

Local and regional wave speed in the aorta: effects of arterial occlusion

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Abstract

Arterial wave speed is widely used to determine arterial distensibility and has been utilised as a surrogate marker for vascular disease. A comparison between the results of the traditional foot-to-foot method for measuring wave speed to those of the pressure–velocity loop (PU-loop) method is one of the primary objectives of this paper. We also investigate the regional wave speed along the aorta, and the effect of arterial occlusion on the PU-loop measured in the ascending aorta. In 11 anaesthetised dogs, a total occlusion lasting 3 min was produced at four sites: upper thoracic, diaphragm, abdominal and left iliac artery. Pressure and flow in the ascending aorta and pressure proximal to the occlusion site were measured, and data were collected before, during the occlusion and after the occlusion had been removed. In control conditions, the wave speeds determined by the PU-loop in the aortic root were systematically lower than those measured by the foot-to-foot method. During thoracic and diaphragm occlusions, mean aortic pressure and wave speed increased significantly but returned to control values after each occlusion had been removed. The PU-loop is an objective and easy to use method for determining wave speed and can be advantageous for use in short arterial segments when local measurements of pressure and velocity are available.

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1. Introduction

Arterial wave speed, often referred to as the pulse wave velocity by physiologists and clinicians, is the speed at which changes in pressure and velocity travel along the artery. The wave speed depends chiefly upon the local properties of the arterial wall [1,2]. It is widely used to determine arterial distensibility [3] and has been used as a surrogate marker for cardiovascular disease including atherosclerosis [4]. Wave speed at other sites may also be of clinical importance; intra-ventricular wave speed has been suggested as an index to quantify ventricular contractility [5] and elastance [6].

In order to use wave speed as a bedside diagnostic tool, several approaches have been proposed to evaluate

wave speed in real-time [7,8]. The most common involves the simultaneous measurement of either pressure or velocity at two sites a known distance apart (L) and determining the time delay between the two measurements (δt), so the wave speed $c = L/\delta t$. These methods are commonly referred to as foot-to-foot methods since the foot of the systolic wave is usually taken as the reference point in the waveform. Probably the earliest application of this method in the arteries used pressure catheters [9], and since then similar measurements have been made by many other researchers [10–12]. Exact determination of the foot of the pressure wave is difficult because of the variability in the pressure waveform that occurs during late diastole and to a lesser degree, in the initial upstroke of the pressure pulse. In order to avoid this difficulty, other researchers have used different reference points. Frank [13] used 1/5 of the ascending slope of the systolic pressure contour, Kapal et al. [14] measured the velocities using four points on the rising limb and recently, Fitch et al. [15] have sug-

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gested using a point on the descending limb of the arterial pressure when pressure is 1 mmHg higher than diastolic pressure. The foot-to-foot method has also been applied to non-invasive velocity measurements using Doppler ultrasound [16] and magnetic resonance imaging [17]. These techniques strive to identify a point on the arterial pressure or velocity waveform that is not affected by reflected waves, which would affect the measurement of the wave speed.

It is important to note that the foot-to-foot techniques determine the time-averaged speed of the wave over the distance between the two measurement sites, which will be the same as the local wave speed only if all the physical properties of the vessel are the same along its length. However, the aorta has different structures and properties at different regions [18], which leads us to expect different wave speeds along the different regions of the aorta. Wave speed measurements can be made more locally using the foot-to-foot method by bringing the measurement sites closer together but the minimum spacing is usually limited by the need for higher temporal resolution [19]. There is thus a need for an alternative method to measure wave speed locally.

Impedance analysis of simultaneously measured pressure and velocity can be used to estimate the local wave speed. At higher frequencies, it is generally accepted that the effects of reflections are minimal because of the increased dissipation, and in the absence of reflections, the ratio between the Fourier transforms of the pressure and velocity is related to the local wave speed [20]. Although this method has been used extensively, its results are somewhat subjective and greatly dependant on the range of frequencies or harmonics used to define the characteristic impedance [21,22].

A different technique for determining the local wave speed from simultaneously measured pressure and velocity at the same site, the pressure–velocity loop (PU-loop) method, has been recently introduced [23]. The slope of the loop during early systole is linear and proportional to the local wave speed. This technique has been tested *in vitro* [24] and used *in vivo* to determine the wave speed in the ascending aorta of patients with cardiovascular disease [25].

