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*Angiology* 2008; 59; 290 originally published online Apr 2, 2008;
DOI: 10.1177/0003319707305692

The online version of this article can be found at:
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Published by:
SAGE Publications
http://www.sagepublications.com

Angiology
Volume 59 Number 3
June/July 2008 290-295
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10.1177/0003319707305692
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# Age and Blood Pressure Levels Modify the Functional Properties of Central but Not Peripheral Arteries

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The effect of age and blood pressure on the carotid and the radial artery distensibilities was investigated. Patients referred to the outpatient clinic of the Department of Internal Medicine and Geriatric Medicine were asked to participate in the study. The carotid and radial artery distensibility coefficients were measured. Linear regression analyses were performed to investigate the associations between determinants and arterial distensibility. The mean age of the participants was 72.3 years, and 41.5% were men. Carotid distensibility decreased with age in adjusted models ($\beta = -0.317$; 95% confidence interval [CI], −0.241, −0.055), whereas the radial distensibility did not decrease. Levels of systolic blood pressure and mean arterial pressure were associated with decreasing levels of carotid distensibility, whereas the diastolic blood pressure and pulse pressure were not associated ($\beta = -0.571$; 95% CI, −0.404, −0.007; $\beta = -0.410$; 95% CI, −0.308, −0.101, respectively). In conclusion, age and blood pressure levels are associated with the distensibility of the central arteries but not with that of the peripheral arteries.

**Keywords:** arterial distensibility; carotid artery; radial artery; aging; blood pressure

Aging affects the complex interaction between stable and dynamic changes involving structural and cellular elements of the vessel wall.[1] With increasing age, elastin, which is stretchable[2] and important for pulsatile properties, becomes thinner and fractured, whereas the amount of collagen, which in contrast to elastin can resist stress, increases. Changes in these components will result in increased arterial stiffness.[3-5] In addition to age, cardiovascular risk factors such as hypertension, and diabetes mellitus may accelerate the arterial stiffening, which has been found to be associated with cardiovascular morbidity and mortality in patients with hypertension,[6-8] end-stage renal failure,[9] and the age.[10-12] Previous studies have shown that age-related arterial changes may differ in different vascular regions[13,14]; centrally, predominantly elastic arteries stiffen progressively with age, whereas peripherally, predominantly muscular arteries may stiffen, albeit much less progressively.[13,15,16] The aim of the present study was to investigate the effect of aging and blood pressure levels on the carotid and the radial arterial distensibilities.

## Methods

### Study Population

Consecutive patients referred to the outpatient clinic of the Department of Internal Medicine and Geriatric Medicine, Erasmus Medical Center, between April and July 2006 were asked to participate in the study. Patients with a cardiovascular event within 6 weeks before the visit were excluded from the study. Informed consent was obtained.

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### Cardiovascular Risk Factors

Information on previous cardiovascular disease, smoking habits, and drug use was obtained by interview. Patients were classified as ever-smokers (current or past smokers) or never-smokers. Patients' height and weight were measured, and body mass index (BMI; weight [kg]/height$^2$ [m]) was calculated. Diabetes mellitus was defined as the use of blood glucose–lowering medication or a fasting serum glucose level equal to or greater than 7.0 mmol/L.[17]

### Blood Pressure Measurements

Blood pressure and heart rate were measured twice on the right arm using an automatic device (Accutorr Plus; Datascope Corporation, Mahwah, New Jersey.). The measurements were obtained after at least 5 minutes of rest with the patient in the supine position. The pulse pressure (PP) was calculated as systolic blood pressure (SBP) – diastolic blood pressure (DBP). The mean arterial pressure (MAP) was calculated as DBP + 1/3 PP. The average of the 2 measurements was used in the analysis. Hypertension was defined as a blood pressure level ≥140/90 mm Hg or the use of antihypertensive medication.

### Arterial Distensibility Measurements

After at least 5 minutes of rest with the patient in the supine position, arterial measurements were performed by Wall Track System 2 (Pie Medical, Maastricht, the Netherlands), using a B-mode ultrasound to identify the right common carotid artery at 1 to 2 cm proximal to the origin of the bulb. The right radial artery was investigated at the antecubital crease. The end-diastolic diameter ($D$), the absolute stroke change in diameter during systole ($\Delta D$), and the relative stroke change in diameter ($\Delta D/D$) were computed as the mean of values measured in 4 seconds of 3 successive recordings. The distensibility coefficient (DC) was calculated by the following equation: $2(\Delta D/D)/PP$ ($10\ MPa^{-1}$).[18] The means of diameter and distension of 3 successive recordings were taken as the subject's readings.

