Simultaneous Measurement of Beat-to-Beat Carotid Diameter and Pressure Changes to Assess Arterial Mechanical Properties

Cristina Giannattasio, Paolo Salvi, Filippo Valbusa, Anna Kearney-Schwartz, Anna Capra, Maria Amigoni, Monica Failla, Lucia Boffi, Fabiana Madotto, Athanasios Benetos, Giuseppe Mancia

Abstract—Use of local arterial distensibility measurements by change in carotid artery diameter divided by pulse pressure has limitations because blood pressure is often taken in a vessel distant or at a time different from where and when change in diameter is taken. In 92 subjects (23 to 91 years of age), carotid artery diameter was continuously measured ecographically, whereas blood pressure was continuously measured simultaneously tonometrically on the contralateral artery, the 2 signals being synchronized via 2 EKGs. Within each cardiac cycle, there was a linear relationship between the changes in vessel diameter and the changes in blood pressure during either the protomesosystole or the diastole after the dicrotic notch. The diastolic slope was displaced upward and steeper than the systolic slope, the pressure–diameter loop showing a hysteresis. Both slopes showed a high reproducibility when data were averaged over a several-second period. There were small differences between consecutive cardiac cycles, suggesting that modulation of arterial mechanical response to continuous changes in intravascular pressure may undergo physiological variations. In the 92 subjects, systolic and diastolic slopes correlated significantly with distensibility values obtained by Reneman formula and exhibited a close inverse relationship with each subject’s age and systolic blood pressure, thereby showing the ability to reflect age- and pressure-dependent large artery stiffening. This method may allow precise assessment of man’s arterial mechanical properties within each cardiac cycle. This highly dynamic assessment may help to collect information on properties of normal and altered large elastic arteries and the mechanisms involved in disease. (Hypertension. 2008;52:896-902.)

Key Words: arterial mechanical properties □ arterial compliance □ arterial distensibility □ systolic blood pressure □ aging □ new method □ stiffness

In the last 2 decades, evidence has been obtained that large elastic artery distensibility undergoes a progressive reduction with aging, and that its values are markedly reduced in hypertension and a variety of other diseases.1-12 It has also been shown that this reduction has adverse clinical consequences because large elastic artery stiffening: (1) provides less buffering to the pressor effect of stroke volume and increases the traveling speed of the pressure wave along the arterial tree, with an increase in the reflected wave phenomenon and a systolic blood pressure elevation13; (2) enhances the traumatic effect of intravascular pressure excursions on the vessel wall, thereby favoring atherosclerosis13; and (3) independently increases, at any blood pressure level, the risk of cardiovascular morbidity and fatal events.14-18

All methods used currently to measure large elastic artery distensibility have limitations. Some methods derive from theoretical models, and their results thus rely on complex and sometimes only partially testable mathematical assumptions.19 Other methods rely on the well-established direct relationship between arterial stiffening and speed of pulse wave traveling along the arterial tree and pulse wave velocity measurements, thus providing an index of arterial distensibility, albeit indirect and dependent on the integrated characteristics of both central elastic and middle-size muscle arteries.19 Still other methods measure the systo-diastolic changes in carotid or aortic diameter in response to systo-diastolic blood pressure excursions, which are, however, often obtained at sites away from where or at times different from when the diameter changes are measured, with inevitable inaccuracies of uncontrollable magnitude.19

In the present study, we describe a method for assessing large elastic artery mechanical properties in man that may avoid some of the above-mentioned inconveniences. The method is based on echographic measurement of continuous properties.
changes in a common carotid artery diameter versus continuous changes in blood pressure measured simultaneously by tonometry from the contralateral artery. This may have several advantages: (1) to relate changes in vessel diameter to the actual changes in intravascular pressure occurring at the same site and time; (2) to provide not just 2 (diastolic and systolic values) but a high number of vessel diameter and blood pressure values across the cardiac cycle, thereby allowing the diameter–vessel relationship to be expressed as a slope; (3) to compare the slope between different cardiac cycles and thus provide information on how this arterial function may vary on a short-time or even a beat-to-beat basis, an issue never addressed before; and (4) to measure the slope separately during systole and diastole, with a more extensive information on arterial mechanical properties.