The aims of this study are: (1) compare the results of the PU-loop method with those of the foot-to-foot method for determining the wave speed, (2) examine the regional wave speed along the aorta using the foot-to-foot method and (3) investigate the effect of arterial occlusion on the PU-loop method for measuring wave speed in the ascending aorta of open-chest anaesthetised dogs.

2. Methods

Experiments were carried out in 11 mongrel dogs (average weight, 22 ± 3 kg, seven males), that were

anaesthetised intravenously with sodium pentobarbital, 30 mg/kg body weight. A maintenance dose of 75 mg/h was given intravenously for the duration of the experiment. Each dog was endotracheally intubated and mechanically ventilated using a constant-volume ventilator (Model 607, Harvard Apparatus Company, Millis, MA, USA). After a median sternotomy, an ultrasonic flow probe (Model T201, Transonic Systems Inc., Ithaca, NY, USA) was mounted snugly around the ascending aorta, approximately 1 cm distal to the aortic valve. ECG leads were connected to both forelegs and the left back leg. Two high-fidelity pressure catheters (Millar Instruments Inc., Houston, TX, USA) were used to measure the pressure in the aortic root approximately 1 cm downstream from the aortic valve, and approximately 1 cm upstream from each occlusion site. The catheter in the ascending aorta was advanced from either the right or the left brachial artery and the catheter at the occlusion site was advanced from the right iliac artery. Snares were placed at four sites: (1) the upper descending thoracic aorta at the level of the aortic valve “*thoracic*”, (2) the lower thoracic aorta at the level of the diaphragm “*diaphragm*”, (3) the abdominal aorta between the renal arteries “*abdominal*” and (4) the left iliac artery, 2 cm downstream from the aorta–iliac bifurcation “*iliac*”. Fig. 1 shows the occlusion sites along the aorta and the average length of each segment.

For each occlusion, data were collected for 30 s at three times: before occlusion, during occlusion (3 min after the snare was applied), and after removing the occlusion (3 min after the snare was removed). The duration of the occlusion was chosen not only because it was used by other researchers [26], but also because we observed that heart rate immediately increased significantly on applying the snare then returned to control conditions after approximately 2 min. An interval of 15 min was allowed between occlusions for recovery. Each dog was occluded at four sites and the sequence of occlusions was varied from dog to dog using a 4×4 Latin-square, in order to eliminate time effects. The distances between the occlusion sites and the measurement site in the ascending aorta were measured *post-mortem* by marking the catheter at each occlusion site as it was withdrawn from the aorta.

To convert the measured flow rate into velocity, we measured the circumference of the ascending aorta *post-mortem*. To compensate for the different phase response of the pressure and flow transducers, the feet of the pressure and velocity waveforms were brought into coincidence prior to carrying out the analysis. Shifting of no more than three sampling intervals (i.e., 15 ms) was required, consistent with the maximum measured lag attributable to the filter in the ultrasonic flow meter used in our experiments [27]. The pressure catheters were calibrated before each experiment against a mercury manometer and all data were recorded at a sampling

