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Retinal Arteriolar Diameters and Elevated Blood Pressure

The Atherosclerosis Risk in Communities Study

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Narrowing and other changes in retinal arterioles may reflect damage due to hypertension, which may predict stroke and other cardiovascular diseases independently of blood pressure level. Newly developed quantitative methods of assessing retinal narrowing are used to determine whether this sign is related only to current blood pressure or whether it also independently reflects the effects of previous blood pressure. Retinal photography was performed at the third examination of Atherosclerosis Risk in Communities (ARIC) Study in 1993–1995, and results are presented for the 9,300 nondiabetic participants aged 50–71 years. Generalized narrowing of smaller arterioles was strongly and monotonically related to current blood pressure in men and women, whether they were taking antihypertensive medications or not, and, independent of current blood pressure, was consistently and monotonically related to blood pressure levels measured 3 and 6 years before the retinal assessment. Arteriovenous nicking was also independently related to both current and previous blood pressures. The patterns of association suggested that these signs reflect both transient and persisting structural effects of elevated blood pressure, in agreement with the scant pathologic literature available. The findings suggest that retinal assessment may be useful for research on the microvascular contributions to clinical cardiovascular diseases. *Am J Epidemiol* 1999;150:263–70.

arterioles; arteriosclerosis; blood pressure; cardiovascular diseases; microcirculation; retinal artery

Narrowing and other changes in retinal arterioles may reflect damage due to elevated blood pressure to arterioles, not only in the retina but possibly in other organs as well. Such damage, in turn, may be associated with the occurrence of strokes, particularly those associated with disease of the smaller arteries and arterioles and perhaps with other cardiovascular complications of hypertension. Some of the retinal vascular signs of severe, long-standing hypertension, such as hemorrhages and arteriolar sheathing, which were well described years ago (1), are now less frequently observed in populations, presumably because of the widespread use of antihypertensive medications. Generalized arteriolar narrowing, believed to be the earliest retinal sign of hypertension (1), has previously been assessed imprecisely, but newer studies have developed more quantitative techniques for its measurement (2).

To understand possible relations between retinal arteriolar diameters and clinical cardiovascular disease, one must understand the relations between retinal arteriolar diameters and levels of blood pressure. A key question is whether generalized retinal narrowing is largely physiologic, i.e., active constriction that is a cause or perhaps the result of current blood pressure levels or whether, at least in part, narrowing indicates persistent or irreversible arteriolar damage. If it reflects arteriolar damage, the narrowing should be related to previous blood pressure levels regardless of the current blood pressure level.

The main hypotheses of this investigation are that measures of retinal arteriolar narrowing are related to current blood pressure levels and to previous blood pressure levels independent of current blood pressure. We also examine the relation of narrowing to the use of antihypertensive medications.

Some of the classic ophthalmoscopic signs of hypertension (e.g., sheathing or hemorrhages) are better understood pathologically than is generalized narrowing, since narrowing is more difficult to assess in his-

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Abbreviations: ARIC, Atherosclerosis Risk in Communities; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; TDR, trunk diameter ratio.

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tologic material. These signs are also analyzed in association with both current and previous blood pressure levels. The question of whether blood pressure is related independently to both narrowing and the classic signs is examined in a companion publication (3).

MATERIALS AND METHODS

The Atherosclerosis Risk in Communities (ARIC) Study is a prospective investigation of factors related to atherosclerosis and the incidence of coronary heart disease in four communities. Atherosclerosis is assessed by using carotid artery ultrasound imaging. In 1987–1989, the study recruited and examined 15,792 men and women selected as probability samples of residents of Forsyth County, North Carolina, the city of Jackson, Mississippi, selected suburbs of Minneapolis, Minnesota, and Washington County, Maryland, who were aged 45–64 years. Only Black residents were selected in Jackson, whereas residents were selected without regard to ethnicity in the other communities. Response rates were 46 percent in Jackson and approximately 65 percent in the other communities. Of those examined at baseline, 14,368 (93 percent of the survivors) returned for a second examination 3 years later (in 1990–1992), and 12,887 (86 percent of the survivors) returned for a third examination 6 years later (in 1993–1995). For addition of an assessment of arterioles to the assessment of large-artery diseases, retinal photography was performed at examination 3, when the participants were aged 50–71 years. For the current analysis, we excluded 38 participants whose race was neither Black nor White and 1,721 who were diabetic or had missing information on diabetes status, since diabetic changes might complicate the interpretation of the associations of retinal signs with blood pressure. For this purpose, diabetes was defined as a fasting glucose ≥7.8 mmol/liter (≥140 mg/dl), a nonfasting glucose ≥11.1 mmol/liter (≥200 mg/dl), or a history of or treatment for diabetes. Of the 11,128 participants eligible for study, 160 (1.4 percent) lacked retinal photographs, and 1,480 (13 percent) had retinal photographs that could not be evaluated. Five participants with occlusion of retinal veins or arteries, 129 with no recorded blood pressure at the first or second examination, two with no recorded blood pressure at the third examination, and 52 with missing information on antihypertensive medication use were also excluded, leaving 9,300 participants for analysis.

