Arterial properties along the upper arm in humans: age-related effects and the consequence of anatomical location

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Submitted 5 May 2009; accepted in final form 26 October 2009

Bjarnegård N, Länne T. Arterial properties along the upper arm in humans: age-related effects and the consequence of anatomical location. J Appl Physiol 108: 34–38, 2010. First published October 29, 2009; doi:10.1152/japplphysiol.00479.2009.—The normal aging process of the brachial artery (BA) wall is of specific interest since it is often selected as a model artery in studies of vascular function. With echo-tracking ultrasound, diameter, absolute diameter change, and intima-media thickness (IMT) were registered in 60 healthy subjects, 21–86 yr (30 men), at a proximal, upper third, and distal arterial site along the upper arm. Blood pressure was recorded noninvasively, and the distensibility coefficient (DC) was calculated. The diameter at the proximal site increased with age from 5.5 ± 0.2 mm in the young subjects to 6.9 ± 0.3 mm (P < 0.01) in the elderly subjects, concomitantly as IMT increased from 0.40 ± 0.01 to 0.65 ± 0.03 mm (P < 0.001). The diameter at the other sites was similar in the young and elderly subjects, whereas IMT increased slightly with age. At the proximal site, DC decreased dramatically from 40.7 ± 2.2 to 10.1 ± 0.8 10^{-3} kPa (P < 0.001) with age, whereas hardly no change was seen in the distal upper arm. The principal transit zone between elastic to predominantly muscular artery behavior seems to be located within the proximal part of the brachial artery, emphasizing the importance of carefully defining the arterial examination site.

distensibility; echo-tracking; intima-media thickness; upper arm

Materials and Methods

THE BUFFERING FUNCTION of large arteries dampens the intermittent ventricular ejections to a more continuous peripheral blood flow, which improves organ perfusion and reduces left ventricular afterload (19, 31). A diminished aortic distensibility has been shown to be an independent risk factor for cardiovascular mortality in several population studies (8, 27, 41). With aging, diameter and wall thickness of elastic arteries increases simultaneously as their distensibility decreases (2, 29, 39). The peripheral muscular arteries seem to be less affected by aging, even if regional differences seem to exist (14, 37).

The brachial artery is of specific interest since it is often used as a demonstrator of vascular function in humans, e.g., in studies of vascular reactivity since endothelial dysfunction is considered to be a key factor in development of atherogenesis (9). It has lately been suggested that local vessel wall properties may affect the response to flow-mediated dilation, an indirect measure of endothelial function (42). Earlier studies on wall properties in the brachial artery have shown conflicting results. We have previously reported a markedly age-related decrease of local arterial distensibility as opposed to others who have found no distinct effect of age on wall mechanics (6, 40). One reason for the diverging results could be the fact that the transition zone between elastic and muscular behavior is within the length of the artery, since a proximal site was selected by Bjarnegård et al. (6), whereas Van der Heijden-Spek et al. (40) scanned the distal part of the upper arm. The aims of the study were 1) to define the arterial wall properties at three anatomically defined sites along the upper arm and 2) to evaluate whether the relation between wall properties and age differs at those sites.

Materials and Methods

Subjects. Eighty healthy, nonsmoking volunteers were examined. In 15 of these, complete data could not be collected from all three examination sites. In addition, three subjects were excluded due to blood pressure of >160/90, and two were excluded because of a capillary plasma glucose of >10 mM. Thus 60 subjects between 21 and 86 yr (30 men) were included. The subjects were divided into three age-categories: young (Y), middle aged (M), and elderly (E) (Table 1). None had a history of diabetes or symptomatic cardiovascular or renal disease, and all were free from cardiovascular medication, and their systolic arm-arm blood pressure difference was <15 mmHg. All subjects gave informed consent to participate in the study, which was approved by the ethics committee of Linköping University Hospital, Sweden.

Measurement of arterial diameter change and intima-media thickness. An ultrasound system (Esaote AU5, Esaote Biomedica, Florence, Italy) equipped with a 7.5-MHz linear array transducer is used for real-time imaging of the vessel. The system is connected to a PC, where the Wall Track System software (WTS2, Pie Medical, Maastricht, The Netherlands) is installed. Details of the technique have been described previously (22, 25). In short, ECG leads are connected to the subject. After visualisation of the artery in a longitudinal section, the scanner is switched to M-mode, and the M-mode line is positioned perpendicular to the anterior and posterior wall. A window of sufficient width to include the envelope from both anterior and posterior wall is chosen, and the radio frequency (RF) signal is transferred to the PC, where it is stored. Automatically, a sample volume is positioned on the media-adventitia transition of the anterior and posterior wall. This automatic detection rarely fails as long as the RF signal amplitude representing the arterial wall is distinctly higher than surrounding signals. Only if the software repeatedly fails to correctly identify the arterial wall, manual adjustment of the sample volume is made before arterial distension waveforms are finally calculated, and the average data is presented on the screen. For intima-media calculation, RF data focusing on the far vessel wall is stored. The averaged envelope for each heart beat is later processed offline, and the mean far wall intima-media thickness (IMT) is presented after automatic calculation.

