qt (p = 0.74). Cardiovascular parameters during baseline, phenylephrine and sodium nitroprusside administration as well as arterial blood gas results (PaO₂ and PaCO₂) are described in Table 4.1.

Bland-Altman scatter plots for all measurements between the IBP(c) and the peripheral sites as well as between IBP(f) and the IBP(m) showed poor agreement with wide LOAs above ± 5 mmHg (Figs. 4.1-4.3, Table 4.2).
The worst agreement with the widest LOA was for SAP between the carotid and metatarsal and the facial and metatarsal, with limits spanning a magnitude of 36 mmHg and a bias (LOA) of 2 (-15 to 19) mmHg and 1 (-16 to 18) mmHg, respectively (Figs. 4.2a and 4.3a, Table 4.2). Visual assessment of the Bland-Altman SAP plots showed a haphazard (non-systematic) pattern of agreement with a marginal bias and data points in both the positive and negative direction of the plot across the spectrum of pressures evaluated (Figs. 4.1a, 4.2a and 4.3a).

There was a general tendency for the MAPc and DAPc to be underestimated by the peripheral arteries as indicated by a positive bias and as illustrated in the plots. However, overestimation did also occur with some points in the negative regions of the plots (Figs. 4.1b, 4.1c, 4.2b and 4.2c). This underestimation of MAP and DAP by the more peripheral vessel (further from the heart) was also present when the facial and the metatarsal were compared (Figs. 4.3b and 4.3c). The bias (LOA) for MAPc and MAPf was 2 (-4 to 9) mmHg and MAPc and MAPm was 5 (-4 to 14) mmHg. Visual inspection of the Bland-Altman Plots showed changing bias for MAPm across the spectrum of measurements compared to a consistent bias for MAPf compared to MAPc (Figs. 4.1b and 4.2b).

The best agreement for DAP and overall was seen between DAPc and DAPf with bias (LOA) of 1 (-3 to 5) mmHg.

Regression analysis on the difference between the carotid and facial artery measurements for SAPf, MAPf and DAPf, Qt explained 20%, 37% and 17% of the variance respectively, with SVR having negligible association as indicated by the influence of the combined Qt and SVR as 20%, 38% and 19% respectively. The
difference between the metatarsal artery and the carotid for SAPm, MAPm and DAPm showed no association with Qt and SVR.
Table 4.2

Overall systolic (SAP), mean (MAP) and diastolic arterial pressure (DAP) data with mean difference (bias), precision, limits of agreement (LOA) their 95% confidence intervals (CI) for upper and lower LOA for invasive blood pressure measurements in 8 horses across the carotid, facial and the metatarsal arteries.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Carotid vs Facial</th>
<th>Carotid vs Metatarsal</th>
<th>Facial vs Metatarsal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bias (mmHg)</td>
<td>Precision (mmHg)</td>
<td>LOA (mmHg)</td>
</tr>
<tr>
<td>SAP</td>
<td>1</td>
<td>6</td>
<td>-11 to 13</td>
</tr>
<tr>
<td>MAP</td>
<td>2</td>
<td>3</td>
<td>-4 to 9</td>
</tr>
<tr>
<td>DAP</td>
<td>1</td>
<td>2</td>
<td>-3 to 5</td>
</tr>
<tr>
<td>SAP</td>
<td>2</td>
<td>9</td>
<td>-15 to 19</td>
</tr>
<tr>
<td>MAP</td>
<td>5</td>
<td>5</td>
<td>-4 to 14</td>
</tr>
<tr>
<td>DAP</td>
<td>4</td>
<td>3</td>
<td>-2 to 10</td>
</tr>
<tr>
<td>SAP</td>
<td>1</td>
<td>9</td>
<td>-16 to 18</td>
</tr>
<tr>
<td>MAP</td>
<td>3</td>
<td>4</td>
<td>-5 to 11</td>
</tr>
<tr>
<td>DAP</td>
<td>2</td>
<td>3</td>
<td>-4 to 9</td>
</tr>
</tbody>
</table>
Bland Altman plots of agreement between invasive blood pressure (IBP) measured between the carotid and the facial arteries. (a) Systolic arterial pressure (SAP); (b) mean arterial pressure (MAP); (c) diastolic arterial pressure (DAP). Solid lines indicate mean difference (bias) and dotted lines indicate limits of agreement (LOA).
Figure 4.2