Methods

Subjects
The study was based on 92 subjects recruited in the outpatient clinic of Monza (Milan, Italy) and Nancy (France). Forty-six subjects were males and 46 were females, ranging in age from 23 to 91 years (age 55 ± 2 years; mean ± SE). All subjects were normotensive (clinic blood pressure < 140/90 mm Hg at repeated visits in the outpatient clinic) or untreated mildly hypertensive patients with no history of chronic therapeutic drug use of any kind or of major diseases. Absence of major diseases was confirmed by physical and laboratory routine examinations. Echo-Doppler examinations of supra-aortic arteries showed no evidence of atherosclerotic plaques, defined as a focal intima-media thickness > 1.5 mm. Nine subjects were smokers, and none had a history of alcohol consumption, although 2 reported occasional drinking. Subjects consented to participate in the study after explanation of its nature and purpose. The study design was approved by the ethics committees of the institutions involved.

Diameter/Pressure Curves
From the separate carotid diameter and tonometry signals, diameter/pressure curves were obtained via specifically designed software (DiaPres; DiaTecne). First, a 4-second period was selected to allow analysis of 3 to 5 diameter/pressure curves depending on the heart rate values. Second, the EKG signal made available by either the tonometric or the ultrasound device were superimposed to obtain an initial alignment of pressure and diameter waveforms. Third, a correction factor of 30 milliseconds was applied to the diameter waveform to take into account the phase error attributable to cardiac electromechanic coupling as well as the delay attributable to propagation of the pressure wave to the carotid artery. Fourth, once aligned, the beginning and the end of the segments to be analyzed within each waveform were identified visually on the 2 beams (Figure 1). The analysis was performed on digitized data after conversion in ASCII mode and consisted of the relationship between the diameter and the pressure changes throughout the cardiac cycle, the diameter changes being expressed in micrometers and the pressure changes in millimeters of mercury. This was followed by calculation of the slope of: (1) the increase in diameter versus the increase in pressure during protomesosystole; and (2) the reduction in diameter versus the reduction in pressure during late diastole (ie, after the dicrotic notch [Figure 1]). During protomesosystole (ie, from the upstroke to the peak systolic pressure and diameter values) and late diastole (the pressure and diameter signals after the dicrotic notch), the diameter and pressure signals were usually both straight (Figures 1 and 2). When dealing with a semiautomatic irregular signal, the least square method was used to search for the straight line that minimized, point by point, the sum of the square of the distances with respect to the irregular line. The diameter and pressure signals during final systolic phase and early diastole were nonlinear and thus were not used.

Protocol
After a light breakfast and a 24-hour abstinence from smoking as well as alcohol- and caffeine-containing beverages, subjects underwent an echo-Doppler examination of the supra-aortic vessels. The protocol was as follows. Blood pressure was measured 3 times from the brachial artery, keeping the subject in the sitting position and using a mercury sphygmomanometer or a semiautomatic device. Next, subjects were placed supine, and brachial blood pressure was measured few more times. A 7.5-MHz probe of an echotracking device (Wall Track System; Pie Medical) was positioned on a common carotid artery, and an arterial tonometry device (PulsePen; DiaTecne) was positioned at the same level on the contralateral vessel, each device being operated by a single investigator. The tonometric signal was calibrated versus supine brachial artery blood pressure values. Finally, after a 10-minute rest, carotid artery diameter and blood pressure were measured continuously and simultaneously for several 5-second periods over a 10-minute time interval.

Data Analysis
In each subject, the slope of the diameter/pressure relationship during protomesosystole and late diastole were averaged separately, first for the carotid cycles within each acquisition period and then for 2 acquisition periods selected randomly over the 10-minute recording time. The values were regarded as reflecting carotid artery compliance of a given individual during systole and diastole, respectively. Averages (± SE) were then calculated for the group as a whole and for subgroups above and below the median age and systolic blood pressure of the entire sample. Data were also normalized for diastolic diameter to obtain distensibility values, which were compared with those obtained from the same set of measurements with a current method of assessing carotid distensibility (ie, the absolute systo-diastolic change in carotid diameter divided by the absolute pulse pressure value and normalized for baseline diameter according to the Reneman formula). Calculation was also made of the systolic or diastolic slope variability for different cardiac cycles within a given acquisition period and for different acquisition periods, using the coefficient of variation of the mean slope value and the SD of the mean change of the second value versus the first one according to the Quan–Shih approach, using the Bland–Altman approach to analyze the data. Statistical comparisons were made by the $t$ test for paired or unpaired observations. A $P < 0.05$ was taken as the level of statistical significance. The univariate Spearman