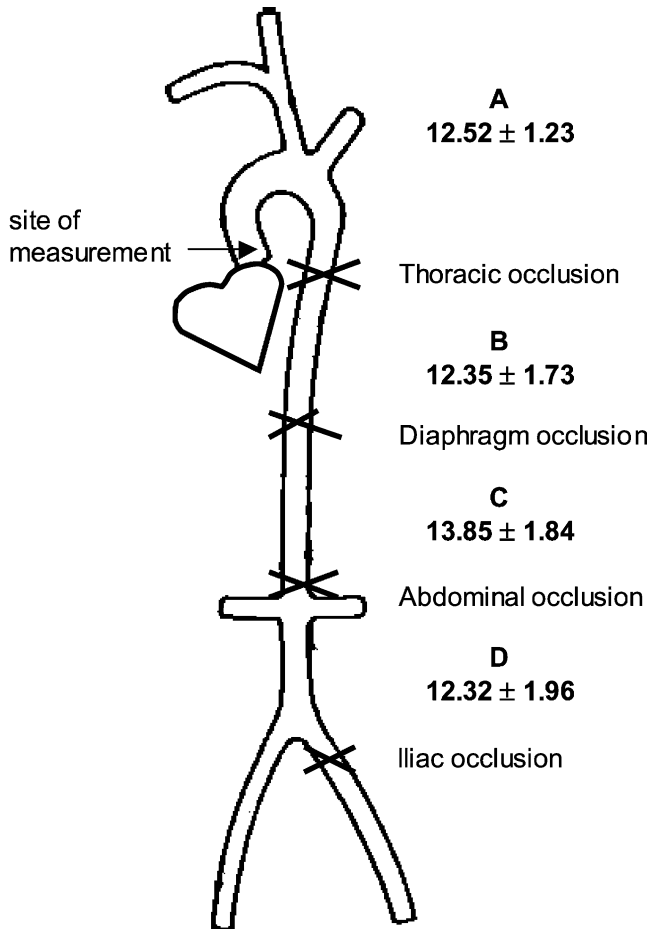


Fig. 1. The occlusion sites along the aorta with the mean and standard deviation of the length of each segment. Distances were measured post-mortem (cm).

rate of 200 Hz and stored digitally. Data were converted into ASCII format using CVSOFT (Odessa Computer Systems Ltd., Calgary, Canada) and were analysed using programs written in Matlab (The MathWorks Inc., MA, USA).

The relative difference between the two methods of measuring wave speed is calculated as the ratio of the difference between the two results (foot-to-foot minus PU-loop) to the average of both results [28]. The change of wave speed due to the occlusion determined by each method is calculated as the ratio of the difference between the two results (during occlusion minus control) to control and presented as (control vs. occlusion). Paired *t*-tests were used in all comparisons and $p < 0.001$ was considered statistically significant.

3. Analysis

The theoretical basis of the PU-loop method for determining wave speed has been described previously [23]. Briefly, the water hammer equation for forward (+) and backward (–) waves is

$$dP_{\pm} = \pm \rho c dU_{\pm} \quad (1)$$

where dP and dU are the pressure and velocity differences across the wavefront, ρ is the density of the blood and c is the wave speed. Eq. (1) can be used for determining the wave speed when the waves passing by the observation site are in one direction only, which is most probably the case during the earliest part of systole. During this time, it is probable that only forward waves are in the ascending aorta because it is too early for the arrival of any reflected waves. Integrating (1) for forward waves produces

$$P_{+} - P_0 = \rho c U_{+} \quad (2)$$

where P_0 is the pressure at end diastole, $t = 0$ and $U = 0$. Eq. (2) is an equation for a straight line relating P_{+} and U_{+} with a slope of ρc . Thus, plotting the measured pressure against the measured velocity over the cycle one obtains the PU-loop, whose slope during the very early part of systole equals ρc , when $P = P_{+}$ and $U = U_{+}$. In all our calculations, we assume the blood density, $\rho = 1050 \text{ kg/m}^3$.

The foot-to-foot method for measuring the wave speed is based on measuring the time that it takes the wave to travel from one observation site to another, a known distance away. We measured this transmission time using a technique similar to that used by McDonald [10]. We shifted the pressure waveform measured downstream at the occlusion site back in time, until its early systolic upstroke superimposed on the upstroke of the pressure waveform measured upstream. In order to improve the technique, we subtracted the diastolic value from each signal so that the initial upstroke of both signals starts from zero, making the superimposition of the initial upstrokes easier, as shown in Fig. 2a. Also, in order to improve the results of this technique, we shifted the downstream pressure waveform back in time in steps that were smaller than a sampling period ($< 5 \text{ ms}$) and the superimposition was detected by eye.

The regional wave speed along the aorta was estimated for each of the four segments shown in Fig. 1 using the foot-to-foot method. The time delay in region B was determined by subtracting the time delay measured in region A from that measured in region AB, giving the wave speed in B. The time delay in region C was determined by subtracting the time delay measured in region AB from that measured in region ABC, giving the wave speed in region C, etc.

4. Results

4.1. Comparison between methods for measuring wave speed

We measured the wave speed in the aorta of each dog under control conditions and compared the results of the foot-to-foot method with those of the PU-loop method.

