Waveform dispersion, not reflection, may be the major determinant of aortic pressure wave morphology

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Submitted 25 April 2005; accepted in final form 13 July 2005

Hope, Sarah A., David B. Tay, Ian T. Meredith, and James D. Cameron. Waveform dispersion, not reflection, may be the major determinant of aortic pressure wave morphology. Am J Physiol Heart Circ Physiol 289:H2497–H2502, 2005.—The objective of this study was to investigate the determinants of aortic pressure waveform morphology in the thoracoabdominal aorta with specific reference to features of potential prognostic value for cardiovascular disease. In particular, we aimed to determine the location of major pressure wave reflection sites within the aorta. Aortic pressure waveforms were acquired with 2-Fr Millar Mikro-tip catheter transducers in 40 subjects (26 men, 14 women), and repeated in 10 subjects, at five predetermined points within the aorta: aortic root, transverse arch, and at the levels of the diaphragm, renal arteries, and aortic bifurcation. Waveforms were analyzed for augmentation index (AI), time to inflection point (TI), and pressure parameters. AI decreased progressively between the aortic root and bifurcation (P < 0.001), and TI increased (P < 0.01). There was the expected progressive peripheral amplification of systolic and pulse pressures and fall in time to peak pressure (all P < 0.001). There was no difference on repeat pullback or between sexes. These data are at variance with the concept that central AI results from the superimposition upon the forward traveling wave, resulting from cardiac contraction, of a pressure wave returning from a peripheral reflection site (11, 19). The site of the putative reflection point has been debated, with some authors suggesting the predominant reflection point to be either at the renal arteries or at the aortic bifurcation and others suggesting that the reflection point has no physical reality but represents the combined effects of reflection from many peripheral sites (8, 9, 14). Consistent with the hypothesis of wave reflection are the findings that increased central augmentation index is associated with increased pulse wave velocity, when the reflected wave would be expected to return earlier in systole because of the decreased transit time, and independently associated with small height (22), when the reflected wave would be expected to return earlier in systole because of the shorter distance to the putative reflection point (15, 16, 22).

According to the hypothesis that central pressure augmentation is caused by the reflection of pressure waves from the periphery, the time to the inflection point on the pressure waveform, marking the putative onset of influence of a reflected wave, would be expected to decrease, and the augmentation index to increase, with distal progression from the aortic root toward the putative reflection point. This hypothesis has been previously tested, and supported, in only two small groups of subjects (14, 18).

METHODS

The study was performed in the cardiac catheterization laboratory of Monash Medical Centre. The study was approved by the institutional Human Research and Ethics Committee and performed in accordance with institutional guidelines. Participants gave written informed consent. Forty subjects, twenty-six men and fourteen women, were studied at the time of clinically indicated coronary angiography (32 subjects) or percutaneous coronary intervention (8 subjects). Mean age was 65 ± 12 yr, mean height 170 ± 8 cm, mean weight 79 ± 14 kg, and mean body mass index 28 ± 5 kg/m². Four subjects were current smokers, and twenty-two had hypertension, nine diabetes mellitus, thirty-four hypercholesterolemia, and nine family history of cardiovascular disease. All subjects were in sinus rhythm at the time of the study.

Data acquisition. Data were acquired under baseline conditions after completion of the clinically indicated procedure. Aortic waveforms were acquired with a 2-Fr Millar Mikro-tip catheter transducer introduced via a 6-Fr multipurpose or right coronary guiding catheter positioned at the aortic root under fluoroscopic control. The Millar transducer was positioned just distal to the tip of the guiding catheter.

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IN NORMAL PHYSIOLOGICAL STATES central systolic blood pressure determines cardiac afterload and is thus a determinant of cardiac work and energy requirement. In both physiological and pathological states central blood pressure is considered to result from the interaction of the heart and systemic vasculature through peripheral resistance and large-artery impedance. Central (as opposed to brachial) blood pressure has been proposed to be important in causing or accelerating cardiovascular pathology and in determining risk (21, 25), and techniques involving aortic pressure “pulse wave analysis” have been proposed to predict cardiovascular risk. If central blood pressure is indeed a more relevant determinant of cardiovascular function than conventional brachial blood pressure or if, as has also been suggested, the difference in central and brachial systolic blood pressure is a risk indicator, knowledge of what determines the central blood pressure waveform is essential to target appropriate intervention.

