Age-Related Abnormalities in Arterial Compliance Identified by Pressure Pulse Contour Analysis

Aging and Arterial Compliance

Gary E. McVeigh, Christopher W. Bratteli, Dennis J. Morgan, Cheryl M. Alinder, Stephen P. Glasser, Stanley M. Finkelstein, Jay N. Cohn

Abstract—The objective of this study was to evaluate age-related changes in pulsatile arterial function. Aging alters arterial pulsatile function and produces consistent changes in the pressure pulse contour. A reduced systemic arterial compliance that can be derived from analysis of the pulse contour is regarded as the best clinical index of impaired pulsatile arterial function and may mark the presence of early vascular damage. We analyzed intra-arterial brachial artery waveforms in 115 healthy normotensive volunteers (83 men, 32 women) and radial artery waveforms obtained with the use of a calibrated tonometer device in 212 healthy volunteers (147 women, 65 men). A computer-based assessment of the diastolic pressure decay and a modified Windkessel model of the circulation were used to quantify changes in arterial waveform morphology in terms of large artery or capacitive compliance, oscillatory or reflective compliance in the small arteries, inertia, and systemic vascular resistance. Large artery compliance and oscillatory compliance correlated negatively with age for both invasive and noninvasive groups \((r=-0.50\text{ and } r=-0.55; \quad r=-0.37\text{ and } r=-0.66; \quad P<0.001\text{ for all})\). The slopes of the regression lines for the decline in oscillatory compliance with age were significantly steeper than those recorded for large artery compliance estimates. The change in blood pressure with age independently contributed to the decrease in large artery compliance but not oscillatory compliance in both groups. Consistent age-related changes were found in the pressure pulse contour by analysis of waveforms obtained invasively or noninvasively from the upper limb. The change in the oscillatory or reflective compliance estimate was independent of blood pressure change and may represent a better marker than large artery or capacitive compliance of the degenerative aging process in altering pulsatile arterial function. (Hypertension. 1999;33:1392-1398.)

Key Words: age ■ compliance ■ resistance ■ impedance

Adaptations in the arterial vasculature play a critical role in influencing cardiovascular hemodynamics with advancing age.\(^1\) The generalized structural and functional changes in the arterial circulation contribute to alterations in regional blood flow, progression of atherosclerosis, and the microvascular abnormalities that occur during senescence.\(^2\) In large arteries, aging results in progressive deposition of calcium salts, fraying and fragmentation of elastin, and an increase in the number and cross-linking of collagen fibers that alter the compliance characteristics of the vessel wall.\(^3\) A rigid aorta is less able to buffer the pulsatile output from the heart; it contributes to an increase in systolic blood pressure and left ventricular afterload and a decrease in diastolic blood pressure and impaired coronary perfusion. Recent evidence suggests that an increase in pulse pressure is accompanied by progressive vessel wall damage and atherogenesis and is associated with an increase in cardiac morbidity and mortality rates.\(^4,5\) In addition, a reduction in diastolic pressure, especially in the presence of coronary artery disease, has been implicated in precipitating cardiac events.\(^6\)

Age-related changes in the vasculature are not confined to large arteries but involve small arteries and arterioles as well.\(^7–9\) Traditionally, age-related hemodynamic adaptations in the small arterial vessels have been characterized by changes in total peripheral resistance that predominantly reflect a reduction in capillary density and changes in the media thickness:lumen ratio.\(^9\) Resistance calculations represent a steady-state measurement based on a circulatory model of continuously fixed pressure (mean arterial pressure) and constant flow (cardiac output). It ignores pressure fluctuations that occur in the circulation, where the compliance characteristics of the arterial vasculature provide the vital buffering function required to smooth pulsatile outflow from the heart.\(^10\) However, endothelial function, elastin, and smooth muscle elements of the small vessels are known to be altered with advancing age, thus impairing the compliance

Received November 10, 1998; first decision November 27, 1998; revision accepted January 22, 1999.