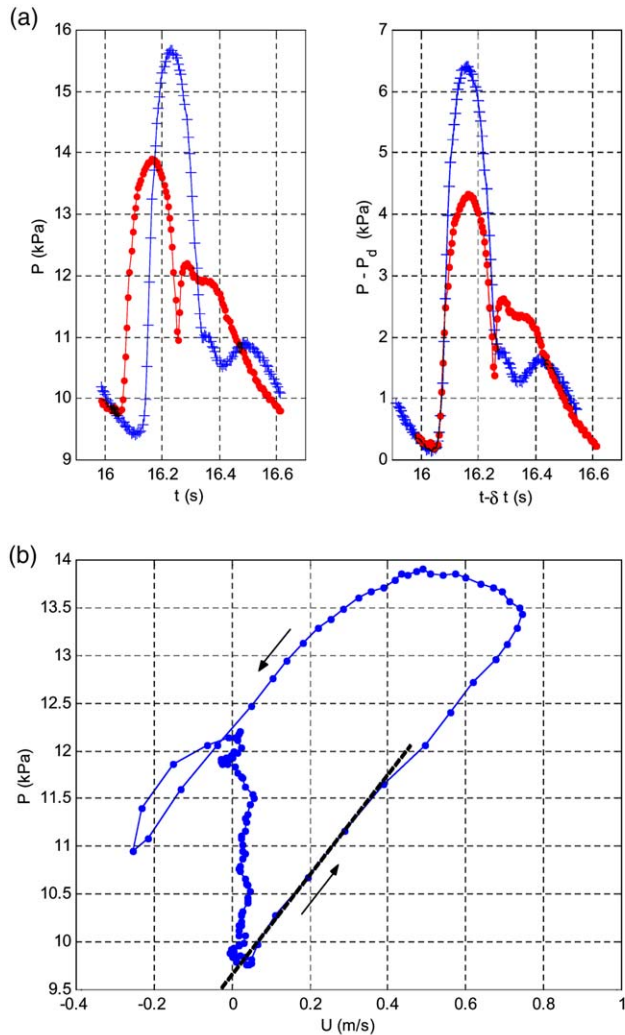


Fig. 2. The wave speed measured by (a) foot-to-foot method. The left panel shows the pressure waveform measured in the ascending aorta (\bullet) and in the iliac artery ($+$). The right panel shows the two waveforms with their diastolic pressure, P_d , subtracted and the iliac waveform shifted so that the initial upstroke of the two waveforms superimpose. The time delay $\delta t = 72$ ms and distance between the two measurement sites is 45.5 cm giving a wave speed of 6.3 m/s. (b) The PU-loop in the ascending aorta for the pressure (\bullet) shown in (a), and the corresponding velocity. The points indicate data sampled at 200 Hz and the initial slope, dashed line, indicates a wave speed of 4.9 m/s. The linear portion corresponding to early systole is fitted by eye and the arrows indicate the direction of the loop.

Foot-to-foot method: a typical illustration of the technique used to calculate wave speed by the foot-to-foot method is shown in Fig. 2a. In this case, the distance between the two catheters was 45.5 cm and $\delta t = 72$ ms giving an average wave speed of 6.3 m/s, over aortic sections ABCD.

PU-loop: a typical example of the PU-loop method for calculating wave speed in the ascending aorta for the above case is shown in Fig. 2b. The initial part of the loop is linear, its slope equals ρc and the wave speed calculated from the slope is 4.9 m/s.

The average wave speed under control conditions, for four breathing cycles, at four different times (the control runs prior each occlusion), for each dog, measured in the ascending aorta by the PU-loop is compared to:

- The average wave speed in segment A measured by the foot-to-foot method under control conditions, for four breathing cycles, for each dog as shown in Fig. 3a, and
- The average wave speed along the whole length of the aorta (segment ABCD), measured by the foot-to-foot method under control conditions, for four breathing cycles, for each dog as shown Fig. 3b.