Bland Altman plots of agreement between invasive blood pressure (IBP) measured between the carotid and the metatarsal arteries. (a) Systolic arterial pressure (SAP); (b) mean arterial pressure (MAP); (c) diastolic arterial pressure (DAP). Solid lines indicate mean difference (bias) and dotted lines indicate limits of agreement (LOA).
Figure 4.3

Bland Altman plots of agreement between invasive blood pressure (IBP) measured between the facial and the metatarsal arteries. (a) Systolic arterial pressure (SAP); (b) mean arterial pressure (MAP); (c) diastolic arterial pressure (DAP). Solid lines indicate mean difference (bias) and dotted lines indicate limits of agreement (LOA).
4.5. Discussion

To the authors’ knowledge, this is the first study comparing direct blood pressure measurements between central and peripheral arteries at different haemodynamic states in horses. The results revealed poor agreement between the carotid, facial and metatarsal arteries as well as between the two peripheral arteries across the pressures evaluated. No influence of systemic vascular resistance was observed on agreement between sites whilst cardiac output marginally influenced agreement between the carotid and the facial arteries. This suggests other factors have greater influence on the disparity observed.

The poor agreement observed between central and peripheral sites, supported our first hypothesis. However, there was a general trend for the facial and metatarsal artery to underestimate the MAP and DAP of the carotid. This underestimation has also been observed in studies in dogs and ponies (Monteiro et al. 2013; Gent et al. 2015). Although, in human studies there are conflicting findings (O’Rourke et al. 1968; Dorman et al. 1998; Mignini et al. 2006). There are no studies in horses investigating the effects of changes to central pressure, even though perfusion of vital organs such as the brain, heart, kidneys, gastrointestinal tract as well as the skeletal muscles and the gravid uterus is determined by blood flow in these conducting arteries. The underestimation of MAP by the peripheral arteries may result in the overzealous treatment of hypotension in clinical cases, albeit maintaining central pressures well above the driving pressure necessary to perfuse these organs.
The agreement between MAP measured at the carotid and peripheral arteries was poor overall, as indicated by wide LOA, with the worse agreement observed between the carotid and the metatarsal artery. The length of the vascular tree in horses could result in a greater degree of dispersion of reflecting sites minimizing the effects of wave reflection and could explain the worsening agreement seen at more peripheral sites (O’Rourke et al. 1968). The poor agreement between the carotid and the facial artery was surprising, however could be due to the facial artery being a branch of the linguofacial trunk, rather than a direct branch of the external carotid. This may result in more sites of wave reflection, contributing to the discrepancy between the readings.

It was surprising that the agreement between all the arterial sites was not better considering this was an experimental study performed under standardized conditions. The LOA in this study were smaller than in the results reported by Gent et al. (2015) in ponies, who were also surprised by the poor agreement observed. The physical factors that can contribute to discrepancies between readings such as the position of the transducers and formation of blood clots or presence of bubbles in the line were all reduced in this study. Each catheter was flushed using a constant flow of saline pressurised to 300 mmHg to prevent clotting and air bubble formation. In addition, each transducer was verified by a laser spirit level to be at the level of the scapulohumeral joint. Technical errors were also excluded by confirming accuracy of equipment prior to and during use. As differences in damping within each measurement system can contribute to poor agreement between arteries, the effect of damping was reduced by using an identical measurement system for each
artery. The lack of difference in the calculated damping coefficient between each transducer and fluid line was also highly supportive that this factor was unlikely to have contributed to the poor agreement. As this was an experimental study, there was no excessive electrical activity from surgical instruments or manipulation of the vascular tree due to surgery that could have interfered with the data.