Figure 1. Original tracings of carotid diameter and simultaneously acquired blood pressure wave. a and b indicate protomesosystolic phase; c and d, late diastole; Press., blood pressure; Diam., carotid diameter.
or Pearson correlation coefficient was used to relate systolic with
diastolic slopes as well as to relate slope values with age systolic
blood pressure and carotid diameter at diastole. Age and blood
pressure were also taken as the independent variables versus systolic
or diastolic slopes as the dependent ones in a multivariate stepwise
analysis.

Results
The average tonometric blood pressure was 114.2±1.9/
70.6±1.1 mm Hg (systolic/diastolic), and the average carotid
diameter at end diastole was 6943±10.9 µm. As shown in the
2 examples of Figure 2, the diameter–pressure curve was
located upward during diastole compared with systole, indicating
a greater slope value in the former than in the latter
phase of the cardiac cycle. There was a close positive
relationship between the slope of the diameter/pressure rela-
tionship during protomesosystole (Figure 1a and 1b) and late
diastole (Figure 1c and 1d), the diastolic slope being, how-
ever, consistently greater than the systolic one (Figure 3). As
shown in Figures 2 and 4, within a given acquisition period,
there was a close relationship between the diameter–pressure
slopes obtained in different cardiac cycles. Yet, comparing
the change shown by a slope to the one obtained in a previous
cardiac cycle, some differences were seen (Figure 4, top and
bottom panels). The coefficient of variation of the mean
systolic slope ranged from 12.6% to 16.1%, with an average
value for the group as a whole of 14.0%. The coefficient of
variation of the mean diastolic slope ranged from 16.7% to
19.4%, with an average value of 18.4%. There was also a
close correlation between the averaged data obtained in 2
acquisition periods (r>0.91 and >0.85 for systolic and
diastolic slopes, respectively), with negligible differences in
mean values. Reproducibility data were similar in men and
women.

Carotid Slopes Versus Carotid Diameter, Age, and
Blood Pressure
There was an inverse relationship between the systolic and
diastolic diameter/pressure slopes and the carotid artery
diameter at diastole (r=-0.37 and -0.42, respectively;
P<0.001 for both), indicating that the ability of the vessel to
change volume when intravascular pressure raised in systole
or decreased in diastole diminished as it became larger. There
was a highly significant correlation between both systolic and
diastolic carotid diameter/pressure slopes and the carotid
distensibility calculated by the Reneman formula (r=0.77
and 0.76 for systolic and diastolic slopes, respectively;
P<0.0001 for both). As shown in the examples of Figure 5,
top panels, both in systole and diastole, the slope of the
The present study shows that the progressive increase in blood pressure tonometrically measured from a common carotid artery during protomesosystole was associated with a linear increase in the carotid artery diameter measured simultaneously at the same level of the contralateral vessel. It further shows that a linear relationship between changes in carotid blood pressure and diameter also occurred when both progressively decreased in the late diastolic phase (ie, after the diastolic notch). Thus, slopes of the diameter–pressure relationship can be obtained from the carotid arteries during most of the ascending and the descending portion of the pulse pressure wave, which provides extensive data on the response of a large elastic vessel to the blood pressure changes within a cardiac cycle and thus on large elastic artery mechanical properties.

Several advantages of the procedure we used for the characterization of carotid artery mechanical properties need to be mentioned. First, the blood pressure and diameter signals were recorded simultaneously, thus avoiding the error that may occur by calculating the stimulus to carotid artery distension from a pulse pressure measured at a different time, an error that may not be trivial because of the pronounced short-term variability in pulse pressure. Second, diameter and pulse pressure were measured at a corresponding carotid artery level, thus quite precisely matching the vessel distension with the pressure wave that caused it. Third, for both diameter and pressure, measurements were continuous and data can thus be expressed as slopes, which is not possible for conventional methods to assess compliance and distensibility in which 2 points only (minimal and maximal values) are available. And fourth, the systolic and diastolic diameter–pressure slopes were obtained over several consecutive cardiac cycles, thus obtaining a large number of values and also providing information on the short-term variability of this
vascular function, a phenomenon that has been impossible to address by the procedures in use so far.