Methods for retinal arteriolar assessment

The retinal photography performed at examination 3 and its interpretation are described in detail elsewhere (3). Briefly, a 45° retinal photograph was taken of one eye, centered on the optic disc and macula. Pupillary dilatation was achieved after dark adaptation, without use of mydriatic drugs. Photographic methods were standardized with written protocols, and photographer performance was monitored with periodic feedback to assure optimal performance. Photographs were evaluated at the Retinal Reading Center, where they were graded for image quality. The photographs were then viewed with an eight-power lens for qualitative stigmata of hypertension, including focal arteriolar narrowing, arteriovenous nicking, arteriolar sheathing, microaneurysms, hemorrhages, and exudates.

For quantitative assessment of the diameters of retinal vessels, the photographs were converted to digital images. Measurements were then made of diameters of all arteries and veins in the area located in an area designated as zone B, which lies between ½ and one disc diameter from the margin of the optic disc. (Zone A, the area within ½-disc diameter, was used for other retinal evaluations.) For arterioles larger than 80 μm at the outer boundary of zone B, the reader also measured the diameters of its two branches just beyond the boundary. Vessel diameters were enlarged in a subsidiary window, the reader marked vessel edge boundaries, and the diameter was measured by computer.

All arteriolar measurements from each eye were summarized by using a calculated "central retinal artery equivalent" (CRAE) developed by Parr and Spears (4, 5), using the following empirical formula:

$$W_c = (0.87\,W_a^2 + 1.01\,W_b^2 - 0.22\,W_aW_b - 10.76)^{1/2}$$

in which W_c is the diameter of each trunk arteriole, W_a is the diameter of the smaller branch, and W_b is the diameter of the larger branch. In the ARIC Study, all of the arterioles in the measured retinal area were used in calculating CRAE. CRAE then represents a summary of the diameters of all measured arterioles, and it is presumed not to be affected by the arteriolar branching pattern. An analogous central retinal vein equivalent (CRVE) was calculated from the formula:

$$W_c = (0.72\,W_a^2 + 0.91\,W_b^2 + 450.05)^{1/2}$$

in which W_c is the diameter of the trunk vein, W_a is the diameter of the smaller branch, and W_b is the diameter of the larger branch. CRAE was divided by CRVE, and the resulting arterial/venous ratio, now, in effect, standardized by dividing by CRVE for such factors as body size and optical magnification, was used as a measure of generalized arteriolar narrowing. Two arterial/venous ratios were calculated depending on use of the arterioles measured beyond zone B when trunks were larger than 80 μm: a ratio that used the branches

beyond zone B and one that used only the arterioles within zone B. All results presented pertain only to the ratio that used branch measurements beyond zone B, since this investigation found it to have a slightly stronger association with blood pressure.

For all trunk arterioles that exceeded 80 μm at the outer boundary of zone B, a trunk diameter ratio (TDR) was calculated as the ratio of the observed trunk diameter to the diameter predicted from the Parr formula using its two measured branches. A large TDR, then, is evidence of a trunk that is large relative to its branches, attributable either to relatively more constriction peripherally or perhaps to passive dilation proximally. A mean TDR was calculated for each person by using all of the arterioles in the diameter range of 80–99 μm. Only 3 percent of all arterioles crossing the outer boundary of zone B were larger than 99 μm.