From the Division of General Internal Medicine (G.E.M.) and the Cardiovascular Division (C.W.B., D.J.M., C.M.A., J.N.C.), Department of Medicine, University of Minnesota Medical School, Minneapolis, Minn; the Department of Epidemiology (S.P.G.) and the Department of Laboratory Medicine and Pathology (S.M.F.), University of Minnesota, Minneapolis. Correspondence to Jay N. Cohn, MD, Cardiovascular Division, University of Minnesota Medical School, Box 508, 420 Delaware St SE, Minneapolis, MN 55455, E-mail cohnx001@maroon.tc.umn.edu

© 1999 American Heart Association, Inc.

Hypertension is available at http://www.hypertensionaha.org

1392
Characteristics and the ability to withstand distending pressures in this section of the vasculature. \(^9,11\)

While it is generally accepted that the structural and functional changes associated with aging impair the compliance of the arterial circulation, these studies have been confined to the large conduit arteries and have emphasized that changes in pulsatile arterial function do not progress in a uniform or consistent manner in all arteries. \(^12–14\) Prior studies that used pulse wave velocity to estimate the stiffness of arterial segments have indicated that the aorta stiffens progressively at an accelerated rate compared with other arterial segments. \(^15\) Echo-tracking technology has revealed that age-related changes in pulsatile function are inhomogeneous within localized arterial segments of elastic and muscular arteries and that the compliance characteristics of the radial artery may paradoxically increase with age. \(^12,13\) In contrast to the marked heterogeneity in the physical characteristics of localized arterial segments with aging, consistent and predictable changes occur in the arterial pulse contour regardless of the site of measurement. \(^16–18\) These changes reflect alterations in total arterial compliance and can be quantified with the pulse contour analysis technique, which provides an assessment not only of the physiological behavior of the large conduit arteries that serve a capacitance function but also of the smaller arteries that represent the predominant site of reflected waves or oscillations in the arterial bed. \(^10,19,20\) With this technique, we have examined the effects of aging on pulsatile systemic arterial function derived from waveforms obtained with the use of invasive intra-arterial catheters and a noninvasive arterial tonometer device.

**Methods**

**Subjects**

Invasive studies were performed on 115 healthy normotensive volunteers (83 men, 32 women). Noninvasive studies were performed on 212 healthy volunteers (147 women, 65 men). Subjects were free from obvious clinical disease, as established by a full history and examination, which included ECG. No subject had a history of cardiac, cerebrovascular, or peripheral vascular disease and none were taking medications at the time of study. Each subject gave written and informed consent, and the studies were approved by the committee on the use of human subjects in research at the University of Minnesota. Repeatability data were obtained from a separate group of 30 normal subjects who were evaluated by the noninvasive method during 3 separate visits at 1-week intervals. At each visit, pulse contour analysis was performed in triplicate over a 15-minute period.

**Procedures**

Invasive studies were performed between 7 and 8 AM in a quiet, temperature-controlled laboratory with the subjects lying supine. All participants fasted for 12 hours before the study. Alcohol, caffeine, and smoking were prohibited during this time. Under local anesthesia (lidocaine 1%) and sterile conditions, an 18-gauge catheter was inserted into the brachial artery of the nondominant arm of each subject and connected to a Statham P23DB pressure transducer with 24-inch fluid-filled pressure tubing. A single-lumen catheter was positioned close to the superior vena cava after percutaneous insertion into a brachial vein. Cardiac output was determined in triplicate by the indocyanine green dye-dilution technique (Waters D400 densitometer). Mean arterial pressure was derived by integrating the area under the pressure pulse waveform. All subjects rested for 30 minutes after the catheter was placed to establish a stable baseline before data were collected.

For the noninvasive studies, radial artery pressure pulse waves were recorded with an arterial tonometer sensor array (model N-500, Nellcor Inc). A waveform was calibrated by the oscillometric method with a cuff on the opposite arm and a calibration system internal to the Nellcor device. The tonometer sensor array adjusted automatically to obtain the optimal waveform and repeated its calibration until the waveform was stable. Cardiac output was estimated from an algorithm that incorporates a multivariate function of age and body surface area in addition to heart rate and ejection time that can be determined from arterial pressure waveforms, measured with the use of invasive or noninvasive instrumentation as described previously. \(^20,23\)

**Beat Marking and Waveform Analysis**

Invasive brachial artery and noninvasive radial artery waveforms were recorded for 30 seconds for each subject in the supine position. Blood pressure waveforms were digitized at 200 samples per second and stored in a personal computer. The data were automatically displayed on the computer screen for visual analysis to confirm that the recorded waveforms were uniform and without artifact. Individual beats, demarcated with the upstroke beat mark as a fiduciary time point, were cross-correlated. Those with a correlation coefficient of <0.95 were discarded. This usually excluded 20% to 25% of the beats from a 30-second sample.

