Effect of Age on Brachial Artery Wall Properties Differs From the Aorta and Is Gender Dependent
A Population Study

Janneke J. van der Heijden-Spek, Jan A. Staessen, Robert H. Fagard, Arnold P. Hoeks, Harry A. Struijker Boudier, Luc M. Van Bortel

Abstract—Compliance and distensibility are wall properties of large arteries, which may play a role in cardiovascular disease. The purpose of this study was to investigate whether the influence of age on these vessel wall properties differs between vascular territories and is gender-dependent. In a population sample of 498 men and women 20 to 79 years of age, diameter, distensibility, and compliance coefficient of the muscular brachial artery were measured with an echo-tracking device. Distensibility of the aorta was measured with the use of pulse-wave velocity. The effects of age and gender were assessed and adjusted for confounding factors such as mean blood pressure, pulse rate, body mass index, smoking, alcohol intake, and antihypertensive treatment. Covariance analysis showed no relation between gender and distensibility of the elastic aorta. Distensibility of the muscular brachial artery was lower in men, whereas men had a larger diameter and larger compliance of the brachial artery. With age, distensibility of the aorta decreased in both sexes to the same extent, whereas distensibility of the brachial artery did not change significantly. With age, brachial artery diameter increased; this increase was more pronounced in women. In men brachial artery compliance did not change with age, whereas in women compliance of the brachial artery increased with age. This study (1) confirms that distensibility of the aorta, an elastic artery, decreases with age. (2) In contrast to the aorta, after adjustment for confounding factors, in both men and women, no relation exists between age and distensibility of the muscular brachial artery. (3) Brachial artery diameter increase with age is more pronounced in women than in men. (4) In contrast to the well-known decrease in arterial compliance of elastic arteries with age, brachial artery compliance is not decreased with age and is increased in women. In conclusion, the effect of age on large-artery wall properties is not uniform but depends on gender and vascular territory. (Hypertension. 2000;35:637-642.)

Key Words: aorta • arteries • compliance • aging • gender

Compliance and distensibility are vessel wall properties of large arteries. Arterial compliance, defined as the absolute change in volume per unit of pressure ($\Delta V/\Delta P$), reflects the buffering capacity of an artery; a decrease in compliance increases cardiac afterload and the risk of cardiac hypertrophy. 1–3 Arterial distensibility, defined as the relative change in volume per unit of pressure ($[\Delta V/V]/\Delta P$), reflects mainly the elasticity of the wall and is considered a determinant of strain on the vessel wall. 4 A local decrease in distensibility might be associated with an increased risk of arterial wall damage, an important feature in atherosclerotic disease. 5 Preservation of distensibility might be important in protecting the arterial wall against damage at a particular site. 6

From 1880 on, several groups have investigated the effect of age on elastic properties of the arterial system. 7 The first studies were postmortem studies, 8–10 later followed by in vivo measurements of regional distensibility. 11,12 At the age of 20 years, the vascular system is considered to be mature, but it is unclear from which age distensibility starts to decrease. Several studies reported the influence of age on wall properties of elastic large arteries. It has been suggested that aortic distensibility reaches its peak at $\approx$10 years of age 11 and starts to decrease in the third age decade. 9,13 With advancing age, elastic arteries, like the aorta and common carotid artery, dilate, become stiffer, and show an increase in wall thickness. 8,11–18 The arterial tree, however, is composed not only of elastic arteries but also medium-sized muscular arteries such as the brachial artery. Whether the effect of age on arterial wall properties of these arteries is similar to the effect on elastic arteries is not known. In addition, no study investigated whether the effect of age is gender dependent. The aim of the present study was to investigate the effects of age and gender on wall properties of the medium-sized muscular brachial artery compared with the elastic aorta in a general population.
Methods
A random population sample was identified in a rural area of Belgium. The population sample was stratified by sex and age (20 to 39, 40 to 59, and 60 years) in an attempt to recruit the same number of subjects in each stratum. From population registers, a random sample of the households was drawn. All household members ≥20 years were eligible except if they were foreign nationals or if the quota of their age-sex stratum had been fulfilled. Of 974 subjects invited, 614 agreed to take part. Of these participants, 116 subjects were withdrawn because of technical and logistic problems. The number of subjects finally considered in the analysis totalled 250 men and 248 women.

