Scientific Contributions

Pressure Wave Reflection Assessed From the Peripheral Pulse
Is a Transfer Function Necessary?


Abstract—Synthesis of the aortic pressure waveform by application of a transfer function to the radial pulse allows the estimation of aortic systolic blood pressure and aortic augmentation index, an index of pressure wave reflection derived from the early systolic component of the waveform. The accuracy of this approach for determining the aortic augmentation index has been questioned, however, and it may be possible to derive similar information without using a transfer function. We compared aortic systolic blood pressure and the aortic augmentation index obtained from carotid and radial arteries with the use of transfer functions. We examined the correlation between the aortic augmentation index and a radial augmentation index obtained without use of a transfer function. Arterial tonometry (SphygmoCor) was performed in 84 subjects including healthy volunteers (n = 30), subjects with essential hypertension (n = 30), and patients with coronary artery disease (n = 24). Effects of nitroglycerine and norepinephrine on aortic and radial augmentation index were examined in 12 healthy volunteers. Values of aortic systolic pressure obtained from radial and carotid arteries by using transfer functions were in acceptable agreement (R = 0.98, difference = −0.9 ± 4.6 mm Hg; mean±SD, n = 84), but those of aortic augmentation index differed especially in control subjects (R = 0.47, difference = −3.8 ± 12.4%). Aortic augmentation index was, however, closely correlated with radial augmentation index (R = 0.96, n = 84). Nitroglycerine and norepinephrine produced parallel changes in the aortic and radial augmentation index. Our findings question the use of a transfer function to obtain the aortic augmentation index but suggest that similar information on central pressure wave reflection can be obtained directly from the radial pulse. (Hypertension. 2003;41:1016-1020.)

Key Words: aorta • hypertension, arterial • pulse

Augmentation of central blood pressure by the return, in systole, of pressure waves reflected from small arteries in the peripheral circulation can be quantified by an aortic augmentation index (AIx; Figure 1).1 AIx depends on ventricular ejection, the timing of reflected waves (determined mainly by pulse wave velocity in the aorta and large arteries and hence, on the stiffness of these arteries), and the amount of reflection (determined mainly by arterial tone at the major sites of reflection). Aortic AIx increases with age and blood pressure2 and is elevated in subjects with other risk factors for cardiovascular disease, including diabetes3 and hypercholesterolemia.4 In patients with end-stage renal failure (a group with high cardiovascular mortality), AIx is highly predictive of cardiovascular mortality.5 AIx could thus be potentially useful in identifying patients who might benefit from treatment aimed at reducing arterial stiffness or arterial wave reflections.

Applanation tonometry provides a noninvasive means for recording high-fidelity arterial pressure,6 and this methodology can be used to estimate aortic AIx. The most widely used approach is to perform radial artery tonometry and then apply a transfer function to calculate the aortic pressure waveform from the radial waveform.7-9 A similar approach can be used to derive aortic AIx from the carotid pulse. Owing to the proximity of the carotid artery to the aorta, the carotid waveform is modified little by the carotid-to-aorta transfer function and, even without the use of a transfer function, can be used to estimate aortic AIx.10,11 Radial tonometry is favored, however, because it is simple to perform and well tolerated. Carotid tonometry, on the other hand, requires a high degree of technical expertise11 to achieve optimal results and does cause minor discomfort. Although use of a radial-to-aortic transfer function for the measurement of central systolic blood pressure (which differs from brachial systolic blood pressure as a result of peripheral amplification) has been established,9,12 the accuracy of this approach for the determination of aortic AIx has been disputed. Aortic AIx depends on higher-frequency information than does systolic blood pressure. The transfer function shows greater between-subject variability at high frequencies8,9 and is therefore, less likely to provide an accurate estimate of aortic AIx than of systolic blood pressure. Previous studies have shown greater variation in the determination of aortic AIx than of central systolic blood pressure.9,13