Systolic amplification, a physical phenomenon causing overestimation of systolic pressures by the peripheral arteries, may have contributed to the lack of agreement. Systolic amplification has been documented in dogs and children with the effects of increasing age decreasing its presence (Nichols & O’Rourke 1998; O’Rourke et al. 2000; Wojciechowska et al. 2012). Although the worst agreement observed in this study was the systolic pressures for both combinations with the carotid and between the facial and the metatarsal, both over and underestimation of the more central arterial site occurred. This is consistent with other studies in humans, horses, ponies and dogs where over and underestimation of the SAP by the more peripheral artery was present. (Mignini et al. 2006; Monteiro et al. 2013; Acierno et al. 2015; Gent et al. 2015; Wilson et al. 2017) It is also possible that age related changes could have contributed to poor agreement due to the increasing stiffness of the carotid artery with increasing age, as two of the horses in this study were > 20 years old (Endoh et al. 2017). However, separate analysis with Bland-Altman plots of the two older horses revealed a similar haphazard pattern of agreement as the younger animals. This suggests that age related vascular changes did not influence agreement in this study.
Another possible factor contributing to poor agreement is attenuation, which occurs as a result of partial blood flow obstruction due to the presence of a catheter in the lumen of an artery. This phenomenon, as opposed to overdamping, was demonstrated in an ex vivo model where erroneous low SAP and DAP readings were observed, especially during times of low SVR (Ercole 2006). This phenomenon could perhaps explain the results in dogs where the more peripheral artery underestimated the SAP of the carotid during hypotensive conditions (Monteiro et al. 2013). However, in our study, visual inspection of the Bland-Altman plots did not show underestimation at lower pressures and regression analysis did not reveal any influence by SVR on the difference between measurements. One of the reasons for the lack of attenuation in our study could be the catheter size, resulting in a relatively small proportion of the carotid artery lumen being occupied. Thus, there was less obstruction to flow in the carotid artery compared to the peripheral arteries (Ercole 2006). Unfortunately, in this study vessel size in relation to catheter occupancy was not measured.

The lack of detectable influence of SVR on agreement, may also reflect the method used to measure cardiac output. In our study, cardiac output was measured using the lithium dilution technique. There is evidence in the literature that the administration of certain drugs can influence the function of the lithium sensor. Recently, Hopster et al. (2017) demonstrated a large bias between lithium dilution and thermodilution during administration of high doses of phenylephrine. However, in an older study at doses similar to those used in the current study, a small bias was observed between lithium dilution and thermodilution during administration of
phenylephrine and sodium nitroprusside (Linton et al. 2000). Moreover, the potential error induced by overestimation of measurements was irrelevant to the outcome of the study as we were not investigating the absolute values of cardiac output.

In the study by Gent et al. (2015), administration of dexmedetomidine caused all but the SAPm to have improved agreement with the carotid in comparison to saline administration. The authors hypothesised that these observations were as a result of vasoconstriction by dexmedetomidine, increasing the damping of the pressure waves in a smaller vessel further away from the heart. This also could be explained by the phenomena described by Ercole (2006) with less attenuation during vasoconstriction. This was not evident in our study, in fact the opposite was observed with the administration of phenylephrine causing a trend of worsening agreement between the MAPm with the MAPc as pressures increased.

The agreement between IBP measured at the facial and metatarsal was also evaluated. In this study we observed better agreement between SAP, MAP and DAP measured at the facial and the metatarsal than in a previous study (Wilson et al. 2017). In addition, the positive bias of the MAP and DAP indicated the more peripheral artery underestimated the pressures of the more centrally located artery in contrast to the non-systematic, haphazard agreement seen in the clinical study. The differences in these results could be explained by the current study being performed under standardized experimental conditions.