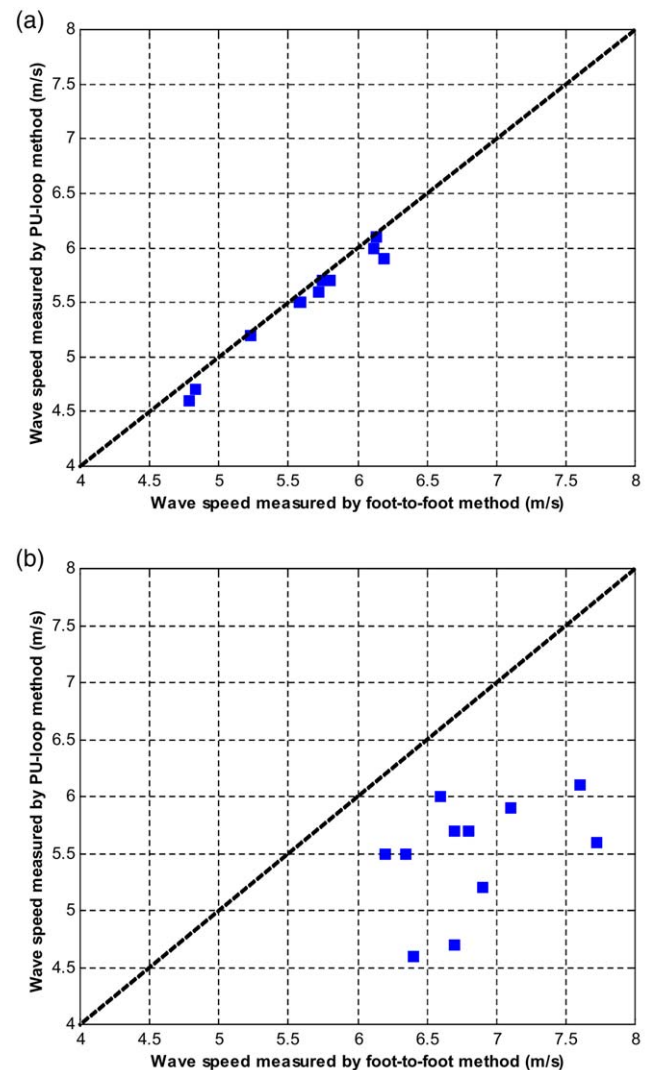


Fig. 3. Average values of wave speed measured by PU-loop method in the ascending aorta and the foot-to-foot method in segment A in (a), where the two methods give similar results, close to the line of identity (dashed line) with a relative difference of 2%. (b) The foot-to-foot method along the whole aorta and the relative difference between the results is 20%. In both cases, the foot-to-foot method gives the higher values. The relative difference is calculated as the ratio of the difference between the two results (foot-to-foot minus PU-loop) to the average of both results.

In these experiments, the average difference between the results of the two methods is 2% (5.6 ± 0.8 vs. 5.5 ± 1.3 m/s, $p < 0.001$) in segment A and 20% (6.7 ± 0.92 vs. 5.5 ± 1.3 m/s, $p < 0.001$) along the entire length of the aorta (segment ABCD). The wave speed given by the foot-to-foot method is consistently higher than the local wave speed in the ascending aorta given by the PU-loop method.

4.2. Regional wave speeds along the aorta

Wave speed is determined by the foot-to-foot method in the four segments shown in Fig. 1.

During control: mean value of the wave speed was lowest in segment A (5.6 ± 0.8 m/s) and increased (6.3 ± 0.9 m/s) in segment B, (7.2 ± 1.1 m/s) in segment C, and (8.7 ± 0.7 m/s) in segment D. Overall average wave speed along the whole aorta is 6.7 ± 0.92 . Fig. 4 shows the average wave speed at the average length of each segment.

During occlusions: wave speed increased in segment A during thoracic occlusion by 28% (5.6 ± 0.8 vs. 7.2 ± 1.2 m/s, $p < 0.001$) and in segment AB during diaphragm occlusion by 18% (6.3 ± 0.9 vs. 7.4 ± 1.1 m/s, $p < 0.001$) compared to their values in control. Wave speed did not change in segments ABC or ABCD during abdominal or iliac occlusions.

4.3. The effect of arterial occlusion on local wave speed

Total arterial occlusion proximally for 3 min caused a significant acute increase in mean aortic pressure during thoracic occlusion by 45% (12.8 ± 1.8 vs. 18.7 ± 3.3

kPa, $p < 0.001$) and by 10% (15 ± 2.5 vs. 16.6 ± 2.2 kPa, $p < 0.001$) during diaphragm occlusion, compared with control values. The acute increase in mean aortic pressure was associated with a significant acute increase in local wave speed in segment A by 25% (6.3 ± 1.5 vs. 7.9 ± 1.5 m/s, $p < 0.001$) during thoracic occlusion and by 10% (5.1 ± 1.2 vs. 5.6 ± 0.9 m/s, $p < 0.001$) during diaphragm occlusion, compared with control values. Once the occlusion was removed, the mean aortic pressure and wave speed reverted to their values at control conditions. There was no significant change in either mean aortic pressure or in wave speed during abdominal and iliac occlusions.