**Data Analysis**

To obtain a measure of arterial compliance, a model was used that divides the total systemic arterial compliance into large artery or capacitive and small artery or oscillatory compliances. The model describes diastolic pressure contours by the following equation:

\[
P(t) = A_1 - A_2 + A_3e^{-A_4t} + A_5e^{-A_6t}
\]

where \(P(t)\) is the diastolic pressure at time \(t\) relative to aortic valve closure. A parameter-estimating algorithm was applied for determination of the best set of \(A\) values for matching the diastolic portion of the measured beat to this equation. These \(A\) parameters, together with an estimate of systemic vascular resistance, determine the 2 compliances. (The methodology and computer software used in this study were developed in collaboration with Hypertension Diagnostics, Inc, whose diagnostic CR2000 instrument uses this methodology.)

In prior studies, the \(A\) parameters were determined by analysis of a single averaged beat that was representative of the 30-second period of arterial pressure pulse data. We and others \(^22\) have noted that high error estimates in the \(A\) parameters may be predictive of variability in repeated measures. Therefore the compliance values for each beat were weighted inversely with respect to an estimate of error and then averaged. The estimate of error was the predicted variance in the compliance divided by a measure of the goodness-of-fit of the model to the data. This approach ensures that individual compliance values with high estimated variance will contribute proportionally less to the overall compliance value. Additionally, end-diastolic distortions were eliminated by defining end-diastole as the point where diastolic pressure is no longer monotonically decreasing.

An impedance index was calculated from the input impedance of the modified Windkessel circuit, with the circuit parameter values determined in the model analysis. The index is a value of the input impedance modulus evaluated at the fundamental frequency, or heart rate. It is represented by a pi circuit that consists of a parallel combination of a compliance and a series combination of inertance and parallel resistance and compliance elements. Similar third-order models of the circulation have been used previously to evaluate the impedance load that opposes left ventricular ejection. \(^23\)

**Statistical Analysis**

Data are presented as mean ± SEM. Mean values were compared with the use of the unpaired Student \(t\) test in the groups that had noninvasive measurements and invasive measurements. The relation between continuous variables were analyzed by linear regression. The independence of association between variables was tested with multiple regression analysis. ANCOVA was used to compare gender and methodological influences on the slopes of regression with age. For repeatability analysis, the intraclass correlation (IC) was used. \(^24\) This statistic estimates the fraction of total variance in a measure that can be attributed to the difference between individuals. This method is preferable to coefficients of
variation in that measures of different magnitudes can be more appropriately compared.

**Results**

Two groups, shown in Table 1, underwent noninvasive and invasive measurements. The groups were well matched with regard to age, height, weight, and body surface area. No significant differences were noted in mean arterial pressure or diastolic blood pressure between groups. Systolic blood pressure was significantly higher in women who underwent invasive studies compared with the noninvasive group (125.5 ± 2.4 vs 119.5 ± 1.2, *P* < 0.001), and heart rate was significantly higher in the group who underwent noninvasive studies. Invasive and noninvasive estimates of large artery and oscillatory compliance were significantly lower and systemic vascular resistance and the calculated impedance to left ventricular ejection were significantly higher in women versus their male counterparts (*P* < 0.01 for all) (Figure 1). The women also were older and shorter, characteristics associated with lower compliance and higher resistance.

Figure 2 illustrates the relation between age and large artery compliance, oscillatory compliance, systemic vascular resistance, and the calculated impedance index for the invasive studies. Large artery compliance correlated negatively with increasing age and decreased by 46% over the age range studied. Oscillatory compliance correlated negatively with increasing age and decreased by 83% over the age range studied. Systemic vascular resistance increased with age by 37% over the age range studied. The total opposition to left ventricular ejection, represented by the calculated impedance index, correlated strongly with age and increased by 76% over the age range studied.