There are aspects of the experimental design that may have influenced results and need to be considered when interpreting the data. Firstly, the horses were
positioned in dorsal recumbency and thus it is not known if the results would be similar in lateral recumbency. In particular, it is not known the impact on pressure measurements when the position of the metatarsal artery is greatly higher than the carotid. This could explain the differences observed between our study and that of other studies where agreement was assessed in ponies positioned in lateral recumbency (Gent et al. 2015). The decision to perform the current study in dorsal recumbency was to enable us to catheterise the carotid artery and the contralateral facial artery, so that flow and pressure in the facial artery was not impacted by the presence of a catheter in the upstream carotid. The use of contralateral arteries also contrasts the study by Gent et al. (2015) where the facial and carotid from the same side was used. Secondly, in our study the carotid arteries were not permanently translocated to a subcutaneous position. It was decided to place the catheter using surgical exposure of the artery to prevent changes in blood flow and thus pressure that could occur due to changes in anatomical alignment. However, it is possible that the cut down technique removed some of the surrounding soft tissue supporting the artery. This could have resulted in changes to elasticity/radial traction of the vessel and resulted in higher systolic pressure and lower diastolic pressure, affecting agreement between the peripheral sites.

Finally, the vasoactive agents’ phenylephrine and sodium nitroprusside were used to manipulate vascular tone to change IBP in order to assess agreement over a wide range of pressures. However, in clinical situations these agents are rarely used and the influence of these drugs cannot replicate clinical situations when changes to vascular tone and cardiac output are due to systemic disease.
Future studies are needed to assess the agreement between IBP measured between central and peripheral in clinical situations in different recumbencies.

4.6. Conclusion and clinical relevance

In conclusion, MAP and DAP of the carotid was generally higher compared to the facial and the metatarsal arteries, which may lead to overzealous treatment of hypotension in clinical cases, albeit maintaining central pressures. Cardiac output and systemic vascular resistance did not largely influence the difference between sites. Mean arterial pressure was closer to the carotid when measured at the facial artery compared to the metatarsal artery in dorsally recumbent horses under isoflurane anaesthesia.

References


Chapter Five

General discussion and conclusion

This thesis describes the completion of a clinical study to investigate the agreement between invasive blood pressure measured at different peripheral locations in anaesthetised horses. A subsequent experimental study was conducted to assess agreement between invasive blood pressure measured at these peripheral sites with a central site over a wide range of pressures.

In the clinical study, we observed poor agreement with wide limits of agreement and a haphazard (non-systematic) pattern of agreement between systolic, mean and diastolic pressures, measured in the facial, transverse facial and metatarsal arteries. This demonstrated that measurements from these sites cannot be used interchangeably. The results of our study have implications for other studies using IBP as an outcome variable and for those validating NIBP devices in horses under general anaesthesia.

The poor agreement observed between blood pressure measured in peripheral sites in clinical cases prompted the question as to which of these peripheral sites provided the most representative measure of central pressure. In addition, we were interested to see if the poor agreement observed in clinical cases could be reproduced in an experimental study, where conditions were standardised and blood pressure was manipulated to obtain a greater range of measurements.
The results of this experimental study demonstrated poor agreement between peripheral sites when compared to the carotid artery and confirmed poor agreement between different peripheral sites. The pressure measured at the facial artery represented those pressures at the carotid better than the metatarsal artery. Due to the poor agreement between peripheral sites and carotid artery, it was evident that no peripheral site provided measures of blood pressure representative of blood pressure measured in the carotid artery. Mean and diastolic pressures measured from the carotid artery were generally higher than the facial and the metatarsal arteries. This underestimation by the peripheral arteries may help to maintain central pressures well above the driving pressure necessary to perfuse central organs when peripheral arterial blood pressure is used to guide interventions. The experimental study also investigated the influence of vascular factors in determining agreement. By measuring these cardiovascular variables, we were able to determine that cardiac output and systemic vascular resistance did not largely influence the difference seen between sites. This finding shows that attenuation of blood pressure did not affect the measured blood pressure in this study (Ercole 2006).

Our research highlights several important aspects about monitoring invasive blood pressure in anaesthetised horses. Firstly, although this technique is considered the most accurate method of monitoring blood pressure, the measurement of pressure at different sites varies. Furthermore, when measured clinically, the choice of peripheral artery to catheterise is dictated by the surgical procedure preventing use of a single artery, even if a suitable site was identified. These results further confirm blood pressure as a poor sole agent for assessing the cardiovascular status of the
horse, however currently it is the only technique available. Further studies are needed to find variables that can be evaluated in conjunction with invasive blood pressure to assess organ perfusion rather than focus on one particular element to guide therapeutics.