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These reservations regarding the transfer function approach prompted us to reevaluate its accuracy and to examine whether information similar to that provided by the aortic Alx can be obtained directly from the radial pulse without the use of a transfer function. That the timing and amplitude of pressure wave reflection influence the radial pulse has long been acknowledged, and a radial Alx (Figure 1) has been described, which might contain information similar to the aortic Alx. We examined the agreement between aortic Alx obtained by applying a transfer function to the radial pulse and aortic Alx obtained from the carotid pulse, with and without the use of a transfer function. We then examined the relation of the aortic Alx (derived from the transformed radial pulse) and the radial Alx derived without the use of a transfer function. We studied healthy subjects and older subjects with hypertension and coronary artery disease to obtain representative samples from groups expected to have low and high values of Alx. In a subgroup of healthy subjects, we administered vasoactive drugs to determine whether the changes in aortic Alx tracked those in the radial Alx.

**Methods**

Studies were performed with the approval of St Thomas’ Hospital Research Ethics Committee and with the written, informed consent of the subjects. Three groups of subjects were studied: healthy volunteers (n=30; mean±SD age, 37±8 years; mean±SD blood pressure, 119±16/69±8 mm Hg; and mean±SD heart rate, 59±10 minutes⁻¹), subjects with uncomplicated essential hypertension with treatment (n=30; age, 51±13 years; blood pressure, 142±22/89±14 mm Hg; and heart rate, 60±9 minutes⁻¹), and patients with coronary artery disease (CAD; n=23; age, 57±8 years; blood pressure, 131±19/79±9 mm Hg; and heart rate, 58±9 minutes⁻¹). Vasoactive treatment in the hypertensive subjects included diuretics (53%), calcium-channel blockers (40%), α-adrenoreceptor antagonists (37%), β-adrenoreceptor antagonists (27%), converting enzyme inhibitors (27%), and angiotensin II receptor antagonists (17%). In the patients with CAD, treatment included β-adrenoreceptor antagonists (95%), nitrates (58%), calcium-channel blockers (25%), diuretics (25%), angiotensin-converting enzyme inhibitors (17%), and α-adrenoreceptor antagonists (8%). Measurements were performed while subjects were supine in a quiet, temperature-controlled environment after at least 15 minutes of rest. Radial and carotid arterial pressure waveforms were obtained by applanation tonometry (Millar Instruments) with Sphygmocor software version 6.3 (Atcor). Three successive recordings were obtained from each artery, and measurements were repeated when the waveform(s) did not pass the automatic quality controls specified by the Sphygmocor software. Brachial arterial blood pressure was measured in triplicate with an oscillometric device (Omron 705CP, Omron) and was used to calibrate the radial pressure pulse. The carotid pressure pulse was calibrated by using the diastolic and mean arterial pressures obtained from the brachial artery measurements. This method for calibrating the carotid pulse to provide an accurate aortic systolic blood pressure has been previously validated. The aortic pulse was synthesized from the radial pulse and from the carotid pulse by using the transfer functions supplied by Sphygmocor. Effects of vasoactive drugs were assessed in a subset of 12 of the healthy volunteers. A similar protocol was used to obtain carotid and radial pressure pulse recordings at baseline and during the last 10 minutes of a 15-minute intravenous infusion of norepinephrine (75 ng · kg⁻¹ · min⁻¹, n=8) or nitroglycerine (100 μg · min⁻¹, n=4).

**Statistics**

Agreement between estimates of the same measurement was assessed by Bland-Altman plots. The mean difference between measurements was used to quantify systematic error and the SD of the differences, the variation in agreement. Pearson correlation coefficients are also presented, with the recognition that these are of limited value in the comparison of closely related measurements. Different measurements (aortic and radial Alx) were compared by regression analysis. A Bland-Altman plot was used to compare aortic Alx with aortic Alx predicted from radial Alx (by using the coefficients of the regression equation of radial vs aortic Alx). P<0.05 was considered significant. All tests were 2-tailed.