---

**TABLE 1. Demographics and Hemodynamics for the Invasive and Noninvasive Blood Pressure Data Sets Grouped by Gender**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Noninvasive Data</th>
<th>Invasive Data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>No./group</td>
<td>65</td>
<td>147</td>
</tr>
<tr>
<td>Age range, y</td>
<td>21–80</td>
<td>22–83</td>
</tr>
<tr>
<td>Mean age, y</td>
<td>42±1.8</td>
<td>45±1.0</td>
</tr>
<tr>
<td>Height, in</td>
<td>70.5±0.34</td>
<td>64.7±0.22</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>85.7±2.0</td>
<td>73.0±1.4</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>2.06±0.02</td>
<td>1.81±0.02</td>
</tr>
<tr>
<td>SYS, mm Hg</td>
<td>87.4±1.7</td>
<td>85.8±0.84</td>
</tr>
<tr>
<td>DIA, mm Hg</td>
<td>124.8±1.7</td>
<td>119.5±1.2</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>64.6±1.3†</td>
<td>69.3±0.9‡</td>
</tr>
</tbody>
</table>

BSA indicates body surface area; MAP, mean arterial pressure; SYS, systolic blood pressure; and DIA, diastolic blood pressure; HR, heart rate.

Within groups, SYS was higher in men and HR was higher in women who underwent noninvasive studies (*P* < 0.01 for both). HR was also higher in women vs men who underwent invasive studies (†*P* < 0.01). Between-group comparisons revealed SYS was significantly higher for women in the invasive group and HR was significantly higher in both men and women for noninvasive vs invasive study groups (‡*P* < 0.01).
Figure 3 illustrates the relations for noninvasive studies. The trends with aging were very similar to those recorded by invasive techniques. Large artery compliance and oscillatory compliance decreased significantly with age by 35% and 90%, respectively. Systemic vascular resistance and the impedance index both correlated strongly with age and increased by 66% and 72%, respectively, over the age range studied.

Illustrative examples of noninvasive radial artery waveforms are displayed in Figure 4. The differences are apparent in diastolic contour in a young subject (a), a middle-aged subject (b), and an elderly subject (c).

Tables 2 and 3 show the slopes of the linear correlations of compliance with age for invasive and noninvasive studies. No significant difference in slopes of the regression lines for large artery compliance estimates were apparent between the invasive and noninvasive studies. By contrast, a significant difference was found for linear regression slopes of oscillatory compliance. Noninvasive data exhibited a significantly steeper decline with age compared with data from invasive studies ($P<0.05$). No differences in the slopes of the regression lines with age were noted when invasive and noninvasive estimates of systemic vascular resistance were compared. Multiple regression analyses revealed that the rise in systolic blood pressure, even within the normal range, significantly reduced the large artery compliance estimates ($P<0.001$). By contrast, the oscillatory compliance was not affected by the change in systolic, diastolic, or pulse pressure.

Invasive data also were examined to identify the relation between age and other hemodynamic measurements. Arterial pressure increased with age (systolic: $r=0.33$, $P<0.001$; mean: $r=0.43$, $P<0.001$; and diastolic: $r=0.20$, $P<0.03$), whereas cardiac output exhibited a nonsignificant decline with age ($r=-0.13$, $P=0.23$). The age-associated increase in systolic pressure was 14% (1.7 mm Hg per decade), mean pressure was 20% (1.6 mm Hg per decade), and diastolic pressure was 9.5% (0.6 mm Hg per decade). The age-associated changes in mean arterial and diastolic blood pressure between groups were similar whether measured by invasive or noninvasive techniques.

Reproducibility data are displayed in Table 4. Repeatability of 3 triplicate measurements are shown in the left column and reproducibility of mean values obtained at 3 successive weekly visits are shown in the right column.

Discussion

Consistent and predictable changes occurred in the arterial pulse contour with advancing age whether recorded inva-
sively or noninvasively from the brachial and radial arteries, respectively. The predominant changes in the arterial pulse contour involve a steepening of the diastolic decay and a diminution in the amplitude and duration of the diastolic waveform in early diastole. These changes are indicative of an age-dependent reduction in large artery (capacitive) compliance and in small artery (oscillatory or reflective) compliance. The analytical technique used in these studies is a modern adaptation of the original description by Frank \(^\text{25}\) of the pulse exhibiting a basic pattern, Grundform, with a superimposed damped oscillation, Grundschwingung.