In our subjects, the systolic and diastolic slopes were almost superimposable when the average values of 2 periods, each made by several cardiac cycles, were considered. This suggests that the value obtained by averaging the data obtained from a short-term period is likely to be representative of the one characterizing the subject under study. However, the systolic and diastolic slopes showed differences, albeit small, when the comparison involved data derived from individual cardiac cycles. This may be attributable to technical errors. However, it is possible that the arterial ability to dynamically change volume in relation to continuous changes in intravascular pressure undergoes some beat-to-beat variability. The procedure we used may allow study of the mechanisms of this variability and their possible alterations with disease.

Several final points should be made. First, both systolic and diastolic slopes showed a highly significant correlation with the measurement of carotid distensibility provided through the same set of data, by the method based on the Reneman formula. However, there were some discrepancies that raise the question of whether taking into account only the 2 extreme pressure and diameter values, as is done with the Reneman formula method, accurately reflects diameter–pressure slopes. Second, during both systole and diastole, the slopes relating the changes in diameter to the changes in blood pressure showed a negative relationship with the arterial diameter, an expected finding because vascular wall tends to become stiffer as the baseline stretching of the tissue components in the wall increases. Third, similar to what was found by use of a conventional method to assess arterial distensibility, the systolic and diastolic slopes showed a progressive reduction with age and systolic blood pressure, each variable independently contributing to the cardiovascular stiffening when a multivariate analysis was performed. Thus, both the systolic and diastolic values obtained by the

Figure 5. Top panels, Carotid artery diameter, pressure, and diameter pressure relationship throughout 1 cardiac cycle in a young (A) and an old (B) subject. Bottom panels, Carotid artery diameter–pressure and diameter pressure relationship throughout 1 cardiac cycle in a normotensive (C) and a hypertensive (D) subject. BP indicates blood pressure; ys, years.
procedure we used can document well-known phenomena such as the age- and blood pressure–related stiffening of large elastic arteries.\textsuperscript{1–12} And finally, the slope of the carotid diameter–blood pressure changes during systole showed a close relationship with that during diastole. However, over the same blood pressure range, the diameter values of the carotid artery were invariably greater during diastole compared with systole, and so was the slope of the diameter–pressure changes. We can speculate that this derives from the viscosity characteristics of the vessel wall, which may oppose and delay vessel distension when blood pressure increases, while favoring return to original diameter when blood pressure falls.\textsuperscript{27–30} If so, the difference between diastolic and systolic diameter–pressure slopes (and possibly between the diameter–pressure hysteresis within a cardiac cycle) may provide information on this determinant of arterial mechanical properties as well as its structural origin. This information might also derive from measurement of the hysteresis of the diameter–pressure loop. However, this was not done in the present study because of the uncertainty about the nature of the nonstraight portion of the loop.

Our technique has some limitations because although the steps taken appeared to satisfactorily align the pressure and diameter signals, other potential errors attributable to variations in electromechanical coupling and different propagation of the pressure wave to the right and left carotid artery could not be completely eliminated. Furthermore, the correct simultaneous recording of carotid blood pressure and diameter needs the availability of 2 expert operators. Finally, the procedure is time consuming, and its use may not be advisable in patients with hemodynamically significant carotid artery plaques to avoid cerebral hypoperfusion by bilateral vessel compression.

Perspectives
The present study shows that slopes of the pressure–diameter relationship can be obtained from the carotid arteries during most of the ascending and the descending portion of the pulse pressure wave, which provides extensive data on the response of a large elastic vessel to the blood pressure changes within a cardiac cycle and thus on large elastic artery mechanical properties. The slope values showed a high within-subject reproducibility, with small differences between consecutive cardiac cycles, and exhibited a close inverse relationship with age systolic blood pressure and the distensibility value obtained by Reneman formula. This new method may allow a precise and in-depth assessment of the mechanical properties of carotid artery in physiology and pathophysiology, with a potential also to investigate the mechanisms involved.

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Disclosures
None.

References


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