The augmentation of central systolic pressure, associated with cardiovascular mortality, is often described by the augmentation index (16). Although not universally accepted, the augmentation of central pressure is widely believed to result from the superimposition upon the forward traveling wave, resulting from cardiac contraction, of a pressure wave returning from a peripheral reflection site (11, 19). The site of the putative reflection point has been debated, with some authors suggesting the predominant reflection point to be either at the renal arteries or at the aortic bifurcation and others suggesting that the reflection point has no physical reality but represents the combined effects of reflection from many peripheral sites (8, 9, 14). Consistent with the hypothesis of wave reflection are the findings that increased central augmentation index is associated with increased pulse wave velocity, when the reflected wave would be expected to return earlier in systole because of the decreased transit time, and independently associated with small height (22), when the reflected wave would be expected to return earlier in systole because of the shorter distance to the putative reflection point (15, 16, 22).

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Waveforms were recorded to a personal computer with Chart for PowerLab (ADInstruments) at 2,000 Hz. After the acquisition of 30 s of data from the aortic root, the guiding catheter and Millar transducer were pulled back together and similar data were recorded from the transverse aortic arch, the level of the diaphragm, the level of the renal arteries, and at the aortic bifurcation. All positions were confirmed by fluoroscopy, and the levels of the renal arteries and aortic bifurcation were also confirmed by angiography. The physical distance between recording sites was measured by the use of a marker catheter. The electrocardiogram was recorded simultaneously with all pressure measurements.

In 10 subjects the catheter and transducer were repositioned at the same point at the aortic root guided by fluoroscopy and the marker catheter. Repeat data were then acquired from the same five aortic points. Data were resampled at 200 Hz for waveform analysis.

_Time-domain waveform analysis._ Ten representative waveforms identified by the onset of the systolic pressure upstroke were analyzed for each subject for each of the five aortic sites. In those subjects experiencing ectopic beats, preectopic, ectopic, and postectopic beats were excluded from analysis. Waveforms were analyzed for waveform characteristics of potential clinical interest with purpose-written software, as previously described (Fig. 1, top; Ref. 10).

_Frequency-domain waveform analysis._ Ten representative waveforms defined by the R-R interval of the electrocardiogram were identified for each aortic site for each subject. These were averaged and subjected to a 256-point fast Fourier transformation spectral analysis, yielding a fundamental frequency of 0.78 Hz for transfer function derivation. Although there was a short time interval between the acquisition of data from the different sites, the average waveforms were assumed to be acquired simultaneously for the purposes of the derivation of transfer functions between the aortic sites using the R wave as the constant reference point (the waveform at the proximal site was defined as the input and that at the distal site as the output of the system). For each subject apparent phase velocities were calculated from the local gradient of the phase of the transfer function between the aortic root and distal sites and the measured distance between the two sites.

_Statistical analysis._ All continuous variables are presented as means (SD) or graphically as means ± SE. The change in waveform parameters with distal progression along the aorta was assessed by repeated-measures analysis of variance. Within subjects simple contrasts were explored to identify where significant differences lay. Significance was taken as $P < 0.05$, and statistical analysis was performed with SPSS 11.0 for Windows (SPSS).

![Fig. 1. Top: schematic representation of the describing parameters used for waveform analysis. Abbreviations are given in Table 1. Bottom: example of recorded pressure waveforms at given points in the aorta. Decreasing augmentation index with distal progression along the aorta is highlighted. From inferior to superior the traces represent the electrocardiogram and pressure waveforms at the aortic root (augmentation index 52.3%), transverse arch (augmentation index 45.0%), level of the diaphragm (augmentation index 20.8%), level of the renal arteries (augmentation index 14.7%) and aortic bifurcation (augmentation index 14.6%) in a single subject, synchronized to the peak of the R wave of the electrocardiogram.](http://ajpheart.physiology.org/)

_AJP-Heart Circ Physiol • VOL 289 • DECEMBER 2005 • www.ajpheart.org_
RESULTS

Waveform characteristics at the five aortic sites, together with noninvasively measured brachial pressures, are detailed in Table 1. An example of waveforms from the five sites in an individual subject is presented in Fig. 1, bottom. Terminology and abbreviations used to describe waveform morphology are given in Fig. 1, top, and Table 1. Mean augmentation index was found to decrease progressively between the aortic root and bifurcation \( (P < 0.001) \) and time to inflection point was found to increase \( (P < 0.01) \) (Fig. 2). Despite this, as expected there was peripheral amplification of systolic and pulse pressures and a fall in the time to peak pressure (all \( P < 0.001 \); Fig. 3). The time to the end of systole also decreased progressively (Fig. 3). Augmentation index was associated with both time to inflection point and heart rate \( (P < 0.001) \) but was not associated with measured pulse wave velocity over any aortic segment. On multiple regression analysis aortic pulse wave velocity was associated with proximal pulse pressure and systolic pressure time integral only \( (P < 0.001) \). Heart rate did not differ by more than 2 beats/min between individual recordings, and the difference cannot explain the progressive differences observed in the waveform parameters between aortic sites. There was no difference with sex or between those who had undergone percutaneous coronary intervention rather than simple angiography. There was also no difference between the first and second pullback in the 10 patients who had the procedure repeated.