All participants refrained from smoking and caffeine-containing beverages for ≥3 hours before being examined. First, the participants were seated and were asked to relax for 5 minutes. The same nurses who had previously visited the participants at home then measured consecutively (5 times) their sitting blood pressure conventionally, with a sphygmomanometer on the left side. Data of systolic blood pressure (SBP) and diastolic blood pressure (DBP) are the mean of 5 measurements. Mean blood pressure was calculated as (2SBP+DBP)/3. The nurses also interviewed the participants about their current health status, smoking (yes/no) and drinking habits (yes/no), and intake of drugs. After 15 minutes of supine rest in a quiet room, aortic and brachial artery wall properties were measured. Vessel wall properties of the aorta were measured with the use of pulse-wave velocity as described below. Vessel wall properties of the right brachial artery were measured with a vessel wall movement detector system. This device measures accurately diastolic diameter (D) and change in diameter during the heart cycle (ΔD). All measurements were made by the same observer. The mean of 3 consecutive measurements (∼15 heart beats) were taken as the patient’s reading.

Brachial artery compliance was expressed as compliance coefficient (CC) and was defined as the compliance per unit of pressure (ΔD). Likewise, brachial artery distensibility was expressed as distensibility coefficient (DC), defined as the relative change in cross-sectional area (ΔA/ΔD), per unit of pressure. Simultaneously with the vascular measurements, blood pressure was measured at the left arm with a semiautomated device (Dinamap). Pulse pressure was calculated as SBP−DBP, ΔP during the heart cycle equals pulse pressure.

From D, ΔD, and ΔP, brachial artery wall properties were calculated by use of the following equations:

\[
(1) \quad DC = \frac{\Delta A}{\Delta D} \Delta P = (2D^2 \Delta D + \Delta D^3) / (\Delta P^2 \Delta D)
\]

\[
(2) \quad CC = \frac{\Delta V}{\Delta P} = \frac{\Delta A}{\Delta D} \Delta P = \pi (2D^2 \Delta D + \Delta D^3) / 4 \Delta P
\]

V is arterial volume. This method has shown good reproducibility.

The vessel wall movement detector system also calculates the delay time from the ECG trigger (R-top) to the 10% level of the ascending limb of the distension waveform of the artery measured. The difference between the delay times to the femoral and carotid arteries was used as an estimate of the carotid-femoral transit time (T). The mean of 3 recordings was taken as the subject’s reading. The distances from the sternal notch to the site of measurement of the common carotid artery and femoral artery were measured with a tape measure. The difference between these 2 distances was used as an estimate of the length of the carotid-femoral segment (Lc-f) . The average pulse-wave velocity (PWV) in this segment was calculated as

\[
PWV = Lc-f / T
\]

which is an estimate of the stiffness of mainly the aortic pathway. PWV is related to aortic distensibility (DC) by the formula:

\[
PWV = \sqrt{1/\rho DC}
\]

where ρ=blood density (Moens Korteweg).

Database management and statistical analyses were performed with SAS software (SAS Institute Inc). The methods of analysis included Mann-Whitney U tests for continuous variables and χ² tests for the dichotomous parameters. To test the influence of gender, an ANCOVA was used with factors for mean arterial pressure (measured by sphygmomanometer), pulse rate, body mass index, smoking, use of alcohol, and antihypertensive treatment. Factors with a value of P>0.10 were dropped from the model. To get the relation between vessel wall properties and age, age was also added as a covariate. To investigate the difference of the age effect among the sexes, the interaction of age and sex was also tested. A value of P<0.05 was considered statistically significant.

The study was approved by the ethics committee of Leuven University, and all subjects gave their written informed consent.

Results
The subjects, 250 men and 248 women, were 50±13 years old, with a range from 26 to 82 years (Table 1). The distribution of age was similar among men and women: 6.0% were 20 through 29 years old, 16.1% 30 through 39, 31.5% 40 through 49, 23.1% 50 through 59, 16.3% 60 through 69, and 7.0% were ≥70 years. The conventionally measured SBP and DBP were slightly higher in men than in women. Current smoking was reported by 160 participants (median 15 cigarettes per day; range 1 to 70), and 113 subjects reported regular alcohol consumption (median 20 g per day; range 1 to 196). A total of 77 subjects were taking antihypertensive treatment either in monotherapy or in combination. Of these, 36.4% (8 men and 20 women) were taking diuretics, 57.1% (22 men and 22 women) were taking β-blockers, 7.8% (4 men and 2 women) were taking angiotensin-converting enzyme inhibitors, and 26.0% (13 men and 7 women) were taking calcium antagonists.

