Peripheral Augmentation Index Defines the Relationship Between Central and Peripheral Pulse Pressure

Shahzad Munir, Antoine Guilcher, Tamra Kamalesh, Brian Clapp, Simon Redwood,
Michael Marber, Philip Chowienczyk

Abstract—Peripheral systolic blood pressure is amplified above central aortic systolic pressure, but the late systolic shoulder of the peripheral pulse may approximate central systolic pressure. Because late systolic pressure also determines the peripheral augmentation index, a measure of pressure wave reflection within the systemic circulation, this implies a direct relationship between amplification and augmentation. We compared the late systolic shoulder of the peripheral pressure waveform with estimates of central systolic pressure obtained using a transfer function in 391 subjects undergoing diagnostic coronary angiography and/or elective angioplasty (30% with insignificant coronary artery disease). In a subset (n=12) we compared the late systolic shoulder of the peripheral pulse with central pressure obtained with a catheter placed in the aortic root. Measurements were made at baseline, during atrial pacing, and during administration of nitroglycerin. Late systolic shoulder pressure closely approximated transfer function estimates of central pressure ($R=0.96$; $P<0.0001$; mean difference±SD: 0.5±5.2 mm Hg). Despite changes in waveform morphology induced by pacing and nitroglycerin (reducing mean values±SE of the augmentation index from 76±3.8% to 66±4.6% and 60±3.3%, respectively), there was close agreement between the late systolic shoulder of the peripheral pulse and measured values of central pressure ($R=0.96$; $P<0.001$; mean difference: 1.7±4.8 mm Hg). In conclusion, the late systolic shoulder of the peripheral pulse closely approximates central systolic pressure and peripheral augmentation index, the ratio of central:peripheral pulse pressure. Interventions to lower augmentation index and peripheral vascular resistance will have multiplicative effects in lowering central blood pressure. (*Hypertension*. 2008;51:112-118.)

Key Words: aorta ■ augmentation index ■ central blood pressure ■ pulse pressure ■ pulse wave analysis

Propagation of the pressure pulse from the left ventricle to the systemic circulation is accompanied by reflections from sites of impedance mismatch. These reflections result in backward traveling pressure waves, which augment pressure at the aortic root, this being quantified by the aortic or "central" augmentation index (AI; cAI; Figure 1).[1–3] At the same time, pulse pressure propagation and reflection within the upper limb results in peripheral amplification of the pressure pulse, so that peripheral systolic pressure (pSBP) measured at the brachial artery, radial artery, or digital artery exceeds central systolic blood pressure (cSBP) at the aortic root.[1,4] Because of the slow rate of change of pressure during diastole, diastolic blood pressure (DBP) is similar at central and peripheral sites (as is mean arterial pressure),[5] but central pulse pressure (cPP) differs from peripheral pulse pressure (pPP). The potential importance of cSBP and cPP was demonstrated in the Conduit Artery Function Evaluation Study, where the difference in outcome between hypertensive regimes was explained by differing central but not peripheral blood pressures, and cPP was predictive of overall outcome.[6]

Augmentation of central arterial pressure and peripheral amplification have been regarded as largely unrelated phenomena, with the former being determined by characteristics of wave propagation in the aorta and by reflections from the head and lower body and the latter by reflections from the upper limb. However, cAI is closely related to the peripheral AI (pAI), a measurement taken direct from the late systolic shoulder ($pSBP_2$) of the peripheral arterial waveform (Figure 1), which, in turn, may approximate cSBP.[7] This implies a direct relationship between amplification and augmentation. The purpose of this study was to investigate how closely $pSBP_2$ equates to cSBP and to define the relationship between AI and cSBP. We first investigated the relationship between $pSBP_2$ and cSBP estimated noninvasively using a transfer function. We then examined the relationship of $pSBP_2$ to cSBP measured invasively at the time of cardiac catheterization. The relationship between central and peripheral pressure is critically dependent on heart rate and tone of muscular arteries.[8–10] We, therefore, made measurements during atrial pacing and during administration of nitroglycerin (NTG) to
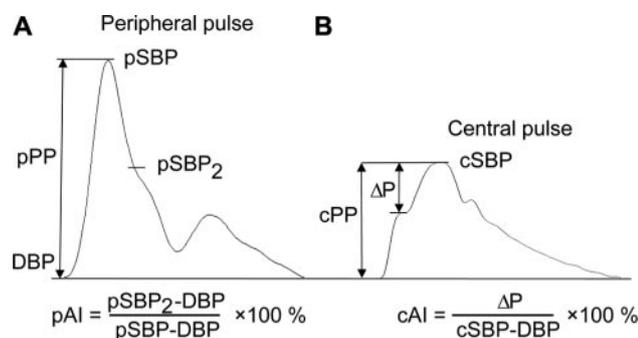
Figure 1. A, Peripheral (digital) arterial waveform showing DBP, pSBP, pSBP$_2$, and the definition of pAI. B, Central (aortic) arterial waveforms showing cSBP, augmentation of central systolic pressure above the first systolic shoulder (ΔP), and the definition of cAI.

determine whether relationships observed at baseline held during these interventions.