There has been increasing interest in the descriptive and quantitative analysis of the arterial pulse contour to provide information about generalized changes in the pulsatile characteristics of the large and small arterial vessels.\(^\text{10,16–20}\) In a recent study from the Baltimore longitudinal study of aging, changes in systolic pressure, the carotid pulse augmentation index, and the aortic pulse wave velocity were reported in 146 male and female volunteers 21 to 96 years of age.\(^\text{26}\) Systolic blood pressure increased 14%, aortic pulse wave velocity increased 2.5-fold, and the augmentation index increased 5-fold over the age range studied. The rise in systolic blood pressure was similar in sedentary and endurance trained individuals despite the 5-fold increase in the carotid pulse augmentation index in the sedentary group and a 2-fold increase in the endurance-trained group. It was concluded that systolic blood pressure was an insensitive marker for differences in arterial stiffness between endurance-trained and sedentary elderly individuals.

The augmentation index uses changes in the pressure waveform during systole and provides a quantitative measure of the incremental increase in the late systolic portion of the arterial pressure waveform.\(^\text{26}\) However, its utility is limited to analysis of waveforms obtained from the more central arteries and in elderly patients an inflection point on the systolic upstroke can be difficult to identify.\(^\text{27}\) Furthermore, changes in the pressure pulse waveform have been well described before significant augmentation of the systolic pressure becomes apparent.\(^\text{28}\) The earliest change in peripheral waveform morphology involves a diminution in the amplitude and duration of the diastolic component, which has been termed the ‘dip waveform’ and is characterized by a steepening of the diastolic decay.\(^\text{29}\)

**TABLE 2. Multiple Regression Analyses of Large Artery Compliance**

<table>
<thead>
<tr>
<th>First Independent Variable</th>
<th>Standardized Regression Coefficient</th>
<th>Second Independent Variable</th>
<th>Standardized Regression Coefficient</th>
<th>(R^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.368</td>
<td></td>
<td>0.135</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.234</td>
<td>DBP</td>
<td>-0.360</td>
<td>0.247</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>-0.354</td>
<td>NS</td>
<td>0.138</td>
<td>0.380</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.210</td>
<td>PP</td>
<td>-0.468</td>
<td>0.329</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>NS</td>
<td>SVR</td>
<td>-0.560</td>
<td>0.339</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**TABLE 3. Multiple Regression Analyses of Oscillatory Compliance**

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Standardized Regression Coefficient</th>
<th>(R^2)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Noninvasive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.664</td>
<td>0.441</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>-0.660</td>
<td>SBP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.643</td>
<td>DBP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.687</td>
<td>PP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.518</td>
<td>SVR</td>
<td>-0.246</td>
</tr>
<tr>
<td>Invasive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-0.552</td>
<td></td>
<td>0.305</td>
</tr>
<tr>
<td>Age</td>
<td>-0.510</td>
<td>SBP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.531</td>
<td>DBP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.530</td>
<td>PP</td>
<td>NS</td>
</tr>
<tr>
<td>Age</td>
<td>-0.419</td>
<td>SVR</td>
<td>-0.268</td>
</tr>
</tbody>
</table>

Regression analyses depicting relative impact of age and each of 4 other variables on oscillatory compliance. Shown are univariate and bivariate regression models for both the noninvasive and invasive methods. Abbreviations as in Table 2.

