The common carotid artery provides significant pressure wave dampening in the young adult sheep☆,☆☆

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ABSTRACT

Background: It has been established that the central elastic arteries of the mammalian circulation dampen the high pulse pressure emanating from the left ventricle, so that the pulsations in distal arterioles, such as in the cerebral circulation, are of lower amplitude than more centrally. However, the contribution of the common carotid artery (CCA) to protection of the cerebral microvasculature from high pulse pressure is not known, specifically to what extent viscoelastic energy dissipation in the arterial wall might contribute to the shock absorbing function of the large conduit arteries.

Methods: Young adult sheep (n = 6) were anaesthetised and their CCAs (n = 7) exposed. Pressure catheters were inserted 10–15 cm apart, proximally and distally in the CCA; a flow probe was placed proximally on the vessel.

Results: The median dp/dt_{max} on the pressure rise of the arterial wave upstroke for the proximal CCA was 619 mm Hg/s and for the distal CCA it was significantly lower, at 197 mm Hg/s (p = 0.0156; n = 7). The median pulse pressure of the proximal CCA was 24 mm Hg/s; distal pulse pressure was significantly lower, at 18 mm Hg/s (p = 0.0156; n = 7). The median flow rate was 0.97 L/min with an interquartile range from 0.51 to 1.15 L/min.

Conclusions: The native CCA in the young adult sheep is an effective "pressure dampener" in the arterial circulation, reducing both pressure slope and pulse pressure, most likely via viscous dampening in the arterial wall.

1. Introduction

The "central" elastic arteries of the mammalian circulation have a "shock absorbing" function in that they serve, when normal, to "dampen" the high pulse pressure emanating from the left ventricle, so that the pulsations in distal arterioles, such as in the cerebral circulation, are of lower amplitude than more centrally. This windkessel function reduces with age, when arterial stiffening results in higher pulse pressure being translated to the cerebral microcirculation, which in turn has been linked with risk of dementia [1].

The contribution of the common carotid artery (CCA) to protection of the cerebral microvasculature from high pulse pressure (if any) in normal young mammals is not known. In particular, it is unclear to what extent viscoelastic energy dissipation in the arterial wall might contribute to the shock absorbing function of the large conduit arteries.

Such energy dissipation is known to reduce both the intensity of the forward-running pressure wave (i.e. the slope of the pressure upstroke) and the overall pulse pressure [2]. An understanding of the mechanisms which act to protect the microvasculature may provide guidance in how to prevent the transmission of pulse pressure to the brain and the associated cognitive decline.

The aim of this study was to examine the effect of the CCA on arterial pressure waves in young adult sheep; particularly, we aimed to assess if the normal CCA "dampens" arterial pressure waveforms.

2. Methods

This study was approved by the Animal Care and Ethics Committee of Charles Sturt University (CSU), Australia, according to protocol number A16091. The studies described were conducted humanely and in compliance with the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes 8th edition (2013).

Young mature (estimated 5–7 years old based on dentition) Border Leister cross bred ewes (Ovis aries, n = 6) weighing 62–100 kg were used for this study.

2.1. Measurement of common carotid dimensions

CCA internal diameter and wall thickness were measured with B-mode ultrasound using a GE Medical Systems Vivid e coupled with a Logiq e 8L-RS transducer probe (GE Healthcare, Chicago, IL, USA) on non-sedated animals in advance of the surgical procedure. Measurement involved positioning the transducer to acquire transverse images of the CCA and measuring the internal diameter (from lateral to medial at the widest point in each image) in duplicate or triplicate at 3 sites along the CCA (caudal, middle, rostral). From 1 to 3 measurements of wall thickness were acquired in 4 animals (in one animal left and right sides were measured). The internal diameter and vessel wall thickness was determined from these measurements.

2.2. Surgical procedure

2.2.1. Anaesthesia and monitoring protocol

The sheep were fasted for 24 h prior to anaesthesia. On the day of the procedure the sheep were premedicated with Buprenorphine (0.01 mg/kg IV via a 22 g needle and syringe) prior to induction of anaesthesia with Propofol (4 mg/kg IV via a 19 g catheter via a cephalic vein). Anaesthesia was maintained using an endotracheal tube with the cuff inflated, and by the provision of isoflurane (1.5–2%) and oxygen via an anaesthetic machine, with ventilation, gas and pressure monitoring. A wide bore stomach tube was placed orally to evacuate the rumen of ingesta and fluid during the procedure to prevent aspiration of ruminal contents.