Methods

Subjects were recruited from those attending Guy's and St Thomas' cardiothoracic unit for diagnostic angiography or elective percutaneous coronary angioplasty. Study 1 was performed before cardiac catheterization; study 2 was performed during catheterization. Subjects with acute coronary syndromes and those with significant valvular disease and rhythm other than sinus rhythm were excluded. Subjects in study 2 had previously undergone diagnostic coronary angiography and were studied immediately before an elective single vessel coronary angioplasty. Further exclusion criteria for this study were composed of significant left main stem disease, a permanent pacemaker in situ, or an ejection fraction (estimated on echocardiography or ventriculography) <30%. Subject characteristics are given in Table 1. The protocols adhered to the principles of the Declaration of Helsinki and were approved by the local research ethics committee, and all of the subjects gave written informed consent.

Study 1: Noninvasive Assessment of Central Blood Pressure (n=391)

Applanation tonometry of the radial artery was performed with subjects seated and after resting for ≥15 minutes using the SphygmoCor system (Atcor). Blood pressure was measured according to British Hypertension Society guidelines using a validated oscillometric device (Omron 705, Omron). The inbuilt software in the SphygmoCor system was used to obtain measurements (pSBP$_2$, pAI, cSBP, and cAI, defined as in Figure 1) using a transfer function to estimate aortic pressure from radial pressure. Mean values of these measurements were obtained from 3 consecutive recordings. Waveforms for which a late systolic shoulder in the radial waveform could not be identified and, hence, for which SBP$_2$ could not be obtained by the inbuilt software were excluded from the analysis.

Study 2: Comparison of Peripheral and Aortic Pressure Waveforms (n=12)

In this study peripheral pressure waveforms were acquired from the digital artery using a servocontrolled finger pressure cuff (Finometer, Finapres Medical Systems). We have shown previously that digital artery waveforms obtained in this way are similar to radial artery waveforms acquired using the SphygmoCor system.[11] A Finometer was used in preference to the SphygmoCor system, because it allowed continuous recordings of peripheral pressure facilitating simultaneous comparison of digital pressure with aortic pressure. The left arm and hand were placed in a neutral position, and the Finopress transducer was attached to the left index finger with the finger ≈10 cm below the level of the heart. Following standard preparations for angioplasty, vascular access to the right femoral artery and right femoral vein was established with hemostatic

Table 1. Subject Characteristics

Characteristic	Value
Sex (male/female), n (%)	303/88 (77/23)
Smokers, n (%)	65 (17)
Age, mean (SD), y	61.7 (10.4)
BMI, mean (SD), kg · m^{-2}	29.7 (5.3)
Past history, n (%)	
Previous myocardial infarction	141 (36)
Treated hypertension	239 (61)
Diabetes mellitus	85 (22)
Heart failure*	86 (23)
Angiographic findings, n (%)	
Nonsignificant disease†	117 (30)
Single vessel	97 (25)
Multivessel	192 (49)
Drug therapy, n (%)	
ACEI/ARB	190 (49)
β-blocker	259 (66)
Calcium channel blocker	149 (38)
Nitrate	143 (37)
Diuretic	75 (19)
Lipid profile, mean (SD), mmol · L^{-1}	
Total cholesterol	4.2 (1.3)
HDL cholesterol	1.1 (0.4)
Triglycerides	1.5 (0.9)

ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor antagonist.

*New York Heart Association >grade 2.

†Normal or minor non–flow-limiting stenosis.

sheaths. In 10 subjects, a Millar SPC-454D (Millar Instruments) high-fidelity pressure-tipped catheter was passed through the femoral arterial sheath over a guide wire and, using fluoroscopic guidance, the tip of the catheter was positioned in the proximal aortic root. The combined frequency response of the catheter and amplifier was flat to >100 Hz. In the remaining subjects (n=2), a standard fluid filled catheter was used. The subject was systemically heparinized with a weight-adjusted dose of unfractionated heparin to reduce the risk of thrombus formation within the catheter. A bipolar temporary pacing electrode was passed via the right femoral venous sheath and positioned under fluoroscopic guidance at a stable site in the right atrium ensuring consistent atrial capture. After ≥10 minutes resting supine when the subject was hemodynamically stable, baseline measurements of aortic root pressure and digital pressure were obtained over a 3- to 4-minute period. Right atrial pacing was then initiated at a rate of 20 bpm above the resting heart rate. Pacing was maintained for ≥60 seconds at the faster rate before simultaneous aortic catheter and digital artery pressure recordings were made. Pacing was then discontinued for the remainder of the study. After the return of heart rate and blood pressure to baseline and further baseline recordings, subjects then underwent a cumulative dose infusion of NTG (10 and 100 μg/min; each dose for 5 minutes) with recording of aortic and digital artery pressures over the last 1 minute of the infusion period.