Study protocol. All subjects refrained from drinking beverages containing caffeine 3 h before the examination, which was performed in supine position in a silent room with temperature of 22–24°C. After 10 min of supine rest, oscillometric upper arm blood pressure (Dinamap PRO 200 Monitor, Critikon, Tampa, FL) was registered bilaterally, and capillary p-glucose was checked. The ultrasound transducer was positioned at three defined sites along the left arm (Fig. 1), where measurements of the arterial distension waveform as well as IMT were repeated at least three times during 4-s-long sequences in the following order: 1) distal axillary artery (AXA),...
LOCAL BRACHIAL ARTERY WALL PROPERTIES

Table 1. Demographics and clinical data of the healthy subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Y (n = 20)</th>
<th>M (n = 20)</th>
<th>E (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men/women</td>
<td>10/10</td>
<td>10/10</td>
<td>10/10</td>
</tr>
<tr>
<td>Age, yr</td>
<td>29 ± 1</td>
<td>49 ± 1</td>
<td>76 ± 1</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>23.6 ± 0.5</td>
<td>25.0 ± 0.5</td>
<td>23.6 ± 0.7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>71 ± 2</td>
<td>76 ± 2</td>
<td>69 ± 3</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.73 ± 0.02</td>
<td>1.75 ± 0.02</td>
<td>1.70 ± 0.02</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>61 ± 2</td>
<td>59 ± 2</td>
<td>63 ± 3</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>112 ± 3</td>
<td>120 ± 3</td>
<td>124 ± 3</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>61 ± 2</td>
<td>71 ± 2</td>
<td>64 ± 2</td>
</tr>
<tr>
<td>Pulse pressure, mmHg</td>
<td>51 ± 2</td>
<td>49 ± 2</td>
<td>59 ± 3</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg</td>
<td>78 ± 2</td>
<td>88 ± 2</td>
<td>84 ± 2</td>
</tr>
</tbody>
</table>

All data, except frequencies, are means ± SE. BP, blood pressure; Y, young subjects (<40 yr old); M, middle-aged subjects (40–59 yr old); E, elderly subjects (>60 yr old).

DC was used to approximate local pulse wave velocity (PWV), since the speed of the pulse wave is related to arterial wall distensibility as expressed in the Moens-Korteweg equation (31).

\[ PWV = \frac{1}{\sqrt{DCP}} \]

where the unit for PWV is m/s and DC is expressed in kPa. Density (p) of blood is assumed to be 1.060 kg/m³.

In the absence of wave reflections, characteristic impedance (Z₀) represents the ratio of change in pressure to change in flow in an artery (31).

\[ Z_0 = \frac{\rho PWV}{A} \]

where the unit for Z₀ is dyne s/m³ and A is the local cross-sectional area in m².

Statistical analysis. Version 15 of the SPSS statistical package was used. For continuous variables, the differences between groups were tested with unpaired Student’s t-test, analysis of covariance (ANCOVA), or ANOVA, followed by post hoc test according to Scheffe. The association between different continuous variables was evaluated by Pearson’s product-moment correlation, whereas multiple linear stepwise regression models were built to test how individual independent variables influenced the dependent variable. For unevenly distributed variables, log transformation of the data was performed before the test. Values are expressed as means ± SE, except as noted. P < 0.05 was considered significant.

RESULTS

Table 2 shows the local wall properties along the upper arm in the healthy subjects. Since only arterial diameter and CC differed when genders were compared, the relation between arterial parameters and age were analyzed with men and women compiled into three age categories.

DC at AXA decreased markedly from 40.7 ± 2.2 in the young to 10.1 ± 0.8 10⁻³ kPa in the elderly (P < 0.001). DC was similar at BAprix and BADist in middle-aged and elderly subjects but slightly higher in the young than in the elderly at BAprix (P < 0.05) and BADist (P < 0.01). The difference between young and elderly decreased and was no longer