Fig. 5 shows the effect of an acute change in pressure on the shape of the PU-loop and the wave speed in a typical dog. The slope of the initial part of the loop became steeper during thoracic and diaphragm occlusions, indicating a higher wave speed than found under control conditions or with distal occlusions. We could not detect any difference in wave speed between control conditions and during the more distal occlusions.

5. Discussion

Total occlusion of the aorta using a snare provides a convenient means for producing acute changes in blood pressure. The changes occurred almost immediately upon applying and releasing the snare. We acknowledge that arterial occlusion may produce a massive sympathetic outflow and aortic occlusions above the renal arteries in particular may activate the renin–angiotensin–aldosterone system, which consequently contributes to blood pressure change. However, the scope of this study is to investigate the effect of arterial occlusion on wave speed as measured by the PU-loop and the foot-to-foot methods, giving attention only to changes in blood pressure. Dissecting the impact of non-hemodynamic parameters such as neuro-hormonal, sympathetic and parasympathetic factors on wall properties, changes in pressure and wave speed requires further investigations and additional measurements.

Wave speed, c , is one of the mechanical properties of an elastic vessel and is a direct measure of its distensibility, D since $c = (\rho D)^{-1/2}$ where $D = (1/A)(dA/dP)$, where A is the cross-sectional area of the vessel and dA is the change in A with change in pressure dP . Thus, the less distensible the wall of the vessel is, the higher the wave speed will be. Lack of aortic distensibility, due to either increased blood pressure or disease, is an important determinant of both left ventricular function and coronary blood flow. Left ventricular load is affected by the stiffness of the aorta during systole, and coronary flow depends on the elastic recoil of the ascending aorta during diastole. Thus, the ability to measure local wave speed in the aortic root may be of a distinct advantage conferred by the PU-loop method.

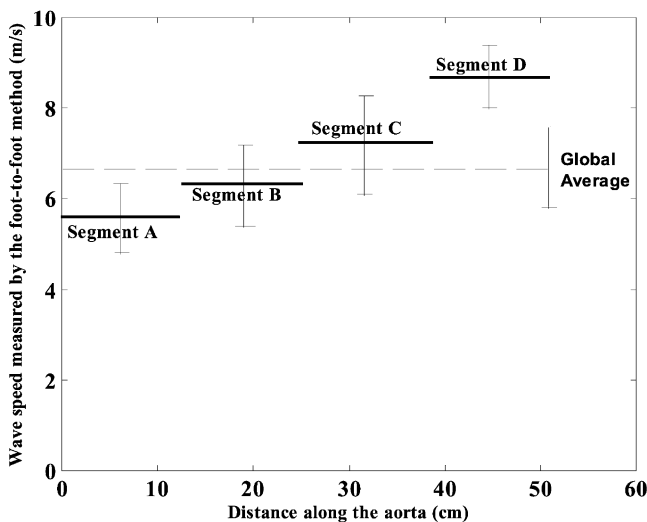


Fig. 4. Wave speed in four segments along the canine aorta. Wave speed gradually increased distally. Overall average wave speed along the whole length of the aorta measured by the foot-to-foot method, dashed line, is 6.7 ± 0.92 m/s, which is 20% higher than that measured in the ascending aorta by the PU-loop method.