The retinal signs are defined as in the paper by Hubbard et al. (3). Focal narrowing was evaluated within the optic disc margin, in zone A, where the vessels are arterial in nature, and in zone B, where the vessels are arterioles. Arteriolar sheathing was assessed in zone B and was considered definite when the arteriolar walls were partially or completely opaque. Arteriovenous nicking was evaluated in zone B, and a definite classification required narrowing of the venous blood column on both sides of the point where a vein crossed under an artery. Retinal microaneurysms were noted as typically round, red capillary ballooning, usually having smooth margins and a diameter of less than 150 μm. Blot and flame-shaped hemorrhages were distinguished. Hard exudates, actually lipid deposits, were detected as bright, yellow-white deposits with sharp margins. Soft exudates, or areas of retinal ischemia, were detected as white, pale yellow-white, or gray-white areas with feathery edges.

At each examination, sitting brachial blood pressure was measured three times with a random zero sphygmomanometer after 5 minutes rest, by trained technicians following a standardized protocol. The average of the second and third readings of systolic and fifth-phase diastolic blood pressures was used in this report. Antihypertensive medication use was recorded at each examination. We defined mean arterial blood pressure at any examination as [(0.33 × systolic pressure) + (0.67 × diastolic pressure)]. Mean arterial pressure measured at examination 3 is referred to as current blood pressure, and the mean of mean arterial pressure at examinations 1 and 2 is referred to as previous blood pressure. Examination 3 cigarette smoking status is dichotomized as current cigarette smokers versus former or never smokers.

Statistical methods

Arterial/venous ratios and TDRs were evaluated in relation to both current and previous blood pressures in gender-specific linear regression models to determine the influence of blood pressure while controlling for age, race, antihypertensive medication use, and cigarette smoking. Logistic regression was used in analogous fashion with the odds of a retinal sign determined by light-box grading (e.g., arterial/venous nicking) as the dependent variable and blood pressures as the independent variables. Means and standard errors adjusted for selected variables presented in the figures were estimated by using linear regression methods; cutoffs for six blood pressure categories were equal intervals (with the exception of the lowest and highest categories) chosen to approximate equal numbers of participants in each category.

All analyses were performed using SAS statistical software (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Characteristics of the study population were generally similar in women and men (table 1). Average age at examination 3 was almost 60 years, approximately 20 percent were Black, 17 percent were current cigarette smokers, and 27 percent used antihypertensive

TABLE 1. Characteristics of the study population, the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1995

	Mean (standard deviation)	
	Women (n = 5,228)	Men (n = 4,072)
Mean age (years)	59.1 (5.5)	59.9 (5.6)
% Black	21.4	16.0
% current smokers	16.9	18.5
% using antihypertensive medication	28.0	26.3
Mean current systolic blood pressure (mmHg)	122.5 (19.0)	123.9 (17.7)
Mean current arterial blood pressure (mmHg)	87.9 (11.9)	90.2 (11.5)
Mean previous* arterial blood pressure (mmHg)	86.5 (10.8)	89.5 (10.1)
Mean arterial/venous ratio	0.85 (0.07)	0.83 (0.07)
Mean trunk diameter ratio†	0.97 (0.08)	0.97 (0.07)
Not using antihypertensive medication		
Mean arterial/venous ratio	0.85 (0.07)	0.83 (0.07)
Mean trunk diameter ratio	0.97 (0.07)	0.97 (0.07)
Using antihypertensive medication		
Mean arterial/venous ratio	0.83 (0.07)	0.81 (0.07)
Mean trunk diameter ratio	0.98 (0.08)	0.98 (0.08)

* Mean of measurement at examination 1 (1987–1989) and measurement at examination 2 (1990–1992).

† Among 4,770 women and 3,675 men.

medications. Men had slightly higher current and previous blood pressure levels. Mean (standard deviation) arterial/venous ratios were 0.85 (0.07) in women and 0.83 (0.07) in men. Both had a mean TDR of 0.97.