**TABLE 4. Repeatabilities for Noninvasive Data**

<table>
<thead>
<tr>
<th>Variable</th>
<th>15-min Repeatabilities</th>
<th>3-wk Repeatabilities*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=30)</td>
<td>(n=30)</td>
</tr>
<tr>
<td>HR</td>
<td>85.2 (75.0–92.1)</td>
<td>69.1 (51.9–82.5)</td>
</tr>
<tr>
<td>SBP</td>
<td>86.0 (76.3–92.5)</td>
<td>71.9 (55.6–84.2)</td>
</tr>
<tr>
<td>MAP</td>
<td>88.8 (80.8–94.1)</td>
<td>72.7 (56.6–84.7)</td>
</tr>
<tr>
<td>DBP</td>
<td>86.4 (76.8–92.7)</td>
<td>74.8 (59.7–86.0)</td>
</tr>
<tr>
<td>C1</td>
<td>73.4 (57.7–85.1)</td>
<td>58.7 (38.6–75.6)</td>
</tr>
<tr>
<td>C2</td>
<td>83.8 (72.8–91.2)</td>
<td>72.6 (56.5–84.6)</td>
</tr>
<tr>
<td>CO</td>
<td>89.6 (82.0–94.5)</td>
<td>90.3 (83.3–94.9)</td>
</tr>
<tr>
<td>SVR</td>
<td>86.8 (77.6–93.0)</td>
<td>83.2 (72.0–91.0)</td>
</tr>
<tr>
<td>ZHR</td>
<td>78.3 (64.6–88.1)</td>
<td>74.5 (59.2–85.8)</td>
</tr>
<tr>
<td>ET</td>
<td>74.2 (58.8–85.6)</td>
<td>72.8 (56.8–84.8)</td>
</tr>
</tbody>
</table>

\(r_I\) indicates interclass correlation; CI, confidence interval; ZHR=impedance; and ET, ejection time. Other abbreviations as in previous tables.

*Each data point consists of the mean of 3 successive measures over 15 minutes.
duration of the pressure waveform that interrupts the mono-
exponential decay of diastole and reflects a change in the
stiffness or compliance characteristics of the arterial blood
vessels.\textsuperscript{29,30} The pulse contour analysis technique segments
the diastolic interval into 2 components: an exponential decay
as a function of large artery compliance and diastolic fluctu-
ation that represents the effects of peripheral wave reflections
that produce a form of damped resonance superimposed on
the basic shape of the pressure waveform.\textsuperscript{31,32} Pressure pulse
waveform reflections arise primarily from discontinuities in
the caliber or elastic properties along vessels in the arterial
system, with the major reflection sites located close to the
high-resistance arterioles.\textsuperscript{33} The decline in the oscillatory
compliance estimate was more closely associated with ad-
vancing age than a reduction in large artery compliance.
Because the arterioles are largely free from atheroma and the
change in oscillatory compliance was independent of blood
pressure change in this population, this estimate may be a
sensitive marker for the effects of the aging process per se
independent of other confounding influences. One possible
explanation for the greater sensitivity of small artery changes
is that the large arteries tend to increase in caliber with
aging.\textsuperscript{34} The effect of a reduction in arterial wall elastic
properties on arterial distensibility might then be counterbal-
anced by a caliber increase in the large arteries but not in the
small arteries. This caliber increase could maintain compli-
ance despite a reduction of distensibility caused by structural
or functional alterations in the wall.

Type 2 diabetes mellitus is often viewed as accelerating the
aging process in arteries.\textsuperscript{35} We have previously reported a
diminution in the amplitude and duration of the diastolic oscil-
latory waveform in diabetic subjects.\textsuperscript{29} These changes occurred
before other morphological changes were noted in the arterial
wave shape and without differences in total peripheral resistance
or cardiac output between groups. Furthermore, the alteration in
the arterial pulse contour occurred in the diabetic subjects before
complications of the disease could be detected. Similar changes
in the pulse contour have been described with other risk factors
for,\textsuperscript{36} or disease states associated with,\textsuperscript{29,30} atherosclerosis. In the
present database we have not attempted to analyze any possible
confounding influence of smoking, hyperlipidemia, or hypergly-
cemia on the effect of aging on arterial compliance. Nonetheless,
changes in the arterial pulse contour appear to provide a sensitive
index to assess and monitor changes in pulsatile arterial function
that are evident before changes in steady-state hemodynamics
occur. Whether altered pulsatile characteristics of the arterial
circulation precede the development of cardiovascular disease or
are a consequence of established cardiovascular disease remains
a matter of debate.\textsuperscript{4} It is noteworthy that the consistent changes
in the arterial pulse contour with aging and disease contrast
markedly with the conflicting results of prior studies that have
examined the influence of aging and cardiovascular risk factors
on local or segmental mechanical wall properties that influence
pulsatile arterial characteristics.\textsuperscript{12,37,38}