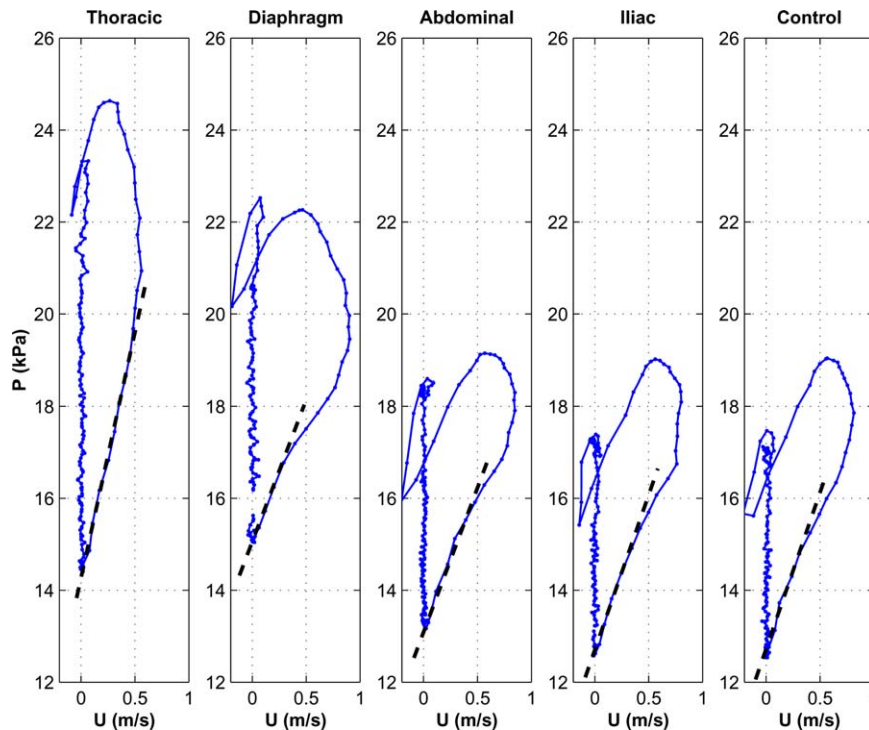


Fig. 5. The effect of arterial occlusion at different sites on the PU-loop and wave speed. During thoracic and diaphragm occlusion, the loop is elevated due to the significant increase in pressure. During thoracic occlusion, the loop became thinner due to the significant decrease in flow and the initial part of the loop became steeper indicating to a wave speed of 8 m/s, which is higher than that of control (6.2 m/s). Neither the shape of the loop nor the slope of its initial part during abdominal and iliac occlusion, were different from those of the control.

Fig. 3 shows that the wave speed calculated by the foot-to-foot method is always higher than that calculated by the PU-loop method. This systematic difference is expected because the foot-to-foot method calculates an average of the wave speeds of all the segments of the aorta between the two measurement sites and wave speed is progressively higher distally. The PU-loop measurement, however is local to the ascending aorta, the most distensible part of the aorta. We note that the wave speed measured by the foot-to-foot method in segment A, although statistically significantly higher, was very close to that determined by the PU-loop method in the ascending aorta.

The results of this research suggest that the PU-loop method for measuring wave speed in the ascending aorta and the foot-to-foot method for measuring wave speed along the aorta differ in a rational way. Whilst the PU-loop measures wave speed locally, the foot-to-foot method measures an average wave speed regionally over a specific distance. Regional wave speed increases distally and its value is always higher than that measured by the PU-loop in the ascending aorta because of the different anatomy and wall structure throughout the arterial bed.

Local wave speed is of clinical benefit, particularly when non-invasive local measurements of pressure and velocity are available. Applanation tonometry has been shown to be an accurate and reproducible technique for

determining the pressure waveform in superficial peripheral arteries [29–31]. In addition, pulsed wave Doppler may be used to determine velocity at the same arterial sites [32,33]. These techniques have recently been used together with the PU-loop to determine wave speed at the carotid, brachial and radial arteries of hypertensive subjects [34]. Also, ascending aortic pressure may be derived from the measurement of the radial artery pressure using the Sphygmocor general transfer function (GTF) [35,36]. When the results of these devices are validated clinically, they may be used together with pulsed wave Doppler for determining wave speed locally in the ascending aorta.

The PU-loop approach for determining local wave speed may provide evidence of early pathological arterial wall change which may not be evident using other non-invasive modalities such as magnetic resonance or ultrasound imaging. On-going work will assess the clinical relevance of local wave speed determined using the PU-loop and non-invasively acquired pressure and flow velocity data in normal volunteers, and patients with hypertension and heart failure.

We conclude that the PU-loop is an objective and easy to use method for determining wave speed and can be advantageous for use in short arterial segments, where it would be difficult to use the foot-to-foot method.

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