Fig. 1. Left: distensibility coefficient (DC) in the young (Y; ●), middle-aged (M; ○), and elderly subjects (E; ▲). DC decreases markedly between site 1 and 2 in Y and M (P < 0.001), i.e., in subjects <60 yr old. An additional drop in DC was seen from site 2 to 3 in all age categories (P < 0.01). Symbols are means ± SE. Right: the three examination sites along the upper arm. 1(AXA), 5–15 mm proximally from the origin of the subscapular artery; 2(BAprix), 5–15 mm distal to the origin of deep brachial artery; 3(BADist), 0–50 mm proximal to antecubital crease.
Aging exerts a marked effect on the cardiovascular system in many ways. Nevertheless, it can be difficult to separate the effect of true normal vascular aging from disease-related changes in Western populations. Cross-sectional studies have shown an age-related increase in arterial diameter, length, and wall thickness. This pattern has been most clearly demonstrated in elastic arteries and peripheral arteries within the lower extremities (2, 14, 31, 36, 37, 39). In elastic arteries, elastin becomes fragmented and degraded because of repeated mechanical loading and oxidative stress and, therefore, is replaced by much stiffer collagen with age, giving rise to decreasing wall distensibility (31). In addition, chemical degradation and calcification may stiffen elastic tissue. Increased metalloproteinases activity and formation of advanced glycation end (AGE)-products are factors that have been suggested to further decrease elastin content and cause cross-links between collagen molecules within the matrix (1, 43). As a significant at BAdist after adjustment for mean arterial pressure (MAP) and body mass index (BMI).

Figure 1 shows DC along the upper arm (left) at the three examination sites (right). DC dropped from AXA to BAdist and further to BAdist in the young and middle-aged subjects, whereas in the elderly subjects DC were similar at AXA and BAdist but dropped from 9.0 ± 0.8 to 5.7 ± 0.4 \(10^{-3}/\text{kPa} \) (\(P < 0.01\)) between BAdist and BAdist.

At all sites, CC was higher in the men, AXA (\(P < 0.01\)), BAdist, and BAdist (\(P < 0.001\)) compared with the women. After adjustment for the larger body size in the men, the gender difference remained significant only at BAdist (\(P < 0.01\)) (Table 3). CC decreased at AXA from 0.97 ± 0.08 in the young to 0.38 ± 0.05 mm²/kPa in the elderly (\(P < 0.001\)). No significant age-related drop in CC was seen in the BA. CC decreased in all three age categories when moving distally along the upper arm, from AXA to BAdist (\(P < 0.001\)), and further from BAdist to BAdist (\(P < 0.01\)) (Table 2).

Arterial diameter was higher in the men than in the women. The average difference was 30% at AXA and BAdist and 23% at BAdist (\(P < 0.001\) for all sites). The diameter was still higher in men after adjustment for body surface area (Table 3). The diameter of AXA increased with age from 5.5 ± 0.2 mm in the young to 6.9 ± 0.3 mm in the elderly (\(P < 0.01\)), concomitantly as IMT increased from 0.40 ± 0.01 to 0.65 ± 0.03 mm (\(P < 0.001\)). In BA, similar diameter of BAdist and BAdist were seen in all age categories, whereas IMT was higher in the elderly than in the young, both at proximally 0.46 ± 0.03 vs. 0.36 ± 0.005 mm (\(P < 0.001\)), and distally 0.43 ± 0.01 vs. 0.36 ± 0.003 mm (\(P < 0.001\)). Both diameter and IMT decreased when moving distally between AXA and BAdist, regardless of age (\(P < 0.001\)). In contrast, no further change was found between BAdist and BAdist.

A negative association between DC and IMT was seen at the level of AXA (\(r = -0.67; P < 0.001\)) but not within BA. In a multiple regression model, age, MAP, BMI, and IMT were included to evaluate their potential influence on AXA DC. DC was mainly influenced by age (\(\beta = -0.61; R^2 = 0.80; P < 0.001\)) and MAP (\(\beta = -0.35; R^2 = 0.05; P < 0.001\)), whereas IMT and BMI were excluded. Within BA, MAP (\(\beta = -0.02; R^2 = 0.21; P < 0.001\)) influenced DC proximally, whereas age was the only variable of significant importance for DC distally (\(\beta = -0.04; R^2 = 0.17; P < 0.01\)).
consequence of the age-related decrease in arterial distensibility, systolic pressure increases, causing a rise in pulse pressure, which is the most important blood pressure parameter for prediction of cardiovascular events in elderly subjects (16). The augmented late systolic aortic pressure may enhance the effect of the normal age process that changes the passive diastolic properties of the left ventricle and predisposes one to left ventricular hypertrophy and interstitial fibrosis. Moreover, it may contribute to the increased incidence of diastolic dysfunction seen even in the absence of left ventricular hypertrophy in the elderly (1). With a variety of techniques, it has been demonstrated that the aortic wall stiffens in a linear or, in elderly, even an accelerated manner with age (29, 36, 39).