An intravenous infusion of physiological saline was given via the cephalic vein catheter at surgical maintenance rates (10 mL/kg/h) for the duration of the procedure. A thermally regulated warming blanket under the sheep was used to maintain body temperature. During the surgical procedures, the sheep's heart rate, respiratory rate, blood oxygen (SpO$_2$) and carbon dioxide (ETCO$_2$) levels, arterial blood pressure and ECG were continually monitored and recorded regularly (every 5 min at least), together with the drugs administered during the procedure.

2.2.2. Surgical technique

The sheep were placed in dorsal recumbency for access to the CCAs. The neck of the sheep and the skin over one of the cephalic veins were clipped, and the skin was prepared with serial applications of an antiseptic and detergent solution (chlorhexidine and cetrimide), 70% alcohol and finally the antiseptic chlorhexidine. The prepped areas were isolated with drapes prior to commencement of the surgical procedure.

Anticoagulation therapy was provided via intravenous delivery of heparin (200 IU/kg loading dose with 100 IU/kg every 30–40 min for the duration of the surgery). Analgesia was further maintained throughout the surgery by the intravenous administration of Buprenorphine (0.01 mg/kg).

Six animals were studied and data were acquired from seven CCAs, as in one animal both sides were interrogated. In the other 5 sheep, the right CCA was studied in four and the left CCA in one, due to abnormally low flow on the right side. An incision via scalpel electrocautery was used to open the skin. The CCA was isolated from approximately 10 cm distal to its origin at the bicarotid trunk [3] which arises from the common brachiocephalic trunk of the aorta, along to within 1 cm proximal to the occipito-vertebral anastomosis. The CCAs were straight in all animals prior to dissection; after dissection in 5 of the 6 animals the vessel was also straight. In one animal the dissected CCA showed significant curvature, taking the shape of a smooth arc from the proximal to the distal ends of the isolated region.

2.3. Blood pressure and flow calibration and measurement

Pressure catheters (1.4F, SPR-671NR, or 3.5F SPR-524, Millar, Houston, TX, USA) and the blood flow transducer (MA8PSB, Transonic, Ithaca, NY, USA) were calibrated prior to use in surgery. Calibration of the pressure transducer was conducted by soaking in water at body temperature for a minimum of 30 min. After soaking, the transducers were held just below the surface of the water and zeroed. Calibration of the Transonic flow probes was according to standard procedures.

Blood pressure was measured at proximal and distal positions on the CCA; flow was measured proximally on the CCA (Fig. 1). The insertion points for the pressure transducers were approximately 10–15 cm apart, depending on the available length of the CCA in the animals. The pressure catheters were advanced approximately 2–5 cm into the proximal vessel and 1–3 cm into the distal end of the vessel. Advancement at the distal end was limited to ensure that the pressure transducer did not pass the occipito-vertebral anastomosis.

The placement procedure for the pressure catheters involved insertion of a sheathed needle (20Gx1 1/4, Surflow L.V. catheter, Terumo, Tokyo, Japan), removal of the needle from the sheath and insertion of the catheter into the vessel via the sheath. The sheath was drawn back along the pressure line and a suture around the catheter at the transducer insertion point was used to seal the artery against bleeding.

As soon as instrumentation was completed, pressure data was simultaneously acquired at proximal and distal pressure catheters, along with flow data via the flow probe.

2.4. Reorientation of pressure transducers in the CCA

In one sheep, after measurements were conducted with the proximal and distal pressure catheters oriented as shown in Fig. 1, the orientation of each of the catheters was reversed, so that the tips with the pressure transducers were pointed towards each other within the CCA. The catheters were advanced such that they "met" at the midpoint of the vessel. They were withdrawn in a stepwise manner, so that the combined distance between them provided a 2–3 cm step increase from the previous measurement point. Pressure data were acquired simultaneously from each pressure transducer at each measurement step.

At the completion of each study, animals were euthanised via intravenous lethal overdose of barbiturate (sodium pentobarbitone 200 mg/kg).