Figure 1 shows the association of arterial/venous ratio with current mean arterial pressure in men and women with and without use of antihypertensive medications. The mean arterial/venous ratios for these four groups are presented in table 1. The arterial/venous ratios, adjusted for age, race, and current cigarette smoking, declined monotonically with increasing blood pressure in all four groups. The arterial/venous ratio association with blood pressure was then evaluated by using gender-specific linear regression models. In a model that also included race, age, medication use, current cigarette smoking, and body height, height was not a significant factor in either women or men, so correction for body size was not considered further. Age and race were retained in further analyses, although each was significant in only one sex. Ten years of age was associated with a slightly lower ratio in men (by 0.005, $p < 0.05$) but not in women, whereas Black race was associated with a lower ratio in women (by 0.008, $p < 0.01$) but not in men. Current cigarette smoking was associated with a smaller arterial/venous ratio by 0.015 in women ($p < 0.001$) and 0.012 in men ($p < 0.001$). Antihypertensive medication use was associated with a lower ratio by 0.005 ($p < 0.05$) in women and 0.014 ($p < 0.001$) in men. In these models, arterial/venous ratio was lower by 0.021 in women and 0.019 in men for each 10-mmHg increment in mean blood pressure ($p < 0.001$ for each sex). An interaction term for treatment and blood pressure, significant for both women and men ($p < 0.01$), showed weaker blood pressure-arterial/venous ratio associations in persons who received treatment, and treatment- and gender-specific models showed arterial/venous ratio declines of 0.025 and 0.013, respectively, in women who were not using and those who were using antihypertensive medication (table 2, model A) per 10 mmHg of current blood pressure and 0.022 and 0.015, respectively, in men ($p < 0.001$ for each of the four associations). Separate analyses in two age groups showed somewhat

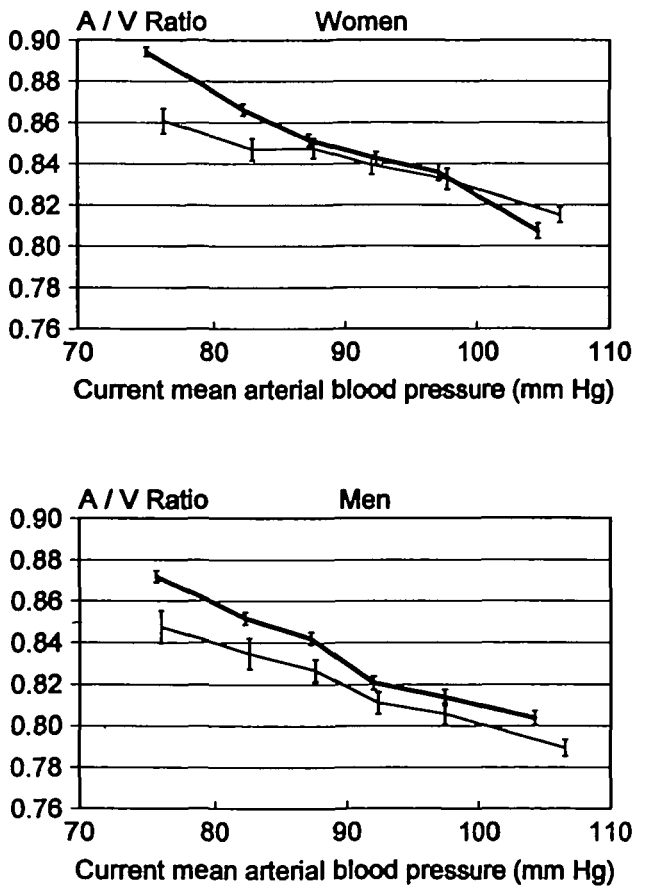

FIGURE 1. Age-, race-, and smoking-adjusted mean (standard error) arterial/venous (A/V) ratio by current mean arterial pressure among those using (thin line) and those not using (thick line) antihypertensive medication, the ARIC Study, 1993–1995. A/V ratio means are plotted at the medians of the following blood pressure groups: 44–<80; 80–<85; 85–<90; 90–<95; 95–<100; and 100–<155 mmHg.