### Statistical Analyses

Mean values with standard deviation and percentages were calculated for continuous and categorical variables, respectively. Univariate linear regressions were performed to investigate whether age, blood pressure levels, and cardiovascular risk factors were associated with the carotid and the radial arterial distensibilities. In these analyses, the carotid and radial DCs were the dependent variables. Multivariate analyses were adjusted for age, sex, MAP, and heart rate. Additional adjustment was made for BMI, smoking, diabetes mellitus, and the use of antihypertensive drugs. Analyses stratified for age to investigate whether the association between age and DC was constant over time in different age groups were performed. All statistical analyses were performed using the statistical package SPSS 10.1 for Windows XP (SPSS Inc, Chicago, Illinois). Statistical significance is assumed at $P < .05$.

**Table 1.** Characteristics of the Study Participants

| | Participants (n = 82) |
|---|---|
| Age, y | 72.3 ± 12.7 |
| Men, % | 41.5 |
| BMI, kg/m$^2$ | 25.9 ± 5.2 |
| SBP, mm Hg | 129.4 ± 16.6 |
| DBP, mm Hg | 70.8 ± 9.5 |
| MAP, mm Hg | 93.6 ± 11.9 |
| PP, mm Hg | 58.6 ± 12.0 |
| Heart rate, bpm | 65.3 ± 11.3 |
| Smokers, % | 57.3 |
| Hypertension, % | 56.1 |
| Diabetes mellitus, % | 9.8 |

NOTES: BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; PP = pulse pressure; bpm = beats per minute.

**Table 2.** Univariate Linear Regression β-Coefficients (95% CI) Describing the Association of Various Variables With the Carotid Distensibility Coefficient

| | β | 95% CI | *P* Value |
|---|---|---|---|
| Age, y | −0.383 | −0.276, −0.082 | <.0001 |
| Men, % | 0.038 | −2.262, 3.191 | .735 |
| BMI, kg/m$^2$ | −0.013 | −0.268, 0.239 | .910 |
| SBP, mm Hg | −0.456 | −0.237, −0.092 | <.0001 |
| DBP, mm Hg | −0.354 | −0.355, 0.090 | .001 |
| MAP, mm Hg | −0.415 | −0.310, −0.105 | <.0001 |
| PP, mm Hg | −0.350 | −0.279, −0.069 | .001 |
| Heart rate, bpm | −0.146 | −0.200, 0.042 | .196 |
| Smokers | −0.156 | −4.547, 0.801 | .167 |
| Hypertension | −0.070 | −3.546, 1.856 | .535 |
| Diabetes mellitus | 0.191 | −0.604, 8.186 | .090 |

NOTES: BMI = body mass index; CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; PP = pulse pressure; bpm = beats per minute.

## Results

Baseline characteristics of the study population are presented in Table 1; the mean age of the 82

**Table 3.** Multivariate Linear Regression β-Coefficients (95% CI) Describing the Association of Various Variables With the Carotid Distensibility Coefficient

| | Model 1[a] | | | Model 2[b] | | |
|---|---|---|---|---|---|---|
| | β | 95% CI | $R^2$ | β | 95% CI | $R^2$ |
| Age, y | –0.317 | –0.241, –0.055 | 0.28 | –0.314 | –0.242, –0.046 | 0.32 |
| SBP, mm Hg | –0.571 | –0.404, –0.007 | 0.23 | –0.279 | –0.301, –0.102 | 0.33 |
| DBP, mm Hg | 0.116 | –0.208, 0.354 | 0.19 | –0.005 | –0.273, 0.268 | 0.32 |
| MAP, mm Hg | –0.410 | –0.308, –0.101 | 0.19 | –0.384 | –0.292, –0.086 | 0.32 |
| PP, mm Hg | –0.202 | –0.229, 0.028 | 0.21 | –0.080 | –0.168, 0.089 | 0.33 |

NOTES: BMI = body mass index; CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; PP = pulse pressure.
[a]Model 1, adjusted for sex, heart rate, and MAP.
[b]Model 2, model 1 + age, BMI, smoking, diabetes mellitus, and the use of antihypertensives.