2.5. Data acquisition and analysis

Data from each pressure probe was acquired via a 2 channel amplifier/interface PCU-2000 signal conditioner unit 320-6580 RevE (ADInstruments, Bella Vista, NSW, Australia). Pressure and flow probe data were digitized at 250 samples/s via an 8 channel data analog/digital
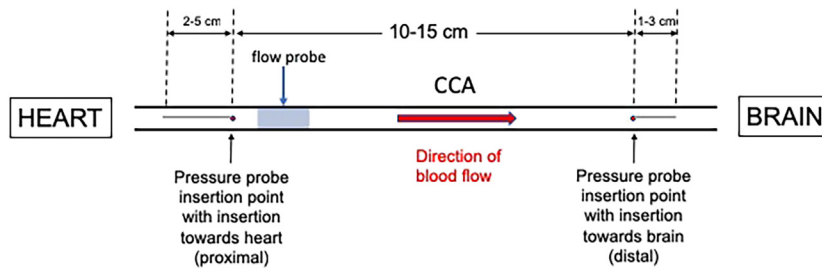
Fig. 1. Positioning of pressure and flow transducers on the CCA.

amplifier (GSV8DS, ME-Systeme, Hennigsdorf, Germany) and transferred to a customised Labview General Graphing Utility v0.2.2 (National Instruments, Austin, TX, USA) run on a PC. Data was analysed using RemLogic™ (Natus Medical Incorporated, Pleasanton, CA, USA) for measurement of the maximum slope (dp/dt_{max}) of the forward wave of the pressure waveform and pulse pressure measured as peak to trough pressure amplitude. For flow, dp/dt_{max} and pressure pulse analysis, the data from continuous runs of a minimum of 38 representative pressure waveforms were analysed automatically using RemLogic™ software.

2.6. Statistical methods

The prospectively defined primary endpoints of the study were: the difference between proximal and distal dp/dt_{max} on the arterial wave upstroke and the difference between proximal and distal pulse pressure. Descriptive data were expressed as median with interquartile range. A non-parametric test of significance, the Wilcoxon signed-rank test was used due to limited sample size, with a test of whether the proximal dp/dt_{max} was higher than the distal dp/dt_{max}; and whether the proximal pulse pressure was higher than the distal pulse pressure (one-sided analysis). Statistical significance was inferred at a one-sided p-value <0.05.

3. Results

The median CCA internal diameter was 5.5 mm, with interquartile range of 5.0–6.9 mm (n = 7). The median CCA wall thickness was 0.77 mm, with interquartile range 0.60–0.83 mm (n = 5). The median CCA flow rate was 0.97 L/min, with an interquartile range 0.51 to 1.15 L/min (n = 7).

Representative proximal and distal CCA pulse pressure waveforms are presented in Fig. 2; in this study the insertion points for the pressure catheters were 15 cm apart and total distance between catheter tips was 19–20 cm. The proximal waveforms present a steep systolic upstroke, with evidence of a reflected wave, as well as the presence of a dicrotic notch and additional low peaks. The distal waveform is much smoother, with a lower gradient on the upstroke and no distinct notches or peaks on the downstroke. The background effect of the respiration cycle is apparent in the gradual overall rise and fall of blood pressure in the sequence in Fig. 2.

The median dp/dt_{max} on the pressure rise of the arterial wave upstroke for the proximal CCA was 619 mm Hg/s, (432–841); the distal CCA dp/dt_{max} was significantly lower (p = 0.0156), at 197 mm Hg/s (77–375), see Fig. 3a. The median pulse pressure of the proximal CCA was 24 mm Hg/s (15–26), and the median pulse pressure of the distal CCA was significantly lower (p = 0.0156), at 18 mm Hg/s (9–20), see Fig. 3b.

3.1. Reorientation of pressure transducers in the CCA

Fig. 4 presents pressure measurements acquired when the pressure transducers were re-oriented so that they were each inserted medially towards the midpoint of the CCA. The pressure measurements from the point where each pressure transducer was midway within the vessel and for each of the steps of withdrawal of the catheters is presented. The two pressure signals were almost identical when placed in the same position and the waveform shape progressively diverges as the distance between sensors is increased.