TABLE 2. Age-, race-, and cigarette smoking-adjusted difference and standard error (SE) in arterial/venous ratio associated with a 10-mmHg difference in mean arterial blood pressure (BP), by hypertensive medication use, the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1995

	Not using antihypertensive medication		Using antihypertensive medication	
	Model A*	Model B*	Model A	Model B
	Women			
No	3,765		1,463	
Current BP				
Difference	−0.025	−0.018	−0.013	−0.010
SE	0.001	0.002	0.002	0.002
p value	<0.001	<0.001	<0.001	<0.001
Previous BP†				
Difference		−0.012		−0.006
SE		0.002		0.002
p value		<0.001		0.009
	Men			
No	3,001		1,071	
Current BP				
Difference	−0.022	−0.017	−0.015	−0.011
SE	0.001	0.002	0.002	0.002
p value	<0.001	<0.001	<0.001	<0.001
Previous BP†				
Difference		−0.009		−0.010
SE		0.002		0.003
p value		<0.001		<0.001

* Model A includes age, race, smoking, and current BP. Model B includes these variables plus previous BP.

† Mean of arterial BPs 3 and 6 years prior to current BP.

weaker associations of arterial/venous ratio with current blood pressure in those aged 60–71 years than in those aged 50–59. Among older, untreated women, the arterial/venous ratio differed between those with current mean blood pressure values of 75 and 95 mmHg by 0.038 compared with 0.059 in the younger group. Corresponding differences in older and younger men were 0.049 and 0.060, respectively. However, the blood pressure-age interaction term was significant only in women ($p < 0.001$).

Figure 2 shows the arterial/venous ratio association with current systolic pressure in untreated men and women. Associations with current diastolic pressure (not shown) resemble those for current mean blood pressure, but those with current systolic pressure are curved, with greater systolic pressure-associated changes in arterial/venous ratio at lower levels of current systolic pressure. Men appear to have lower arterial/venous ratios than do women at most current systolic pressure levels.

Separate linear regression models were run for women and men who were taking and those who were not taking antihypertensive medications with arterial/venous ratio as the dependent variable and age, race, current smoking, current mean blood pressure, and previous blood pressure as independent variables (table 2, model B). Both current and previous blood pressures were significantly negatively associated with arterial/venous ratio in all models. The associations with previous blood pressure found after adjustment for current blood pressure and these other variables are shown in figure 3.

Mean TDR was related positively to current mean blood pressure in both sexes, whether treated or not treated for hypertension, as shown in figure 4 ($p < 0.05$ in each group when tested in a linear model with age and race adjustment). The mean TDRs for these four groups are indicated in table 1. TDR associations with previous blood pressure after controlling additionally for current blood pressure were weak, inconsistent by group, and not statistically significant.

Associations of the retinal signs determined by lightbox grading with blood pressure were assessed by using multiple logistic models that included age, gender, race, smoking, and both current and previous mean blood pressures. Odds ratios for the retinal signs corresponding to 10 mmHg higher levels of blood pressure are shown in table 3. For current blood pressure, odds ratios were positive, approximately 1.5 or greater, and significant at $p < 0.05$ for focal narrowing, whether measured within the optic disc, zone A or B, blot hemorrhages, flame hemorrhages, and arteriolar sheathing, and borderline significant for arterial/venous nicking,