**Table 4.** Univariate Linear Regression β-Coefficients (95% CI) Describing the Association of Various Variables With the Radial Distensibility Coefficient

| | Model 1[a] | |
|---|---|---|
| | β | 95% CI |
| Age, y | –0.071 | –0.118, 0.061 |
| SBP, mm Hg | –0.057 | –0.086, 0.051 |
| DBP, mm Hg | –0.010 | –0.126, 0.115 |
| MAP, mm Hg | –0.038 | –0.112, 0.079 |
| PP, mm Hg | –0.070 | –0.125, 0.065 |

NOTES: CI = confidence interval; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP = mean arterial pressure; PP = pulse pressure.
[a]Model unadjusted.

participants was 72.3 years, and 41.5% were men. The carotid distensibility decreased significantly with age in models adjusted for sex, heart rate, and MAP (β = –0.317; 95% confidence interval [CI], –0.241, –0.055; Tables 2 and 3, Figure 1A). After adjustment for BMI, smoking, diabetes mellitus, and the use of antihypertensive drugs, estimates only slightly changed. Increasing levels of SBP and MAP were associated with the carotid distensibility (β = –0.571; 95% CI, –0.404, –0.007; β = –0.410; 95% CI, –0.308, –0.101, respectively; Table 3, Figure 1B and D). Diastolic blood pressure and PP were not associated with the carotid distensibility in adjusted models. There were no associations found between age and blood pressure levels and the radial distensibility (Table 4). Age, sex, and MAP were important determinants of arterial stiffness, explaining 27.8% of variance in carotid distensibility.

In analyses stratified for age, the mean age in quartiles was 53.2, 70.5, 78.2, and 84.9, respectively. In adjusted models, the DC of the carotid artery decreased with age through quartiles (β = –0.703; 95% CI, –0.860, –0.145; β = –0.546; 95% CI, –2.703, 0.243; β = –0.538; 95% CI, –2.333, –0.514; β = –0.173; 95% CI, –0.968, 0.400, respectively).

## Discussion

In the present study performed in patients referred to the outpatient clinic of Department of Internal and Geriatric Medicine, carotid distensibility decreased with age, whereas the radial distensibility did not decrease. Similarly, the SBP, MAP, and PP were inversely associated with carotid distensibility.

Several studies have described arterial changes associated with aging. A study in 39 subjects aged 6 to 81 years showed an increase in stiffness of the common carotid artery, abdominal aorta, femoral artery, and radial artery with age.[19] The association was only significant for the aortic and the carotid arteries. Another study performed in 149 patients referred to an outpatient clinic of internal medicine found that carotid intima-media thickness increased and carotid distensibility declined with age.[13] The radial intima-media thickness was also increased with age, but no associations were found with the radial distensibility. These investigators also found an association between diameter and aging, but no data were reported on blood pressure levels and arterial distensibility.

In the present study, the carotid distensibility decreased with increasing levels of SBP, MAP, and PP. The PP presented the strongest association with carotid distensibility, being itself an expression of increased arterial stiffness and considered a clinical surrogate. Age-related vascular changes involve structural and functional changes. This tissue fatigue consists of thinning and fracturing of elastin, an increased