Differences in vessel wall properties between men and women are shown in Table 2. Because vessel wall properties can be influenced by confounders, which might differ between men and women, values were calculated and adjusted for confounders such as mean arterial pressure, pulse rate, body mass index, smoking, use of alcohol, and antihypertensive treatment. After adjustment, PWV of the aorta, a mea-

<table>
<thead>
<tr>
<th>TABLE 1. Characteristics of the Study Population</th>
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<tbody>
<tr>
<td>Item</td>
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<tr>
<td>Men</td>
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<td>-------</td>
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<tr>
<td>n</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Body height, cm</td>
</tr>
<tr>
<td>Body weight, kg</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
</tr>
<tr>
<td>Blood pressure, mm Hg*</td>
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<tr>
<td>Systolic</td>
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<tr>
<td>Mean</td>
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<tr>
<td>Diastolic</td>
</tr>
<tr>
<td>Heart rate, bpm</td>
</tr>
<tr>
<td>Smokers</td>
</tr>
<tr>
<td>Drinking alcohol</td>
</tr>
<tr>
<td>Antihypertensive treatment</td>
</tr>
<tr>
<td>Contraceptive pill</td>
</tr>
</tbody>
</table>

*Data are mean ± SD or number of subjects with percentage in parentheses.
†Percentage of women 20 to 55 years of age with oral contraception. Mean blood pressure=(2SBP+DBP)/3.
‡Statistical significance: P<0.01, §P<0.001.
sure of aortic distensibility, was not different between men and women. Distensibility of the brachial artery was larger in women \( (P, 0.001) \), but diameter and compliance of the brachial artery were smaller \( (P, 0.001) \) in women compared with men.

Descriptive analysis of the effect of age on vessel wall properties in men and women is shown in Figures 1 and 2. Figures 1a and 2a show mean±SEM values of the vessel wall properties for each 10-year age class before adjustment for confounders mentioned above. In a further step of the analysis, a linear as well as a curvilinear (ie, including both age and the quadratic term of age) model were fitted to the relations between age and large-artery wall properties for men and women separately. These analyses showed that a linear model (Table 3, unadjusted values) was sufficient to fit all age relations. All individual data were recalculated according to the adjusted linear regression model and are shown in Figures 1b and 2b.

PWV of the aorta increased with age to the same extent in both sexes. Although visual inspection of adjusted data suggests a more pronounced decrease in brachial artery distensibility in women than in men, the linear regression model could neither in men nor in women show a statistically significant change in brachial artery distensibility with age (men: \( P=0.76 \); women: \( P=0.61 \)) after adjustment for confounders (Table 3). Visual inspection of the relation between age and brachial artery diameter or compliance is in accordance with the linear regression model: After adjustment for confounders (Table 3) with advancing age, brachial artery diameter increased more in women \( (P=0.013) \) than in men. Brachial artery compliance increased in women \( (P=0.002) \), whereas it remained unchanged in men.

**Discussion**

The present study investigated whether the well-known decrease in aortic distensibility with age was also present in the muscular brachial artery and whether it was similar in men and women. Changes in vessel wall properties with age are not only the effect of aging but also can be the effect of other interrelating factors that change with age. From previous studies blood pressure, body mass index, and antihyperten-

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**TABLE 2. Vessel Wall Properties in a Random Population**

<table>
<thead>
<tr>
<th>Artery</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
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<tbody>
<tr>
<td></td>
<td>Men, n=250</td>
<td>Women, n=248</td>
</tr>
<tr>
<td>Aorta†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWV, m/s</td>
<td>7.0±1.9</td>
<td>6.7±2.1</td>
</tr>
<tr>
<td>Brachial artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter, mm</td>
<td>4.55±0.60</td>
<td>3.65±0.57</td>
</tr>
<tr>
<td>DC, $10^{-6}$kPa</td>
<td>20.9±9.9</td>
<td>24.4±12.0</td>
</tr>
<tr>
<td>CC, mm²/kPa</td>
<td>0.33±0.13</td>
<td>0.25±0.12</td>
</tr>
</tbody>
</table>

Results are mean±SD.

*Data adjusted for mean arterial pressure, pulse rate, body mass index, current smoking, current alcohol intake, and use of antihypertensive treatment.

†Measurements available in 242 men and 243 women.

Statistical significance: \( \dagger P<0.01 \), \( \ddagger P<0.001 \).
sive treatment have been identified as confounding factors. The effects of other factors, such as smoking and pulse rate, are not always clear. In the present study, to get the relation between vessel wall properties and age, values were adjusted for mean auscultatory blood pressure, pulse rate, antihypertensive treatment, body mass index, smoking, and use of alcohol for each gender.