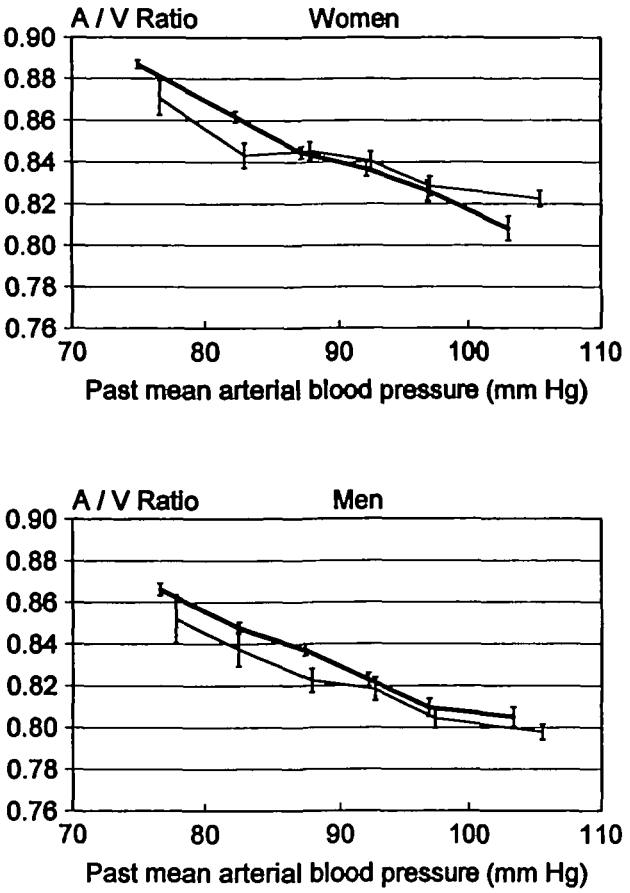

FIGURE 3. Age-, race-, smoking-, and current blood pressure-adjusted mean (standard error) arterial/venous (A/V) ratio by past mean arterial pressure among those using (thin line) and those not using (thick line) antihypertensive medication, the ARIC Study, 1987–1995. A/V ratio means are plotted at the medians of the following blood pressure groups: 55–<80; 80–<85; 85–<90; 90–<95; 95–<100; and 100–<163 mmHg.

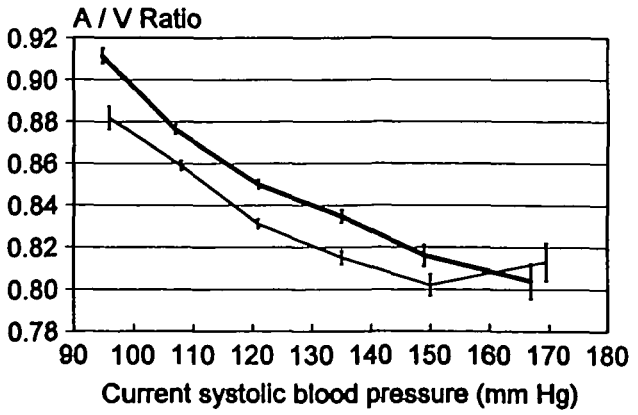

FIGURE 2. Age-, race-, and smoking-adjusted mean (standard error) arterial/venous (A/V) ratio by current systolic pressure among men (thin line) and women (thick line) not using antihypertensive medication; the ARIC Study, 1993–1995. A/V ratio means are plotted at the medians of the following blood pressure groups: 63–99; 100–114; 115–129; 130–144; 145–159; and 160–258 mmHg.

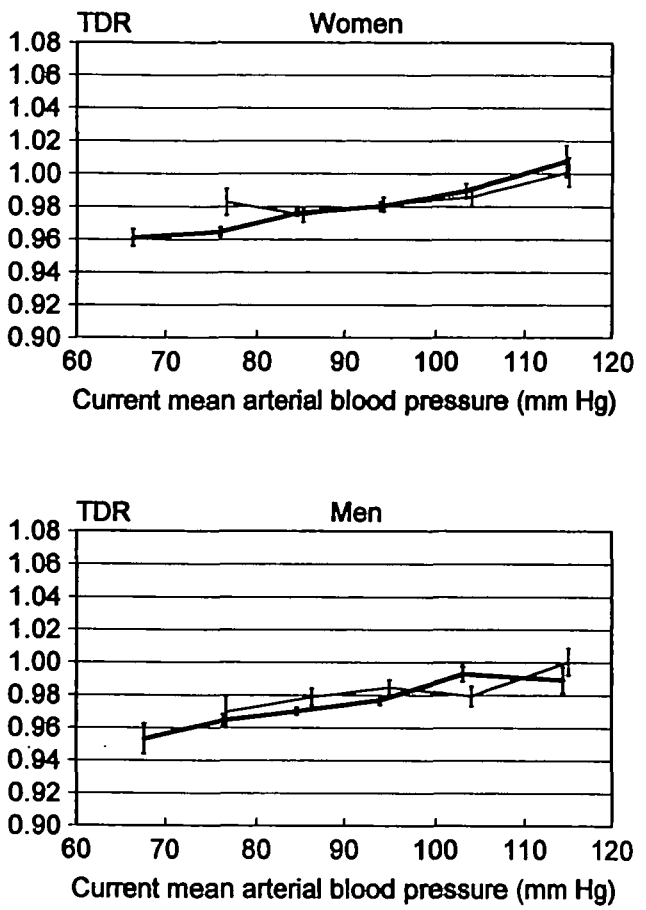

FIGURE 4. Age-, race-, and smoking-adjusted mean (standard error) trunk diameter ratio (TDR) by current mean arterial pressure among those using (thin line) and those not using (thick line) antihypertensive medication, the ARIC Study, 1993–1995. Mean TDR is plotted at the medians of the following blood pressure groups: 51–<70; 70–<80; 80–<90; 90–<100; 100–<110; and 110–147 mmHg. In those using antihypertensive medication, the lowest group was omitted.