Nevertheless, when interpreting invasive blood pressure measured in particular peripheral arteries, from our research we have made the following observations. In the clinical study the smallest limits of agreement were observed between mean arterial pressures in the transverse facial and the metatarsal arteries. This observation was surprising due to the distance between the arteries. In contrast, in the experimental study, with the smallest limits of agreement being present between the two arteries in close proximity i.e. the facial and the carotid artery. That being said, the limits of agreement were still in excess of our predetermined acceptable LOAs. It was expected that arteries in close anatomical proximity such as the facial and transverse facial and the facial and carotid, would have better agreement than what we observed. Explanations for this poor agreement could include the separate origins of these arteries as well as the cut down technique utilized in the experimental study, which removed some of the surrounding soft tissue supporting the artery in turn changing the elasticity/radial traction of the vessel.

The better agreement seen between arteries further away from each other (the transverse facial and the metatarsal artery) in the clinical study was contrasted in the experimental study where the worst agreement was observed between the carotid and the metatarsal artery. Poor agreement was expected due to the length of the
vascular tree, resulting in a greater degree of dispersion of reflecting sites minimizing the effects of wave reflection and could explain the worsening agreement seen at more peripheral site (O’Rourke et al. 1968). These conflicting results could be due to the standardized experimental conditions of the second study and perhaps the wider range of pressures that allowed a different relationship to emerge. It would have been advantageous to have catheterised the femoral artery to assess agreement between the femoral and carotid artery and the femoral and metatarsal artery, and ascertain the pressures changes along the arterial tree.

The findings of both studies are relevant to interpreting data from other studies and the experimental design of future studies including those validating non-invasive blood pressure devices and those using invasive blood pressure as an outcome variable. Studies to date have used peripheral arterial sites interchangeably, presumably on the assumption that measurements of blood pressure would be comparable from different sites. The results of these studies, particularly those comparing blood pressure techniques, should be interpreted cautiously based on the findings outlined in this thesis. The facial and transverse facial artery has been used interchangeably in several studies including a non-invasive blood pressure validation study by Heliczer et al. (2016) where the NIBP device was used on the tail and a cardiovascular study by Risberg et al. (2016). The poor agreement observed in the clinical study could have explained why the accuracy and precision was low in the Heliczer study. Other arterial combinations such as the metatarsal and the facial artery or combinations of all three main sites has been used in other non-invasive
blood pressure monitor validation studies and retrospective studies (Hofmeister et al. 2008; Hatz et al. 2015; Drynan et al. 2016).

Studies using blood pressure as an outcome variable, also need to be compared carefully when blood pressure was measured using different arteries in different studies.

In conclusion the poor agreement with wide LOA and a haphazard (non-systematic) pattern of agreement between SAP, MAP and DAP measured in the facial, transverse facial and metatarsal arteries demonstrates that measurements from these sites cannot be used interchangeably. This has implications for studies that use IBP as an outcome variable and for studies determining agreement between blood pressure measured using NIBP and IBP devices in horses under general anaesthesia. The poor agreement between peripheral sites and the carotid artery also indicate that no site provided a good representative of this more central pressure. In the experimental study mean and diastolic arterial pressures of the carotid was generally higher compared to the facial and the metatarsal arteries, which may lead to overzealous treatment of hypotension in clinical cases, albeit maintaining higher central pressures.

5.1 Future perspectives

It is worth noting that in this study, peripheral blood pressure was compared to only one central site, the carotid artery. Comparisons of peripheral sites to pressure measured in other conducting vessels such as the femoral artery would be required to confirm that this finding is relevant to other pairs of arteries.
Our research raises even more questions about interpretation of invasive blood pressure measurements in anaesthetised horses. Further research is required to evaluate and assess the factors that do influence agreement as to deepen our understanding of the pressure driving perfusion to the vital organs and major muscle groups as well as the influence of position on agreement.
References