**Results**

**Central Systolic Blood Pressure**

Values of central systolic blood pressure computed from the radial pulse by using the radial-to-aortic transfer function were in close agreement with those computed from the carotid pulse by using the carotid-to-aortic transfer function (Figure 2). Correlation coefficients were 0.87, 0.99, and 0.99 in control, hypertensive, and CAD groups, respectively. Mean±SD differences between values obtained from the transformed radial and carotid waveforms in the respective groups were 0.03±5.3, −2.0±4.7, and −1.0±3.4 mm Hg. The overall correlation coefficient for all groups was 0.98 and mean difference, −0.9±4.6 mm Hg. Two SDs (the Bland-Altman statistic giving the confidence limits within which, assuming a normal distribution, 95% of readings will be in agreement) of the difference between the 2 measures of central systolic blood pressure was 9.2 mm Hg.

**Aortic Alx**

Mean values of aortic Alx estimated from the transformed radial waveform were 8.3±8.7, 27.9±10.6, and 29.5±11.8% in the control, hypertensive, and CAD patients, respectively. Agreement between aortic Alx estimated from the transformed radial and transformed carotid waveforms was rela-
tively poor (Figure 3), with correlation coefficients of 0.47, 0.83, and 0.84 and mean differences of -3.8±12.4, -8.8±6.0, and -5.8±7.1 mm Hg for the control, hypertensive, and CAD groups, respectively. The overall correlation coefficient for all groups was 0.84 and mean difference, 6.2±9.2%. The SD of the difference (2SD=18.4%) was substantial in comparison with the difference of 20% seen between mean values of AIx in the control and hypertensive/CAD patients. Similar results were obtained when aortic AIx obtained from the transformed radial pulse was compared with aortic AIx estimated directly from the carotid artery without using a transfer function (overall correlation coefficient, 0.86; 2SD of the difference, 22.6%).

**Comparison of Aortic With Radial AIx**

There was a close correlation (R=0.92 within each group and R=0.96 for all groups; Figure 4) between aortic AIx obtained by applying a transfer function to the radial waveform and the radial AIx obtained without use of a transfer function. For comparison with previous data, a Bland-Altman plot was constructed for the difference between aortic AIx and AIx estimated from the regression line relating aortic to radial AIx. 2SDs of the difference were 5.4%, less than that seen for the difference between aortic AIx derived from radial and carotid waveforms by using transfer functions. Changes in aortic AIx produced by nitroglycerine and norepinephrine were correlated with those in radial AIx (R=0.93, P<0.0001; Figure 5).

**Discussion**

The use of a transfer function to estimate central systolic blood pressure from the radial pulse has been established in patients undergoing cardiac catheterization (in whom direct measurements of aortic pressure can be obtained).7-9 In some of the validation studies, the accuracy of the transfer function for determining aortic AIx was also assessed, and in these the discrepancy between values of AIx obtained from a transfer function and measured values was higher than that for systolic blood pressure.8,9 In the present study, we have compared the agreement between measures of aortic blood pressure and of aortic AIx obtained by transfer functions applied to the radial and carotid pressure waveforms. Estimates of central systolic blood pressure were within acceptable limits of agreement in all groups of subjects, with the mean difference and SD of the difference being <2 and <5.3 mm Hg, respectively, in each group of subjects. This is consistent with validation studies in which aortic pressure estimated from the radial pulse has been compared with direct intra-aortic recordings.9,12 In contrast to central systolic pressure, estimates of aortic AIx derived from the radial and
Carotid waveforms showed relatively poor agreement, especially in young healthy subjects. In these subjects, there was no significant correlation between values of aortic AIX derived from radial and carotid waveforms, and the Bland-Altman 2SD statistic of the difference was 24.8% units. This difference is large in comparison with physiological changes. A change of ~14%, for example, is seen in association with 10 years of ageing. This discrepancy between values of AIX derived by applying transfer functions to the carotid and radial arteries suggests that one or the other or both of the transfer functions are of limited accuracy in predicting aortic AIX, especially in healthy subjects. Because the carotid artery is close to the aorta, carotid and aortic waveforms are similar, and the carotid-to-aortic transfer function is close to unity. Reconstruction of the aortic waveform from the carotid waveform is thus less sensitive to the exact form of the transfer function. Indeed, the aortic AIX can be estimated from the carotid without use of a transfer function. We found a similar discrepancy between aortic AIX derived by application of a transfer function to the radial waveform and aortic AIX estimated from the radial, irrespective of whether a transfer function was applied to the carotid waveform. The majority of the error is thus most likely to reside in the radial-to-aortic transfer function. The discordance in accuracy with which central systolic blood pressure and aortic AIX can be derived from the radial-to-aortic transfer function is consistent with the characteristics of the transfer function. The transfer function is a “generalized transfer function” calculated from transfer functions from individual subjects. It is thus possible to calculate the 95% confidence intervals that express the interindividual spread of the transfer function. Systolic blood pressure is determined by the coefficients for the lower frequencies, and these show much less spread than do those for the higher frequencies that influence AIX. The effect of this is illustrated in Figure 6: when a radial-to-aortic transform is applied to a typical radial waveform by using the upper and lower 95% confidence limits for the coefficients, there is little variation in systolic pressure but marked variation in the aortic AIX.