4. Discussion

We have shown that the native CCA in sheep is a highly effective "pressure dampener" with significant reduction of dp/dt_{max} along its length, as well as a significant reduction in pulse pressure. These data suggest that the CCA in humans may also be an important site of dampening of the arterial wave intensity.
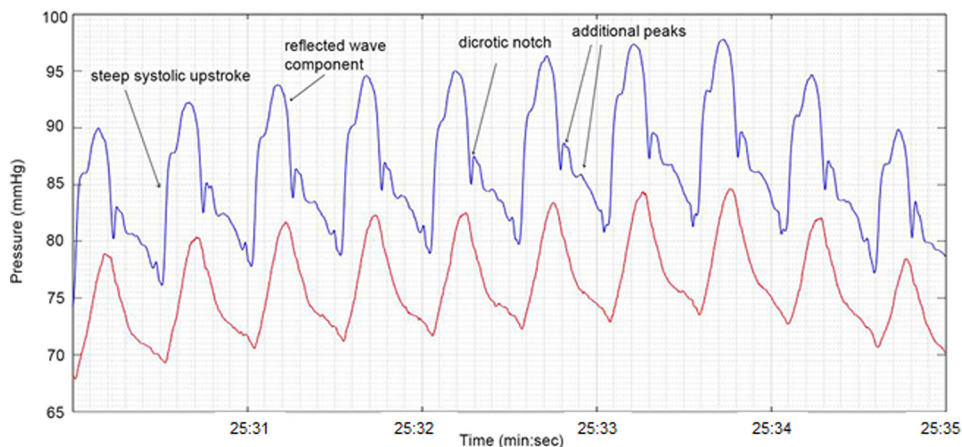

Fig. 2. Pressure waveforms from proximal and distal pressure acquisition positions on the CCA in a sheep. Proximal pressure (blue), distal pressure (red).
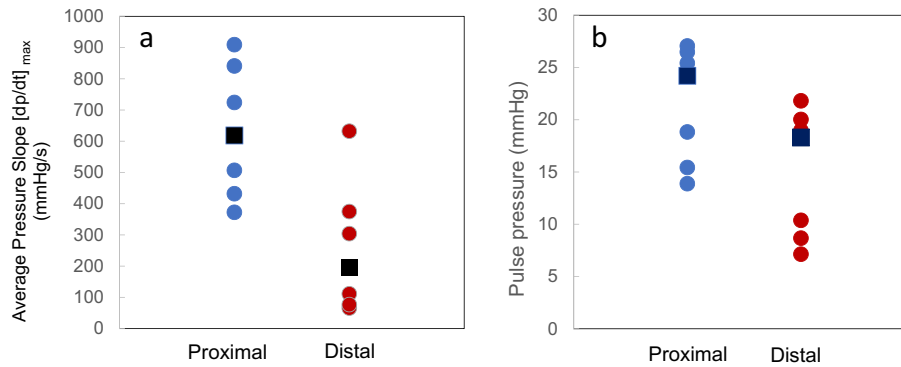
Fig. 3. Scatterplot of average pulse pressure slope dp/dt$_{max}$ (a) and average pulse pressure (b) for proximal and distal waveforms for each study. Median values are shown as squares, other data points are circles.

Understanding the site of arterial wave dampening may have relevance in the pathogenesis of cognitive decline and/or dementia, in humans. Vessels stiffen in older animals, leading to increased distal dp/dt$_{max}$ with consequences evident in the cerebral circulation. There has been a rapid growth in research studies correlating the association of high blood pressure and high pulse pressure with negative effects on cognition and/or risk of Alzheimer's disease [1,4,5]. A recently published study [6] from the Whitehall II cohort suggested SBP ≥130 mm Hg at age 50 but not at age 60 or 70 was associated with increased risk of dementia. Increased blood pressure in the brain leads to susceptibility to microhaemorrhage, which has been associated with dementia [7]. This is interesting as possible pressure dampening of CCA pulse pressure could ameliorate distal pulse pressure, providing benefit in older individuals.

There are two mechanisms that are proposed to operate in large arteries to protect the microvasculature from high pulse pressure. The first is high total arterial compliance, which in combination with vessel resistance creates a windkessel effect [8]; compliance decreases with aging, mainly due to a loss of aortic compliance, which leads to high pulse

pressures both centrally and peripherally. The second is pressure dampening due to viscoelastic energy dissipation in the arterial wall [2,9] which has received much less attention in the context of hypertension and aging. Given that purely elastic distension (i.e. compliance) causes steepening of the pressure upstroke as it propagates [9], whereas viscous energy dissipation in the arterial wall causes attenuation of the pressure upstroke and pressure pulse [2], our data is entirely consistent with the latter mechanism playing a role in protecting the downstream vasculature from both high pulse pressure and high wave intensity (i.e. pressure accelerations). Energy dissipation due to disturbed flow could also contribute to the pressure difference observed, but this is unlikely to be the major mechanism (noting that blood velocities in excess of 120 cm/s would be required to account for a pressure drop of 7 mm Hg).