microaneurysms, and soft exudates. For previous blood pressure, however, the only significant association was with arterial/venous nicking. Separate analyses by gender were performed for the more frequent signs, focal narrowing, and arterial/venous nicking (not shown). Focal narrowing at each location measured was associated with current blood pressure at $p < 0.05$ in both men and women, but not with previous blood pressure. Arterial/venous nicking was associated at $p < 0.05$ with both current and previous blood pressure in women and with previous blood pressure in men.

DISCUSSION

For nondiabetic men and women aged 50–71 years, this study shows that increments in blood pressure levels are associated significantly and monotonically over the entire range of blood pressures seen, with smaller arterial/venous ratios and slightly greater TDRs. Reduced arterial/venous ratios with larger TDRs indicate generalized narrowing, particularly in the more peripheral arterioles located approximately one disc diameter from the optic disc. The findings were consistent in both men and women and with whether they had received antihypertensive medications or not. Narrowing was also significantly, monotonically, and consistently related to blood pressure levels measured 3 and 6 years before the retinal assessment after adjustment for current blood pressure levels. The arterial/venous ratio differences associated with current blood pressure differences, despite their consistency and the high levels of statistical significance, were small, on the order of 0.02 per 10 mmHg of mean blood pressure, or approximately 30 percent of the standard deviation of arterial/venous ratio in the population. Clearly, a careful quantitative technique such as

TABLE 3. Association of current and previous blood pressure (BP) with hypertensive retinal signs determined by light box grading, the Atherosclerosis Risk in Communities (ARIC) Study, 1987–1995*

		No. with sign†	Current blood pressure		Previous blood pressure	
			OR‡	95% CI‡	OR	95% CI
Focal narrowing, zone B	Severe/definite vs. questionable/none	673	1.98	1.81, 2.16	1.04	0.94, 1.15
Focal narrowing within disc	Severe/definite vs. questionable/none	302	1.60	1.41, 1.81	1.02	0.88, 1.18
Focal narrowing, zone A	Severe/definite vs. questionable/none	402	1.75	1.57, 1.95	1.06	0.94, 1.21
Arterial/venous nicking	Severe/definite vs. questionable/none	544	1.10	1.00, 1.21	1.28	1.15, 1.43
Blot hemorrhage	Definite vs. questionable/none	79	1.64	1.32, 2.05	0.91	0.69, 1.20
Flame hemorrhage	Definite vs. questionable/none	52	1.43	1.10, 1.87	1.02	0.74, 1.41
Microaneurysm	One or more vs. questionable/none	174	1.17	1.00, 1.38	1.13	0.94, 1.36
Soft exudate	Definite/questionable vs. none	48	1.21	0.90, 1.64	1.09	0.78, 1.54
Hard exudate	Definite/questionable vs. none	26	0.94	0.61, 1.45	1.16	0.72, 1.87
Arteriolar sheathing	Severe/definite/questionable vs. none	22	1.52	1.00, 2.33	0.98	0.59, 1.62

* A separate model was estimated for each sign; independent variables included current BP, previous BP, gender, age, race, and current cigarette smoking. The unit change is 10 mmHg.

† The number of individuals at risk in each model ranged from 8,947 to 9,300.

‡ OR, odds ratio; CI, confidence interval.

the one used here is required to obtain the precision needed to show these relations.