Mean arterial blood pressure differed significantly among the five aortic sites \( (P < 0.05; \text{Fig. 4}) \), with post hoc analysis revealing the mean arterial pressure to be significantly higher at the diaphragm than at all other sites \( (P < 0.05) \). However, the difference between the mean arterial pressure at the aortic root and the diaphragm was small \( 3.6 \pm 4.6 \text{ mmHg} \). The pattern of diastolic pressure was similar to that of mean arterial pressure (Fig. 4), with a significant difference between sites \( (P < 0.001) \) and diastolic pressure being higher at the diaphragm than at all other sites \( (P < 0.001) \). Again, mean differences between the aortic root and diaphragm were small \( 3.4 \pm 3.4 \text{ mmHg} \). The differences between noninvasively measured brachial and aortic root mean arterial pressure and diastolic pressure were also small \( 5.6 \pm 5.6 \text{ mmHg} \), respectively.

Magnitude and phase diagrams for the average transfer functions between the aortic root and the four distal aortic sites are depicted in Fig. 5. There is variability in the slope of the phase of the transfer functions, and looking particularly at the transfer functions between the aortic root and diaphragm and more distal sites, the slope appears flatter for the lower than the
higher harmonics, in keeping with higher phase velocities for the lower frequencies. The pattern of the calculated phase velocities for most subjects was consistent with this, with the measured foot-to-foot pulse wave velocity of the arterial pressure waveform being similar to the average apparent phase velocity of the higher frequencies (>3 Hz) (Fig. 5). However, in some individuals there were peaks of apparent phase velocity at differing specific harmonics, suggestive of significant wave reflection at these particular frequencies (Fig. 5).

**DISCUSSION**

The progressive decrease in augmentation index and corresponding increase in time to the inflection point with distal progression along the aorta was contrary to the expected findings according to the hypothesis that the inflection point marks the onset of influence of a reflected pressure wave. Although our findings for the time to inflection differ from those of two previous small studies, there are previously published waveforms that appear consistent with our observations (14, 18, 20). Our findings for other waveform characteristics are in accordance with previously published data, with the expected peripheral amplification of systolic pressure and pulse pressure and increase in delay in the foot of the pressure wave and decrease in time to peak pressure (9, 12, 20). It might be argued that, because our pressure recordings were not acquired simultaneously from the different aortic sites, there may have been some systematic change in the physiological condition of the subjects between recordings that might account for our findings for time to the inflection point. However, the finding that there was no difference when the measurements were repeated in a group of 10 subjects suggests that this was not the case. It is interesting to speculate that the differences in mean and diastolic pressures at the diaphragm, and apparent nonlinear changes in systolic pressure and time to inflection point, may be due to external constraints on the aorta as it traverses the diaphragmatic hiatus, leading to apparent increase in local aortic stiffness. However, the differences between mean arterial pressure and diastolic pressure at the

![Fig. 3](http://ajpheart.physiology.org/)  
Fig. 3. Peripheral amplification of pressures and fall in times to peak pressure and end of systole with distal progression in the aorta. Bars indicate SE.

![Fig. 4](http://ajpheart.physiology.org/)  
Fig. 4. Mean and diastolic pressures at 5 aortic sites. Mean difference between aortic root and diaphragm in mean arterial pressure is 3.6 (SD 4.6) mmHg and in diastolic pressure is 3.7 (3.4) mmHg. Bars indicate SE.
different aortic sites were small, as were the differences between noninvasively measured brachial and aortic root measurements of both mean and diastolic pressures. Indeed, the latter lie within the criteria set by the Association for the Advancement of Medical Instrumentation for equivalence for blood pressure measuring devices (26). Thus the assumption that mean and diastolic pressures are equivalent throughout the arterial syste (9), which is often adopted, remains reasonable on the basis of this data.