Digital and Radial Artery Pressure Calibration and Waveform Analysis

In study 1, radial artery pressure waveforms were calibrated from brachial artery measurements of blood pressure. Aortic waveforms were calibrated using the SphygmoCor software assuming peripheral

Table 2. Peripheral and Central (Transfer Function) Blood Pressure and AIs

Measure	Mean (SD)
Peripheral blood pressures and AI	
pSBP, mm Hg	132.9 (19.3)
DBP, mm Hg	76.5 (10.5)
MAP, mm Hg	95.2 (12.9)
pPP, mm Hg	56.4 (16.0)
$pSBP_2$, mm Hg	121.6 (19.7)
pAI, %	79.6 (11.8)
Central blood pressures and AI	
cSBP, mm Hg	122.1 (18.6)
cPP, mm Hg	45.6 (15.2)
cAI, %	26.1 (9.7)

MAP indicates mean arterial blood pressure (see Figure 1 for definitions of $pSBP_2$, pAI, and cAI).

diastolic and mean arterial pressures to be equal to aortic diastolic and mean pressures, respectively. Equality of peripheral and central diastolic and mean pressure has been demonstrated previously when peripheral pressure is measured invasively.[5] In the invasive study, absolute measurements of aortic pressure were available, and peripheral digital artery pressure was calibrated from invasively acquired mean and diastolic pressure. Pressure waveforms were sampled at 1000 Hz and stored on disk for offline analysis using in-house software developed in MatLab (Matlab, Mathworks USA, version 7). Waveforms were filtered using a fifth-order Butterworth low-pass filter with cutoff frequency of 22.5 Hz. The points P_1 on the aortic pressure waveform and $pSBP_2$ on the digital waveform were determined by first identifying local minima and maxima of the first derivative of the pressure signal (to identify consecutive changes in the gradient of the waveform) and then defined by the intersection of tangents to the curve at these points. This algorithm was applied to an ensemble average of ≥ 10 waveforms and, in addition, to individual waveforms with a mean value of SBP_2 calculated from values for individual waveforms ($n \geq 10$). Values of SBP_2 identified by the algorithm were marked on the waveform and were verified by inspection of the waveform.

Statistics

Subject characteristics are expressed as means (SDs). Except where stated, results are expressed as means±SEs. Bivariate comparisons were made using Pearson's correlation coefficient. Agreement between measures was assessed by Bland-Altman plots and quantified by the mean value and SD of the difference between the 2 measures. Changes in hemodynamic measures after NTG and pacing were assessed using ANOVA for repeated measures. All of the tests were 2 tailed, and $P < 0.05$ was considered significant.

Results

Study 1: Noninvasive Assessment of Central Blood Pressure (n=391)

Hemodynamic measurements are summarized in Table 2. There was a close correlation between $pSBP_2$ and cSBP ($R = 0.96$; $P < 0.0001$; Figure 2). Furthermore, absolute values of SBP_2 and cSBP were similar with the mean difference (SD) between $pSBP_2$ and cSBP being 0.5 (5) mm Hg. The difference between $pSBP_2$ and cSBP was significantly less than that between pSBP and cSBP (11 [7] mm Hg; $P < 0.0001$ for comparison with the difference between $pSBP_2$ and cSBP). cAI was closely correlated with peripheral AI ($R = 0.86$; $P < 0.0001$; Figure 3).
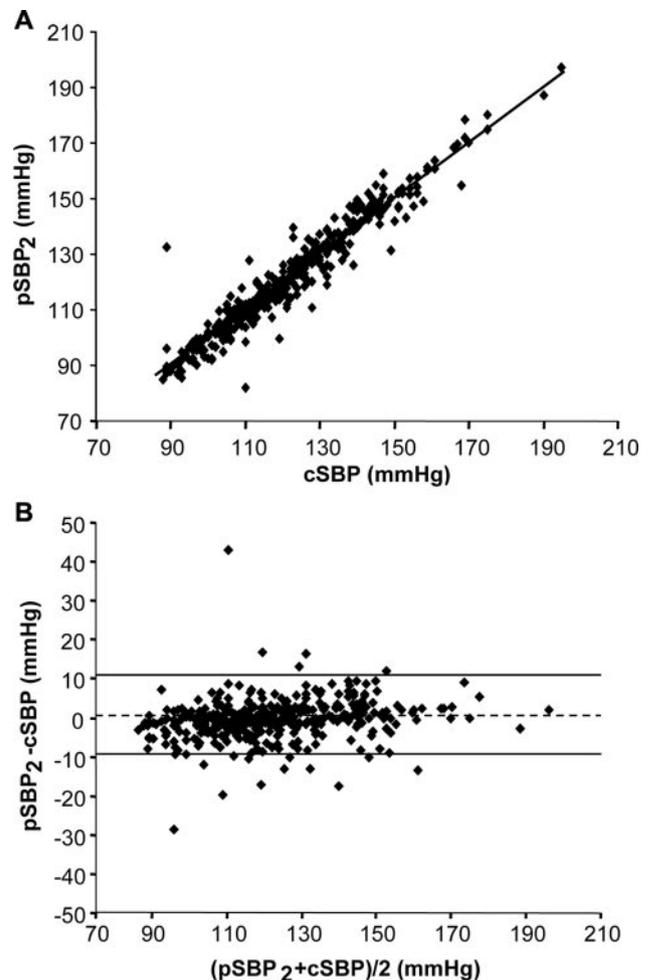
Figure 2. A, Correlation between $pSBP_2$ of the peripheral pressure waveform and cSBP estimated using a transfer function. The solid line is the line of identity. B, Bland-Altman plot showing agreement between $pSBP_2$ and cSBP. The broken line is the mean difference, and the solid lines are mean difference ±2 SD.