Cardiovascular function can vary dramatically among el-
derly individuals, which reflects the interindividual variabil-
ity between age, disease, and lifestyle related effects on
vascular hemodynamics.\textsuperscript{2} Although the determinants that
influence pulsatile arterial function are incompletely under-
stood, modifiable constitutional and lifestyle characteristics
can significantly contribute to arterial compliance. The rise in
blood pressure with aging, even within the normal range, was
associated with a reduction of the large artery compliance
estimates in this study. Atherosclerosis also has been impli-
cated in the alteration of the pulsatile characteristics of blood
vessels.\textsuperscript{39-40} However, the relation between altered mechani-
cal properties of blood vessels and atherosclerosis is complex
and probably involves both structural and functional influ-
ces that have led to conflicting reports in the literature.\textsuperscript{41}

An attractive hypothesis consistent with the data are that
altered endothelial function is at the root of the large and
small artery compliance reduction with aging. Endothelial
release of nitric oxide (NO) is impaired with aging, athero-
sclerosis, and diabetes.\textsuperscript{42-44} Reduced NO would not only
produce vasoconstriction, which would reduce compliance,
but would also facilitate vascular smooth muscle growth that
would add a structural component to the increase in arterial
stiffness. We have previously shown that the short-term
administration of fish oil supplements to patients with diabe-
tes mellitus enhanced NO production or activity from the
endothelium and significantly improved pulsatile arterial
function without influencing cardiac output, total peripheral
resistance, or blood pressure.\textsuperscript{45} These data provide support for
the concept that therapy that favorably influences endothelial
function can improve the pulsatile characteristics of the
arterial circulation and potentially contribute to the cardio-
vascular protective actions of these compounds.

An understanding of the age-related physiological changes
that occur in the arterial system is crucial in order to
appreciate the influence of age on the occurrence of cardio-
vascular disease and its response to treatment. Diagnostic
procedures are currently designed to assess the extent and
severity of vascular disease after the development of symp-
toms or when morbid events occur. The diagnostic challenge
must be to detect abnormal structure and function in the
vascular system before the development of symptoms or
signs of cardiovascular disease.\textsuperscript{46} By providing a direct
assessment of abnormal structure or tone in the arterial
vasculature, alterations in arterial compliance may improve
risk stratification and identify individuals with early vascular
damage who are predisposed to future vascular events.\textsuperscript{47}

Utilization of data from pulse contour analysis is depend-
ent on the reliability and reproducibility of the measurement.
Data on repeatability of measurements both at a single visit
and on 3 weekly visits indicate that the compliance measure-
ments are as reproducible as other noninvasive measurements
such as heart rate and blood pressure. Furthermore, the close
correlation between aging and compliance assessed at a
single time point suggests that this measurement provides
reliable and reproducible information.

Despite the strong negative correlations of arterial compli-
ance with age demonstrated in these studies, considerable
individual variability was noted. This may indicate differ-
ences in the rate of vascular aging among individuals or
reflect variations in the generalized effects of subclinical
atherosclerosis superimposed on the aging process. Longitu-
dinal studies will be required to confirm whether impaired
compliance characteristics of the arterial vasculature can
serve as a marker for vascular injury and future cardiovascular events. With the advent of noninvasive technologies that have the capability to accurately track changes in the pulse contour over time, this goal can now become a reality.18,20

In summary, these studies confirm by pulse contour analysis the previous observation that large artery compliance falls with age. They demonstrate for the first time that a measure of small artery or oscillatory compliance also falls with age. They demonstrate for the first time that a

[1] L. Hajdu MA, Heistad DD, Siems JE, Baumbach GL. Effects of aging on small artery or oscillatory compliance also falls with age. They demonstrate for the first time that a


[10] Freis ED, Heath WC, Luchsinger PC, Snell RE. Changes in the carotid pulse contour over time, this goal can now become a reality.18,20


Age-Related Abnormalities in Arterial Compliance Identified by Pressure Pulse Contour Analysis: Aging and Arterial Compliance
Gary E. McVeigh, Christopher W. Bratteli, Dennis J. Morgan, Cheryl M. Alinder, Stephen P. Glasser, Stanley M. Finkelstein and Jay N. Cohn

Hypertension. 1999;33:1392-1398
doi: 10.1161/01.HYP.33.6.1392

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/33/6/1392

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/