In contrast to the marked age-related decrease of distensibility that is seen in elastic arteries, muscular arteries are much less affected. PWV along the extremities increases only slightly with age in most population studies (31), and most studies on local peripheral artery distensibility have shown no effect of age (37, 40). As a consequence of the altered arterial properties, pulse pressure amplification decreases, whereas augmentation index increases in response to aging. Interestingly, central augmentation index seems to reach a plateau at ~60 yr of age without increasing further in elderly subjects (28, 29), suggesting that increases in central arterial stiffness and forward wave amplitude, rather than reflected wave amplitude, cause the increasing systolic pressure and pulse pressure seen at higher age.

The arteries along the arm are rarely affected by atherosclerosis or aneurysm formation in contrast to the lower extremities, making the muscular brachial artery suitable as a model in experimental studies of vascular reactivity. Several vasoregulatory substances are synthesized by the endothelium, among them NO, with ability to regulate lumen diameter of muscular arteries and arterioles. Impairment of endothelium-dependent, NO-mediated vasodilatation is an early marker of endothelial dysfunction that accompanies atherosclerosis (9). Administration of an exogenous NO donor, such as nitroglycerin, increases arterial lumen, tenses the parallel collagen and elastin fibers concomitantly as the reduced tension in smooth muscle has the opposite effect on distensibility (3, 4). Thus basal endogenous NO production might be of importance in the regulation of arterial distensibility in humans (38).

Sympathetic nerve activity seems to modulate mechanical wall properties of muscular arteries, although the net effect alteration of smooth muscle tone has on arterial distensibility differs between earlier studies, showing either increased (5), unchanged (5a), or decreased (33) distensibility in response to smooth muscle relaxation. A reduction of sympathetic discharge by brachial plexus anesthesia increases distensibility (18), whereas sympathetic stimulation by cold pressor test, mental stress, or smoking reduces wall distensibility (13, 17, 26). An age-related increase in sympathetic discharge could be a factor of importance for the age-related decrease in distensibility seen in the proximal part of the upper arm (Fig. 1) (15, 30). However, this effect seems small since earlier findings in our laboratory show no effect of sympathetic stimulation on proximal BA wall mechanics (7).

Earlier studies on carotid-radial pulse-wave velocity or local radial artery distensibility implicate that aging has no or only minor influence (10, 12, 31). Studies on wall properties in the brachial artery on the other hand have shown conflicting results. We have reported an age-related exponential decrease of local arterial distensibility as opposed to others who have found no distinct effect of age on wall mechanics (6, 40). One reason for the diverging results could be the fact that the transition zone between elastic and muscular behavior is within the length of the artery, since the reported sites for investigation were the proximal and distal part of the upper arm (6, 40). This is supported by our findings that showed a marked age-related effect on the mechanical properties in the proximal part of the upper arm, whereas hardly any effect was seen in the distal part (Fig. 1). Furthermore, the data in the most proximal part are closely related to the behavior seen in the adjacent elastic carotid artery (21, 32). Wall thickness might also influence wall mechanics, although data from the carotid artery, an area more susceptible to atherosclerosis than the upper arm, suggest that IMT must exceed a threshold thickness that represents an atherosclerotic manifestation before distensibility is affected (11, 20, 34). In the present study, the IMT variations did not restrict wall distensibility at any of the three examination sites (data not shown), in agreement with findings at other arterial locations (24, 35).

It seems likely that the age-related structural remodeling that predominantly affects elastic arteries with increasing collagen-to-elastin ratio and the fatigue due to cyclic stress explains the equalization of distensibility seen in elderly subjects between proximal and distal sites along the upper arm (23, 31). Since local vessel wall properties may affect the response to flow-mediated dilation, it seems to be of considerable interest in studies of endothelial function to be aware of the local wall behavior as well as the anatomical transit zone between elastic and muscular artery wall behavior (42).

Correct measurement of the local blood pressure is crucial for accurate calculation of the local vessel wall distensibility. Invasive pressure is gold standard, whereas applanation tonometry is a noninvasive option at locations where the pulse can be reached from the body surface, which unfortunately excludes the use of tonometry in the present study. It is likely that upper arm cuff pressure slightly overestimates systolic axillary artery pressure due to pressure amplification along the arterial tree (31), resulting in a minor underestimation of the true drop in DC/increase in PWV along the upper arm, at least in young subjects.

In summary, this study shows that the aging process affects arterial wall mechanics in a differential manner along the upper arm. Proximally distensibility decreases markedly concomitantly as diameter and wall thickness increase, whereas only a modest age-related change is seen distally. Thus the principal transit zone between elastic and muscular behavior seems to be located in the proximal part of the upper arm, which emphasizes the importance to select the distal arterial segment of the brachial artery when vascular reactivity and endothelial function are studied.

**GRANTS**

This study was supported by Futurum—the Academy of Health Care, Jönköping County Council, the funds of Linköping University Hospital, the Swedish Research Council (no. 12161), and the Swedish Heart-Lung Foundation.
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