Study 2: Comparison of Peripheral and Aortic Pressure Waveforms (n=12)

Both pacing and NTG produced marked alterations in waveform morphology (Figure 4 and Table 3). NTG had no significant effect on diastolic pressure but reduced both peripheral and central systolic and pulse pressures, with a greater effect on central pressures than on peripheral pressures. The higher dose of NTG (100 μg/min) reduced pSBP and pPP by 13±5.0 and 11±4.3 mm Hg, respectively (each $P < 0.05$) and reduced cSBP and cPP by 23±3.3 and 21±2.3 mm Hg, respectively (each $P < 0.001$ and $P < 0.01$ for comparison of central versus peripheral measures, respectively). NTG (100 μg/min) also reduced pAI and cAI by 20±3.0% and 30±6.7%, respectively (each $P < 0.001$). Pacing was associated with a small increase in diastolic pressure and no significant change in pSBP or cSBP but a reduction in the pPP of 6.0±2.8 mm Hg ($P < 0.05$) and a greater reduction in the cPP of 11±2.1 mm Hg ($P < 0.01$ compared with baseline and $P < 0.05$ compared with change in pPP). Pacing also reduced pAI and cAI (by 11±1.6% and 12±4.4%, respectively; each $P < 0.05$ compared with baseline). For both interventions cAI changed in parallel with pAI (Figure 5).
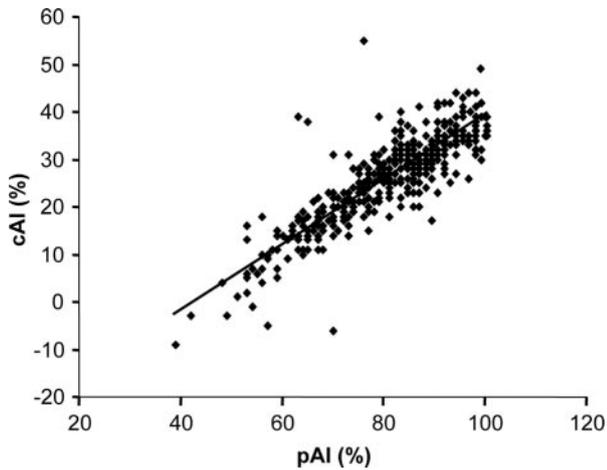
**Figure 3.** Correlation between the pAI and cAI derived using a transfer function.

Using the intersecting tangent algorithm applied to an ensemble average of ≥ 10 consecutive cardiac cycles, SBP_2 was identified in all but 6 of 48 waveforms. Applying the algorithm to individual cardiac cycles with $pSBP_2$ calculated as an average from values obtained from each cardiac cycle gave virtually identical results and was successful in all but 3 of 48 waveforms. Subsequent inspection of these waveforms (which were all from the same subject) revealed the traces to be of poor quality with baseline drift and high-frequency noise. Despite the alterations in waveform morphology induced by pacing and NTG and the differential effects of these interventions on pSBP and cSBP, $pSBP_2$ closely approximated true cSBP ($R=0.96$; $P<0.0001$; Figure 6). The mean (SD) difference between $pSBP_2$ and cSBP was -1.8 (4.0) mm Hg at baseline and -1.7 (4.8) mm Hg under all conditions (baseline, pacing, and after NTG), whereas the difference (under all conditions) between pSBP and cSBP was 25 (24) mm Hg.