Because the findings for augmentation index and time to the inflection point appear inconsistent with the theory of pressure wave reflection, the question arises as to what else might be responsible for this phenomenon. Because it has long been known that the apparent phase velocities of different frequencies within the arterial pressure waveform differ, with higher velocities for the lower frequencies (14, 17, 23), consistent with our data, it is conceivable that the phenomenon of central pressure augmentation may arise because of frequency dispersion. The foot of the arterial waveform and the augmentation point are dependent on high-frequency components of the waveform (5, 17) and would therefore be predicted to become relatively delayed compared with the lower-frequency components with distal waveform progression. This concept was first described by Bramwell and Hill (3) in 1923, in relation to relative delay in wave front progression, and would be expected to result in the types of progressive changes along the aorta that have been demonstrated in this study, with relative delay of both the foot of the pulse wave and inflection point relative to the peak. The concept is not inconsistent with the previously described association between a short time to inflection and small stature, although this association was not evident in our data, because height might simply represent a surrogate measure of aortic diameter and pulse wave and phase velocities are determined not only by properties of the arterial wall but also by the physical dimensions of the vessel, with pulse wave velocity being inversely proportional to the square root of the radius (Moens-Korteweg equation) (4). The previously described association between a short time to inflection and pulse wave velocity might also be explained because the latter is largely equivalent to the phase velocity of the higher frequencies in the pulse pressure waveform (17). Alternatively, if the systemic arterial system is modeled as an asymmetric T tube, reflections from the shorter (cephalic) branch would be progressively delayed and attenuated with distal progression in the longer branch as reported. We feel, however, that there is unlikely to be sufficient energy reflection from this mechanism to account fully for our observed waveform morphologies.

Changes in the phase velocities of the higher frequencies, with or without changes in the lower frequencies, would be expected to result in a change in the degree of frequency dispersion, which would be reflected by changes in time to the inflection point and augmentation index. This phenomenon also provides a possible explanation for the previously described dissociations between pulse wave velocity and augmentation index observed, for example, after caffeine ingestion, when pulse wave velocity has been described to remain elevated while the augmentation index has returned toward baseline levels, and with oral vasoactive drugs (7, 13, 24). It may be that differential effects on the phase velocities of high and low frequencies are responsible for observations that appear inconsistent with wave reflection phenomena.

We do not suggest that the influence of wave reflection should be completely dismissed. In any wave guiding system reflection, dispersion and attenuation will be operative and will be dependent on both guide dimensions and wave frequency. The findings for the increasing amplitude, particularly of the sixth harmonic, of the average transfer functions between the aortic root and progressively more distal sites presented in Fig. 5 suggest that significant reflection of this harmonic may be occurring either at, or distal to, the aortic bifurcation but that there is substantial attenuation of the reflected wave at more proximal sites with much reduced contribution of the reflected wave at the aortic root. The interpretation of apparent phase velocities is also complicated by any wave reflection. We have demonstrated variation in the transfer function phase, which was significantly more marked in the individual than average transfer functions and has previously been accepted to indicate the presence of wave reflection (23). In addition to this, the peaks in apparent phase velocity seen at individual frequencies in some subjects are highly suggestive of significant wave
reflection at these frequencies. This may explain the finding that, although there was progressive reduction in augmentation index with distal progression along the aorta as analyzed by repeated-measures analysis of variance, there was variation at different sites in individuals with a locally increased augmentation index, consistent with only a very localized impact of reflected waves on the augmentation index.

Although pressure wave reflection may play a role in the manifestation of the augmentation of central systolic pressure, it does not appear to be solely, or perhaps even primarily, responsible for the phenomenon, and indeed the term itself may be a misnomer. The possible contribution of frequency dispersion to this phenomenon merits further investigation.

In terms of the practical application of our findings, it is often proposed that central augmentation index is a measure of pressure reflection and of aortic stiffness that might predict risk and response to treatment. This is based on assumptions regarding reflection phenomena—our results raise questions regarding this interpretation and may therefore impact directly on diagnosis and treatment of cardiovascular risk. Pulse wave velocity is associated with cardiovascular outcome (1, 2, 6). Because dispersion depends on differences in pulse wave velocity of different frequency components and as such may provide further indication of risk than group velocity measurement, it may also be a potential surrogate end point to clinical trials of agents aimed at directly modulating arterial stiffness.

GRANTS

This study was supported by a Grant in Aid from the National Heart Foundation of Australia (G 01M 0343). S. A. Hope is supported by Medicine International and Faculty Postgraduate Research Scholarships from Monash University and a Cardiovascular Research Centre PhD Scholarship from Monash Medical Centre.

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