Higher current blood pressure was also associated with focal narrowing, blot and flame hemorrhages, arteriolar sheathing, arterial/venous nicking, microaneurysms, and soft exudates. However, among these retinal signs determined by light-box grading, previous blood pressure was associated only with arterial/venous nicking after adjustment for current blood pressure levels. The lack of association of the retinal signs determined by light-box grading other than nicking with previous blood pressure was unexpected. Microaneurysms, however, are not specific to hypertension (6), and focal narrowing is difficult to measure reliably. Retinal signs determined by light-box grading other than nicking, focal narrowing, and microaneurysms were infrequently observed in this population, and the numbers were probably inadequate for reliable assessment of their independent associations with current and previous blood pressure, since current and previous blood pressure are correlated.

Since generalized narrowing and arterial/venous nicking were related to previous blood pressure independently of current blood pressure levels, these signs may, in part, reflect persisting or permanent changes in the arterioles. The probability of a structural component to arteriolar narrowing is supported by the detailed histologic examinations reported by Harnish and Pearce (7), who studied 12 eyes, both postmortem and by ophthalmoscopy over the months prior to death, from eight patients who died with severe hypertension. Repeated ophthalmoscopy showed focal narrowings to be either stable or transient, although transient narrowings usually recurred in the same arteriolar segments. The pathology of narrowed arterioles usually revealed normal medial thickness with intimal and medial cellular crowding, interpreted as signs of active constriction, a functional change. However, medial atrophy and a uniform fibrous or sometimes hyperplastic intimal thickening were often superimposed. These histologic changes in narrowed arterioles occurred in the absence of any clinically observable retinal signs other than narrowing. However, as expected, more severe pathology was seen in the arterioles that, on ophthalmoscopy, showed sheathing or the other signs classically attributed to sclerosis.

The observations by Leishman (8) led to the hypothesis that hypertensive, narrowed arterioles eventually become fibrotic, with subsequent passive dilation in the more proximal portions. Consistent with this view, Hill and Dollery (9) found that in a group of very severely hypertensive patients whose diastolic pressures fell precipitously after drug treatment, nephrectomy, or myocardial infarction, the smaller retinal arterioles dilated, whereas arterioles larger than 50 μm often showed diameter reductions after lowering of blood pressure. In the ARIC Study, the association of TDR with elevated blood pressure (figure 4) suggested dilation of trunk arterioles larger than 80 μm relative to their branches or, conversely, relatively greater constriction in the branches. However, TDR was not related to previous blood pressure after adjustment for current blood pressure, and this suggests that passive dilation of larger arterioles due to persisting fibrotic or atrophic changes was not frequent at the levels of hypertension found in the ARIC Study population.

Current use of antihypertensive medications was significantly associated with smaller arterial/venous ratios in both men and women. This was observed in men at all mean blood pressure levels and in women at mean blood pressure levels lower than 90 mmHg. We speculate that this fact, like the associations of arterial/venous ratio with previous blood pressures, is further evidence that arteriolar narrowing is, in part, due to structural or pathologic changes in the vessels. We reason that the arterial/venous ratios are smaller for persons using antihypertensive medications than for untreated persons with the same current blood pressures because of the persisting effects of the higher blood pressures they experienced before receiving treatment. We have no explanation, however, for the exceptional finding in treated women with mean blood pressure greater than 90 mmHg. Furthermore, for both men and women who received treatment, the arterial/venous ratio-blood pressure slopes were less steep than for those who were not receiving treatment (table 1), i.e., narrowing was associated less strongly with treated than with untreated blood pressure levels. This may also be evidence of the persisting effects of previous blood pressures in treated persons.

Results of the study could be biased by missing data, since 1 percent of eligible participants had no retinal photographs and 17 percent of the photographs could not be graded. As Hubbard et al. (3) show, gradability is related to age and race. However, we do not have any reason to believe that the associations of the retinal findings to blood pressure adjusted for age and race would be affected by the missing data.

In conclusion, a new quantitative assessment of retinal arteriolar narrowing shows a relation to even modest blood pressure elevations and to previous blood pressure after accounting for current blood pressure, suggesting that narrowing may, in part, reflect persisting arteriolar pathology due to hypertension. Similar evidence suggests a structural pathologic component to arterial/venous nicking as well. If narrowing and nicking are indeed indicators of the pathologic effects of hypertension on arterioles, carefully standardized ophthalmoscopy may be useful in population studies for assessing the role of arteriolar pathology in diseases of the brain and other organs.

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