Discussion

Propagation of the arterial pressure wave along the upper limb amplifies high-frequency (ie, rapidly changing) components of the pressure wave.[12] In addition, these components are shifted in phase arriving before low-frequency components. This results in augmentation of peripheral radial/digital systolic pressure above cSBP. The late systolic shoulder or point of augmentation of the peripheral pressure wave may relate to the relatively sustained peak of central pressure,

which, because it is of lower frequency than the upstroke of the pressure wave, arrives at the periphery later and remains of approximately constant amplitude. $pSBP_2$ would then be expected to approximate cSBP. Alterations in arterial stiffness and wave reflection, which influence the upstroke of the pressure wave, will influence pSBP relative to cSBP but should have relatively little influence on the relation between $pSBP_2$ and cSBP. In our noninvasive study, $pSBP_2$ closely approximated the transfer function–derived estimate of cSBP in a relatively large group of subjects with a wide range of waveform morphology and central and peripheral blood pressures. Although this agreement between $pSBP_2$ and estimated cSBP could have arisen as a result of the transfer function process itself, these results suggest that $pSBP_2$ will provide a similar estimate of cSBP to that obtained by the transfer function.

To confirm the relationship between $pSBP_2$ and cSBP, we made direct measurements of aortic pressure at rest and during administration of NTG and pacing, interventions known to modify waveform morphology and/or the relationship between peripheral and central blood pressure. NTG reduces AI and has a greater effect on central than on peripheral blood pressure.[10] Heart rate is negatively associated with AI, and increases in heart rate produced by pacing reduce AI.[8] The present results confirm those of previous studies with NTG reducing both cAI and pAI and producing a greater reduction of central than of peripheral blood pressure. Pacing at 20 beats above baseline also reduced cAI and pAI and had a differential effect on central and peripheral systolic pulse pressure. Despite the changes in waveform morphology and differential effects on central and peripheral pressures produced by NTG and pacing, $pSBP_2$ closely approximated cSBP at baseline, during NTG, and during pacing. These results confirm those of the noninvasive study. Taken together, results of the 2 studies suggest that the relationship between $pSBP_2$ and cSBP holds true across a wide range of subjects and during interventions that modify waveform morphology and influence central/peripheral blood pressure. The results are consistent with those obtained by Pauca et al[7] in hypertensive and elderly subjects. Further invasive studies to confirm the relationship between $pSBP_2$ and cSBP would be useful, especially in children and young adults who were not represented in our sample and during interventions that increase arterial stiffness or wave reflections.
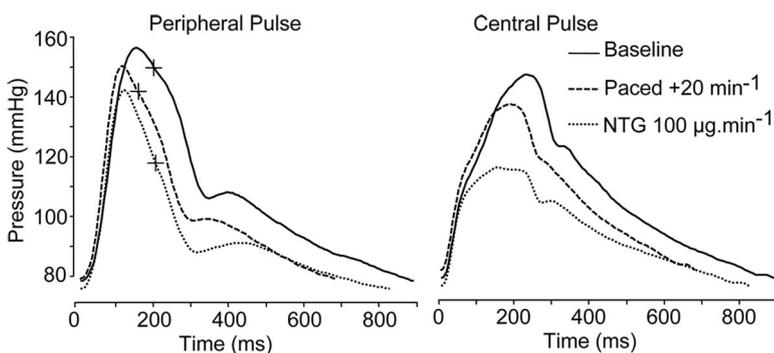
Figure 4. Peripheral arterial and central aortic waveforms recorded after pacing at 20 beats above baseline and after NTG (100 μg/min). The $pSBP_2$ is identified ($+$) and closely approximates cSBP.

Table 3. Peripheral and Central Blood Pressure and Pulse Contour Measures During Administration of NTG and After Pacing

Measurement	Baseline, mean±SE	NTG, mean±SE		Paced, mean±SE
		10 μg · min^{-1}	100 μg · min^{-1}	
Heart rate, min^{-1}	60±2.1	61±2.8	65±3.0†	81±2.2†
pSBP, mm Hg	147±10.7	138±11.5	134±8.0*	145±12.2
DBP, mm Hg	65±2.9	65±2.5	63±2.4	69±2.2*
MAP, mm Hg	90±3.3	85±2.4*	81±2.4†	92±2.4
pPP, mm Hg	82±10.6	74±11.8*	71±8.4*	76±12.1*
pSBP$_2$, mm Hg	124±5.6	109±4.6†	108±4.3†	118±5.2*
pAI, mm Hg	76±3.8	66±3.6†	60±3.3†	66±4.6†
Central pressures and contour measures				
cSBP, mm Hg	127±5.8	113±4.4†	105±3.7†	121±5.5
cPP, mm Hg	63±5.0	48±4.7†	42±3.8†	52±5.1†
cAI, %	36±4.7	19±4.4†	6.6±7.4†	23±5.8*

See Figure 1 for definitions of pSBP$_2$, pAI, and cAI.
*$P<0.05$ vs baseline.
†$P<0.01$ vs baseline.