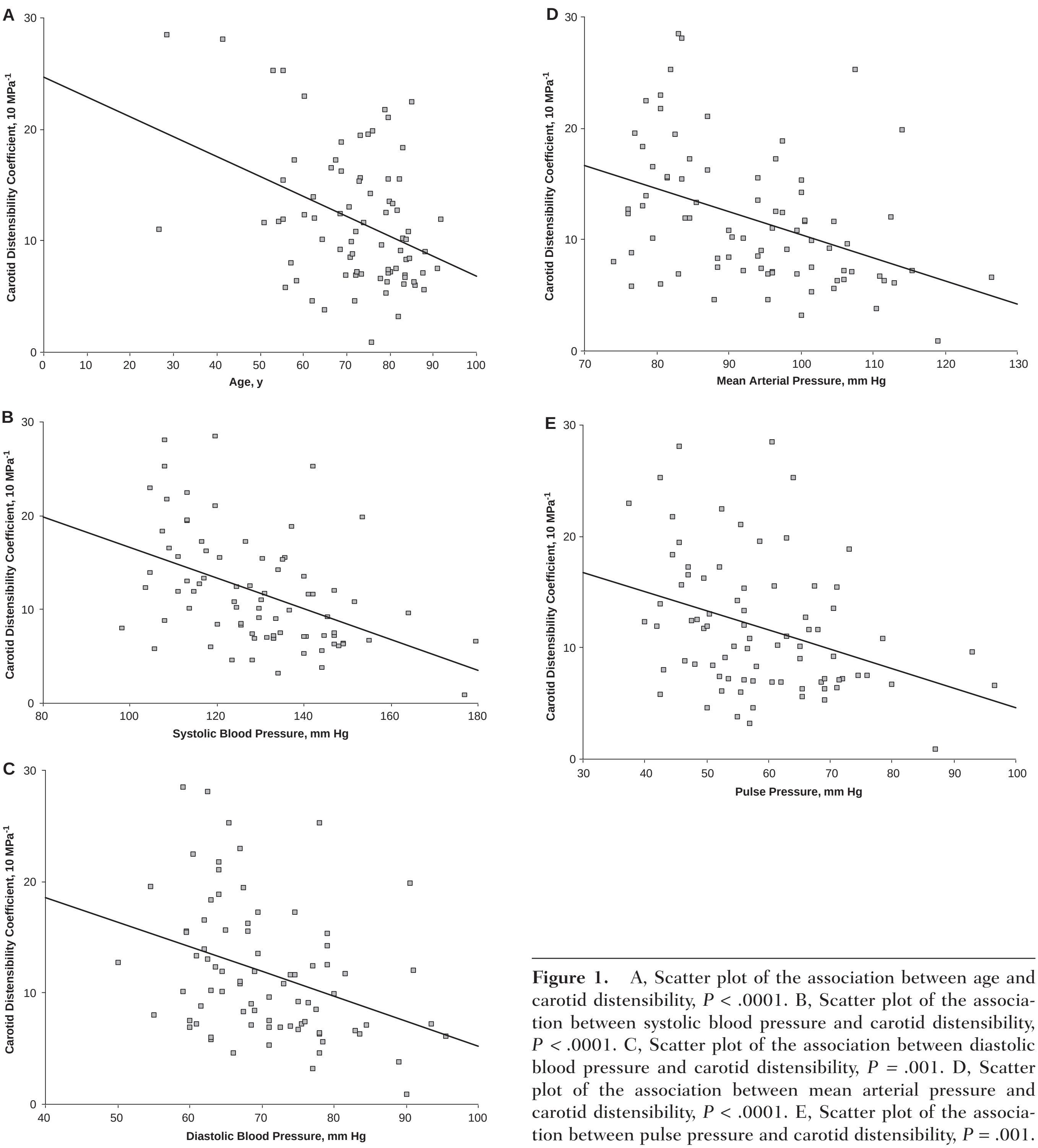


**Figure 1.** A, Scatter plot of the association between age and carotid distensibility, $P < .0001$. B, Scatter plot of the association between systolic blood pressure and carotid distensibility, $P < .0001$. C, Scatter plot of the association between diastolic blood pressure and carotid distensibility, $P = .001$. D, Scatter plot of the association between mean arterial pressure and carotid distensibility, $P < .0001$. E, Scatter plot of the association between pulse pressure and carotid distensibility, $P = .001$.

collagen deposition in the tunica media, and an increase in arterial diameter, resulting in alterations in the buffering capability of the large arteries. Normally, the balance between elastin and collagen is regulated by a slow dynamic process of production and degradation. Because of an inflammatory environment, overproduction of collagen and diminishing of elastin take place.[1] Arterial stiffening due to aging is amplified by the presence of hypertension and diabetes mellitus.[1] These age-related vascular changes seem to be nonuniform throughout the arterial tree, with more marked alterations in the elastic arteries than in the muscular arteries.[13,16,20,21]

We found an association between different age groups and carotid DC; however, the effect of age on the DC was no more significant in subjects in the last quartile of age. It has been speculated that a higher comorbidity at older age might decrease this association, but because we adjusted our models for comorbidity, this hypothesis seems to be unlikely. A minimal elasticity could be required for a normal blood circulation, indicating that distensibility should remain above zero. This could explain a decrease in association. With aging, the peripheral resistance increases moderately, and a tendency to increasing SBP and PP becomes apparent. Because higher blood pressure levels induce hypertrophy of the vessel wall, a vicious circle is established.[20] A high peripheral resistance induces an increase in SBP and DBP, whereas central stiffness tends to increase SBP but to decrease DBP. In young people, blood pressure is mainly determined by peripheral resistance, whereas in the elderly people, central stiffness is the most important determinant.[22] Hypertension induces structural arterial changes, such as vessel wall remodeling and changes in extracellular matrix.[23] Especially, the central elastic arteries are prone to these structural changes, whereas distal muscular arteries seem to be less sensitive.[13,24] This heterogeneity may explain our findings.

The present study has some limitations. First, the cross-sectional design may limit our ability to infer a causal relationship between age, blood pressure levels, and measures of arterial distensibility. Second, a relatively small number of patients were included in the study; therefore, the generalizability of our findings may be difficult.

In conclusion, in a group of consecutive patients, we found that age and blood pressure levels influenced the functional properties of the elastic central arteries but not the muscular peripheral arteries.

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