Whereas use of a transfer function is required to determine central systolic blood pressure from the radial artery, it might not be necessary to assess central pressure wave reflection. That the form of the radial pulse is determined largely by the systemic circulation has been acknowledged since Frederick Mahomed developed the sphygmograph in 1872, and the influence of pressure wave reflection within the systemic circulation on the radial waveform has been emphasized by O’Rourke and colleagues (Kelly et al). The whole concept of a transfer function is that the influence of the upper limb on radial pulse (however complex with regard to differential effects on the various frequency components) differs little between subjects. A transfer function can neither add nor subtract information contained within the radial waveform, and therefore, it should be possible to infer central pressure wave reflection directly from the radial waveform as well as from the transformed waveform. In the present study, we observed a close correlation (R>0.92 in all groups) between the aortic AIX derived by application of a transfer function to the radial waveform and the radial AIX calculated directly from the radial waveform without use of a transfer function. Indeed, the correlation between these indices was greater than that between values of aortic AIX derived from radial and carotid waveforms by using the transfer function approach. Furthermore, when changes in AIX were induced by vasoactive drugs, there was a highly significant correlation between changes in aortic AIX obtained from the transfer function and
radial AIx. That a close relation between aortic and radial AIx should exist is not, as discussed above, unexpected. What is surprising is the simple, approximately linear form of the relation. This means that radial AIx may provide an equally good measure of central pressure wave reflection and has the advantage that it is not dependent on a relatively arbitrary manipulation of the waveform derived from observations made in selected groups of subjects.

In conclusion, our findings question the use of a transfer function to obtain accurate measurements of aortic AIx but suggest that similar information on central pressure wave reflection can be obtained directly from the radial pulse.

Perspectives
Systolic blood pressure and the contour of the pulse waveform differ between central and peripheral arteries. With the recognition that important information relating to arterial wave reflections can be derived from the contour of the aortic pulse, there has been much interest in the estimation of the aortic waveform from more accessible peripheral arteries. A common approach is to use applanation tonometry to obtain the radial or carotid pressure waveform and then to apply a mathematical “transfer function” to synthesize the aortic waveform and hence, to derive the aortic AIx, a measure of arterial pressure wave reflection. The present study compared estimates of aortic systolic blood pressure and the aortic AIx obtained from carotid and radial pulse waveforms by using a transfer function. Those of aortic systolic blood pressure were within acceptable limits of agreement, but those of aortic AIx showed wide variation, especially in healthy subjects. Despite the complexity of the transfer function, an AIx obtained directly from the radial pulse without use of a transfer function showed a close linear correlation with the aortic AIx (estimated by using the transfer function). These findings suggest that the transfer function is of limited value in estimating central arterial wave reflection from the radial pulse and that the same information might be obtained directly from the radial pulse. Future studies should evaluate the use of measurements obtained directly from the peripheral pulse for risk stratification and to identify patients who may benefit from antihypertensive or other treatment.

References
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