Our study suggests that a transfer function is not necessarily required to estimate cSBP because this can be estimated directly from a peripheral pressure waveform. The accuracy of the transfer function approach for estimating central blood pressure has been questioned.[13,14] However, it is now accepted that inaccuracies in the use of the transfer function relate mainly to the calibration of peripheral blood pressure rather than to the accuracy of the transfer function, per se.[15] When peripheral pressure waveforms are calibrated from invasive recordings, the transfer function has been extensively validated.[3,16] Indeed, the equality of pSBP$_2$ and transfer function estimates of cSBP in this study further supports the validity of the transfer function. Estimation of central pressure direct from the peripheral pulse will be subject to exactly the same calibration error as in the transfer function–derived values. It has the advantage of simplicity and potentially avoids bias that may arise when the transfer function is applied to subjects with characteristics that may differ from the group in which it has been derived. A disadvantage of the use of pSBP$_2$ is that it is sometimes difficult to detect. However, our results suggest that this may be because of ensemble averaging of the waveforms, which removes fine

detail. Application of the intersecting tangent algorithm that we used for individual cardiac cycles with subsequent averaging of pSBP$_2$ was successful in all of the waveforms of reasonable quality.

Because SBP$_2$ equates to central pressure and, together with diastolic pressure, determines pAI, there is a simple relationship among pAI, cPPs, and cPPs:

$$pAI = (pSBP_2 - DBP)/(pSBP - DBP) \times 100\%$$

$$\text{because } cSBP = pSBP_2$$

$$pAI = (cSBP - DBP)/(pSBP - DBP) \times 100\%$$

$$\text{or } pAI = cPP/pPP \times 100\%$$

Thus, pAI defines the ratio of cPP:pPP. Because AI depends only on the shape of the arterial waveform, this relationship will be independent of the calibration of the arterial waveform. This is of critical importance given that errors induced by peripheral calibration are the main source of error when estimating central pressure from peripheral pressure.[15] pAI may be regarded as the amount by which central pressure is reduced relative to peripheral pressure independent of the accuracy of blood pressure measurement and technique used to calibrate the peripheral blood pressure waveform.

The present study also addresses the relationship between pAI and cAI. We have observed previously that cAI, estimated by means of a transfer function, and pAI are strongly correlated and change in parallel in response to alterations in vasomotor tone.[17] Results of this study confirm these findings and extend them showing that cAI measured directly from the aortic waveform changes in parallel with pAI. Central augmentation and peripheral amplification have been regarded previously as independent phenomena with central augmentation dependent on the tone of muscular arteries and pressure wave reflection within the systemic circulation. The present study shows that central augmentation is closely related to peripheral augmentation and, hence, to the ratio of cPP:pPP.
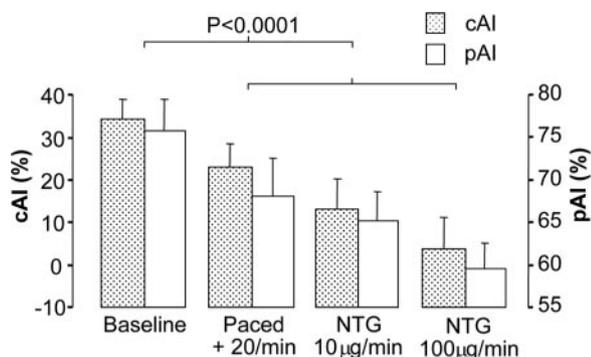
Figure 5. Mean SE values of pAI and cAI at baseline, during pacing at 20 beats above baseline, and during intravenous infusion of NTG.
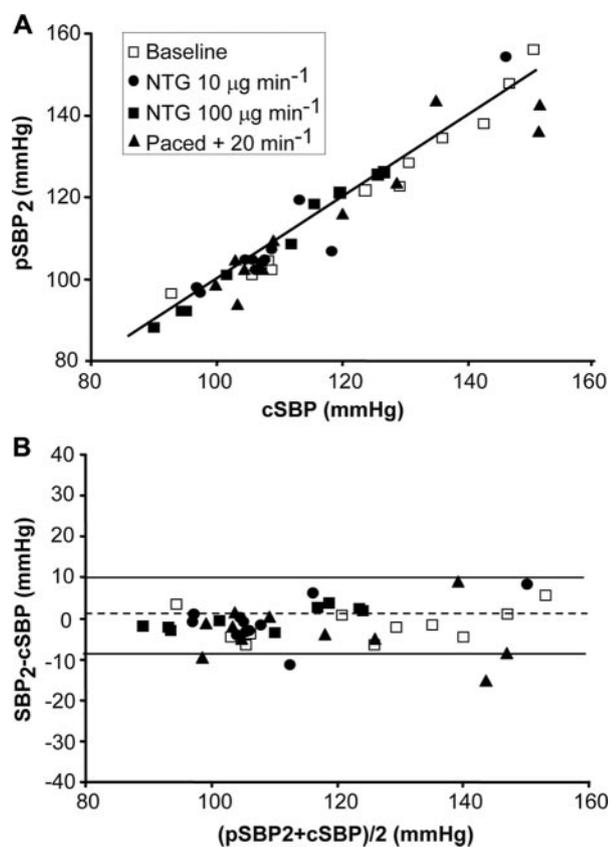
Figure 6. A, Correlation between $pSBP_2$ of the peripheral pressure (digital) waveform and cSBP measured with a catheter in the aorta at baseline, during pacing at 20 beats above baseline, and during intravenous infusion of NTG. The solid line is the line of identity. B, Bland-Altman plot showing agreement between $pSBP_2$ and cSBP. The broken line is the mean difference, and the solid lines are mean difference ±2 SD.