Gender Differences in a Random Population

In this population sample, distensibility of the aorta did not differ between men and women. Kupari et al., who investigated men and women 36 and 37 years old, also reported a gender independence of the aortic stiffness. Laogun and Gosling, however, showed a higher aortic distensibility in women 15 to 45 years old compared with age-matched men. This contradictory result could be due to the use of a smaller study population in the latter study. In addition, in this study no corrections were made for confounders such as mean arterial pressure and body mass index, which are important determinants of large-artery properties and often differ between men and women. Also in the present study, the unadjusted data showed a higher aortic distensibility in women compared with men. However, after adjustment there was no difference. One reason could be a difference in smooth muscle tone and vessel wall structure (elastin/collagen) between men and women, possibly related to hormonal influences, for instance, effects of estrogen. Constitutional differences between men and women also might play a role. Diameter of the brachial artery was larger in men compared with women. Other authors also showed larger diameters of different arteries in men. Because the caliber of vessels is related to body size (height and weight) and the size of women is smaller than of men, this could explain the smaller vessel diameter in women. Because of the larger diameter in men, compliance of the brachial artery was higher in men than in women, despite the lower distensibility of the brachial artery.

Effect of Age and Gender

Distensibility of the aorta decreased with age in both sexes to the same extent. These results confirm earlier studies. Several studies showed that distensibility of another elastic artery, the carotid artery, also decreases with age. In contrast, the present study showed that distensibility of the muscular brachial artery was not related to age, as already observed by Kawasaki and coworkers. In addition, the present study showed that this was the case for both men and women.

The mechanism by which aging causes a decrease in distensibility of the aorta and common carotid artery is not fully clear. Several hypotheses have been proposed. First, the fatiguing effect of cyclic stress on the elastic fibers could play a role. Aging may lead to degeneration of the elastic fibers, with stretching and remodeling of the arterial wall resulting in a

**TABLE 3. Relation Between Vessel Wall Properties and Age**

<table>
<thead>
<tr>
<th>Artery</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men, Slope, (age) 1×10^{-3}</td>
<td>Women, Slope, (age) 1×10^{-3}</td>
</tr>
<tr>
<td>Aorta†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PWV, m/s</td>
<td>90.0±7.6¶</td>
<td>95.3±9.4¶</td>
</tr>
<tr>
<td>Brachial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter, mm</td>
<td>5.9±2.9§</td>
<td>19.8±2.6¶</td>
</tr>
<tr>
<td>DC, 10^{-3}/kPa</td>
<td>-90.4±48.3§</td>
<td>-188.1±60.6</td>
</tr>
<tr>
<td>CC, mm^2/kPa</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Regression coefficients ± SE. *Adjusted for mean arterial pressure, pulse rate, body mass index, current smoking, current alcohol intake, and use of antihypertensive treatment. †Measurements available in 242 men and 243 women. Statistical significance: ‡P<0.1, §P<0.05; ¶P<0.01; ‖P<0.001.
loss of elasticity and a parallel increase in collagen and mucopolysaccharides. This hypothesis is supported by the observation that the decrease in distensibility with age is proportional to the increase in collagen with age.34 Degeneration of elastin fibers also may explain arterial dilation with age. This dilation is greater in elastic than in muscular arteries, as would be predicted from theory. Second, with age, vascular smooth muscle cells accumulate in the arterial wall. Third, atherosclerosis could play a role.34,35 The exact relation between atherosclerosis and arterial wall stiffness is still unclear. Besides, it has been shown that in a population without atherosclerosis, compliance decreased with age.13 Fourth, early and advanced wave reflections, seen with increasing age, could boost pulse pressure and decrease distensibility.36

In the present population sample, the diameter of the brachial artery increased with age. The results concerning changes in diameter of the brachial artery with age are not consistent in the literature. Some authors have found an increase in diameter,14 whereas others have found no relation between age and arterial diameter.14 There also appears to be a gender difference: in the present study the increase in diameter of the muscular brachial artery was more pronounced in women than in men.

Compliance of the brachial artery was not related to age in men. Surprisingly, compliance of the brachial artery increased with age. This increase was statistically significant in women but not in men. The increase in compliance of the brachial artery is caused by a larger diameter, without a statistical change in distensibility. The increase in arterial diameter with age is also found in other arteries.16–18 It has been suggested that the larger diameter with age is due to loss of elastic fibers in the arterial wall. Because brachial artery elasticity (reflected by distensibility) appears to be not significantly changed with age, an alternative explanation could be an adaptive remodeling of the brachial artery. If this latter hypothesis is true, then this adaptive remodeling of the brachial artery with age may be more pronounced in women than in men.

In conclusion, this study confirms that distensibility of the aorta, an elastic artery, decreases with age. This study shows that (1) in contrast to the aorta, after adjustment for confounding factors, in both men and women no relation exists between age and distensibility of the muscular brachial artery. (2) Brachial artery diameter increase with age is more pronounced in women than in men. (3) In contrast to the well-known decrease in arterial compliance of elastic arteries with age, brachial artery compliance is not decreased with age but even increased in women. (4) The effect of age on large-artery wall properties is not uniform but depends on gender and vascular territory.

Acknowledgments
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References


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