4.1. Study limitations

There are important differences between the length of the CCA in the sheep model examined in this study and the length in humans (as well
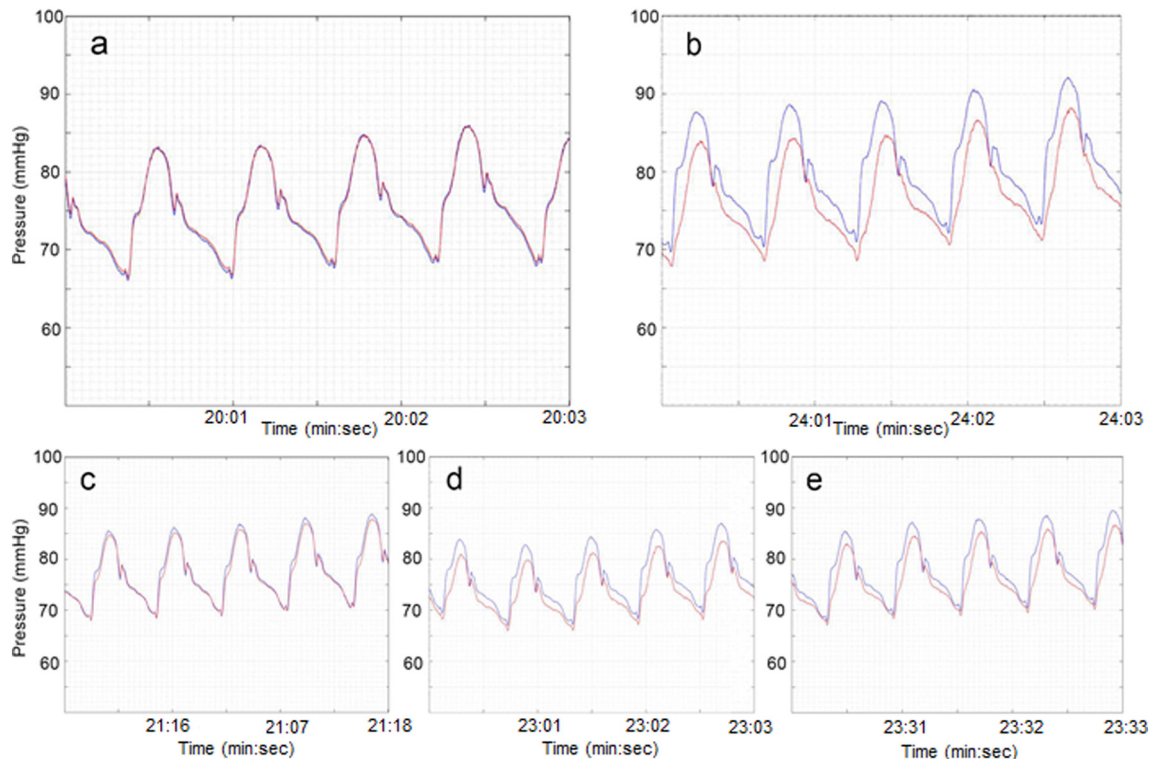

Fig. 4. Pressure waveforms from catheters inserted to midway between pressure probe insertion points, with stepwise withdrawal. (a) Pressure transducers at the midpoint; (b) separated by 9 cm; (c) intermediate separations of 2 cm; (d) 5 cm; (e) 7 cm. Proximal pressure (blue), distal pressure (red).

as in other aspects of cardiovascular structure and function). The length of the CCA from bifurcation at the aorta to bifurcation to internal and external carotid arteries in humans is around 12–13 cm, with some variation due to gender and age [10]. In this study the length of the CCA in the sheep from the bicarotid trunk to the occipito-vertebral anastomosis was approximately 20–25 cm, hence about twice the length of the human CCA. The dependence of the length of the vessel on the dampening effect was apparent from the assessment of the effect of distance between pressure catheter tips on dampening of the pulse pressure waveform, see Fig. 4.

Furthermore, it is possible that surgical exposure of the vessels led to underestimation of the dampening effect of the CCA. Exposure of the vessels surgically has been found to reduce vessel compliance by 10–20%, compared to measurements through intact tissue [11]. We also cannot exclude pressure "drift" during these experiments, however this would not affect the key variables evaluated in this study, namely dp/dt_{max} and pulse pressure.

5. Conclusion

The native CCA in the young adult sheep is an effective "pressure dampener" in the arterial circulation, reducing both pressure slope and pulse pressure, most likely via viscous dampening in the arterial wall. Further studies could explore older sheep or device implants, to assess potential ways to alter the abnormal stiffness in the older CCA for improved pulse pressure wave dampening.

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