However, it is unlikely that the relationship between central augmentation and peripheral amplification results from a relation between propagation characteristics of the upper limb and those of the systemic circulation. Propagation characteristics of the upper limb are thought to remain constant for a given frequency content (this being the basis of the transfer function approach for estimation of central from peripheral pressure). Furthermore, in the present study we observed parallel changes in augmentation and peripheral amplification after pacing, an intervention unlikely to alter upper limb propagation by a mechanism other than a shift in frequency of the arterial pressure wave. It is more likely that the close relationship between augmentation and peripheral amplification is explained by both measures being influenced by a shift in the frequency spectrum of the central arterial pressure wave consequent on either a change in heart rate (as induced by pacing in the present study) or alterations in the tone of muscular arteries that determine systemic impedance, pressure wave reflection, and the frequency content of the arterial waveform. The relationship between augmentation and cSBP explains why both measures are related to cardiovascular outcome[6,18] and that adverse outcome associated with high augmentation can be explained by high central pressures.

Twin studies have shown that AI has much higher heritability than simple blood pressure traits and that a combination of genetic and environmental factors account for the majority of the variance in AI.[19] The present study suggests that these same factors will have a direct influence on the relationship between peripheral and central blood pressure. Given the emerging evidence on the importance of central blood pressure in determining cardiovascular outcome,[6] it may be that such genetic determinants of AI are as important or more important than those of peripheral systolic blood pressure on "blood pressure–related" cardiovascular outcome. Similarly, environmental factors associated with increased AI will effectively increase cSBP above pSBP. Most but not all studies suggest increased pressure augmentation in subjects with diabetes,[20–23] and this could explain why subjects with diabetes benefit from the reduction of blood pressure to lower levels than in nondiabetic subjects.

The efficacy of antihypertensive drugs to lower cSBP will be determined by effects on both AI and peripheral blood pressure, and effects on cSBP can be predicted from the relationships established in the present study. AI is determined by arteries proximal to resistance vessels, rather than by resistance vessels traditionally thought to be the target of antihypertensive drugs.[3] Drugs or drug combinations that have a dual action on muscular arteries and resistance vessels will, thus, have multiplicative effects on cSBP. Nitrates are known to reduce AI and cSBP to a greater extent than peripheral blood pressure.[10] Drugs that stimulate endothelium-dependent NO release also reduce AI without effect on peripheral blood pressure[24–26] and can, therefore, be expected to lower cSBP.

Perspectives

pSBP is amplified above central aortic systolic pressure, but the late systolic shoulder or point of systolic augmentation in the peripheral pulse closely approximates cSBP. pAI approximates the ratio of cPP:pPP. There is a close relationship between cAI and pAIs, so central pressure augmentation and amplification of pPP are closely related. This explains the prognostic impact of AI in terms of central blood pressure, identifies conditions associated with increased augmentation as benefiting from more aggressive blood pressure reduction, and suggests that interventions to lower AI and peripheral vascular resistance will have multiplicative effects on central blood pressure.

Disclosures

P.C. was a shareholder in Micro Medical Ltd until March 2005. The remaining authors report no conflicts.

References

1. Nichols WW, O'Rourke MF. *McDonald's Blood Flow in Arteries. Theoretical, Experimental and Clinical Principles*. London, United Kingdom: Arnold; 1998.
2. O'Rourke M. Mechanical principles in arterial disease. *Hypertension*. 1995;26:2–9.
3. O'Rourke MF, Pauca AL. Augmentation of the aortic and central arterial pressure waveform. *Blood Press Monit*. 2004;9:179–185.

4. Wilkinson IB, Franklin SS, Hall IR, Tyrrell S, Cockcroft JR. Pressure amplification explains why pulse pressure is unrelated to risk in young subjects. *Hypertension*. 2001;38:1461–1466.

5. Pauca AL, Wallenhaupt SL, Kon ND, Tucker WY. Does radial artery pressure accurately reflect aortic pressure? *Chest*. 1992;102:1193–1198.

6. Williams B, Lacy PS, Thom SM, Cruickshank K, Stanton A, Collier D, Hughes AD, Thurston H, O'Rourke M. Differential impact of blood pressure-lowering drugs on central aortic pressure and clinical outcomes: principal results of the Conduit Artery Function Evaluation (CAFE) study. *Circulation*. 2006;113:1213–1225.

7. Pauca AL, Kon ND, O'Rourke MF. The second peak of the radial artery pressure wave represents aortic systolic pressure in hypertensive and elderly patients. *Br J Anaesth*. 2004;92:651–657.

8. Wilkinson IB, MacCallum H, Flint L, Cockcroft JR, Newby DE, Webb DJ. The influence of heart rate on augmentation index and central arterial pressure in humans. *J Physiol*. 2000;525:263–270.

9. Wilkinson IB, Mohammad NH, Tyrrell S, Hall IR, Webb DJ, Paul VE, Levy T, Cockcroft JR. Heart rate dependency of pulse pressure amplification and arterial stiffness. *Am J Hypertens*. 2002;15:24–30.

10. Kelly RP, Gibbs HH, O'Rourke MF, Daley JE, Mang K, Morgan JJ, Avolio AP. Nitroglycerin has more favourable effects on left ventricular afterload than apparent from measurement of pressure in a peripheral artery. *Eur Heart J*. 1990;11:138–144.

11. Millasseau SC, Guigui FG, Kelly RP, Prasad K, Cockcroft JR, Ritter JM, Chowienczyk PJ. Non-invasive assessment of the digital volume pulse: comparison with the peripheral pressure pulse. *Hypertension*. 2000;36:952–956.

12. Karamanoglu M, O'Rourke MF, Avolio AP, Kelly RP. An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. *Eur Heart J*. 1993;14:160–167.

13. Hope SA, Tay DB, Meredith IT, Cameron JD. Use of arterial transfer functions for the derivation of aortic waveform characteristics. *J Hypertens*. 2003;21:1299–1305.

14. Cloud GC, Rajkumar C, Kooner J, Cooke J, Bulpitt CJ. Estimation of central aortic pressure by SphygmoCor requires intra-arterial peripheral pressures. *Clin Sci (Lond)*. 2003;105:219–225.

15. O'Rourke MF, Adji A. An updated clinical primer on large artery mechanics: implications of pulse waveform analysis and arterial tonometry. *Curr Opin Cardiol*. 2005;20:275–281.

16. Gallagher D, Adji A, O'Rourke MF. Validation of the transfer function technique for generating central from peripheral upper limb pressure waveform. *Am J Hypertens*. 2004;17:1059–1067.

17. Millasseau SC, Patel SJ, Redwood SR, Ritter JM, Chowienczyk PJ. Pressure wave reflection assessed from the peripheral pulse: is a transfer function necessary? *Hypertension*. 2003;41:1016–1020.

18. London GM, Blacher J, Pannier B, Guerin AP, Marchais SJ, Safar ME. Arterial wave reflections and survival in end-stage renal failure. *Hypertension*. 2001;38:434–438.

19. Snieder H, Hayward CS, Perks U, Kelly RP, Kelly PJ, Spector TD. Heritability of central systolic pressure augmentation: a twin study. *Hypertension*. 2000;35:574–579.

20. Brooks BA, Molyneaux LM, Yue DK. Augmentation of central arterial pressure in Type 2 diabetes. *Diabet Med*. 2001;18:374–380.

21. Fukui M, Kitagawa Y, Nakamura N, Mogami S, Ohnishi M, Hirata C, Ichio N, Wada K, Kamiuchi K, Shigeta M, Sawada M, Hasegawa G, Yoshikawa T. Augmentation of central arterial pressure as a marker of atherosclerosis in patients with type 2 diabetes. *Diabetes Res Clin Pract*. 2003;59:153–161.

22. Wilkinson IB, MacCallum H, Rooijmans DF, Murray GD, Cockcroft JR, McKnight JA, Webb DJ. Increased augmentation index and systolic stress in type 1 diabetes mellitus. *QJM*. 2000;93:441–448.

23. Lacy PS, O'Brien DG, Stanley AG, Dewar MM, Swales PP, Williams B. Increased pulse wave velocity is not associated with elevated augmentation index in patients with diabetes. *J Hypertens*. 2004;22:1937–1944.

24. Chowienczyk PJ, Kelly RP, MacCallum H, Millasseau SC, Andersson TL, Gosling RG, Ritter JM, Anggard EE. Photoplethysmographic assessment of pulse wave reflection: blunted response to endothelium-dependent beta2-adrenergic vasodilation in type II diabetes mellitus. *J Am Coll Cardiol*. 1999;34:2007–2014.

25. Wilkinson IB, Hall IR, MacCallum H, Mackenzie IS, McEniery CM, van der Arend BJ, Shu YE, MacKay LS, Webb DJ, Cockcroft JR. Pulse-wave analysis: clinical evaluation of a noninvasive, widely applicable method for assessing endothelial function. *Arterioscler Thromb Vasc Biol*. 2002;22:147–152.

26. Hayward CS, Kraidly M, Webb CM, Collins P. Assessment of endothelial function using peripheral waveform analysis: a clinical application. *J Am Coll Cardiol*. 2002;40:521–528.

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