Retinal Vessel Diameters and Their Associations with Age and Blood Pressure

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Purpose. To describe the cross-sectional relationship between retinal arteriolar and venular diameters with age and blood pressure.

Methods. A population-based study was conducted in Beaver Dam, Wisconsin ($n = 4926$, age range, 43–84 years). Retinal photographs of right eyes taken at the baseline examination (1988–90) were digitized. All arterioles and venules located in the area between one-half and one disc diameter from the optic disc margin were measured with a computer-based program. These measurements were combined to provide the average diameters of retinal arterioles and venules of each eye, and the association with age and blood pressure (BP) was analyzed.

Results. After controlling for gender, hypertension, diabetes, serum glucose and lipids, cigarette smoking, and body mass index, retinal arteriolar diameters were found to be decreased by 2.1 μm (95% confidence interval [CI], 1.5–2.7) for each decade increase in age, and by 4.4 μm (95% CI, 3.8–5.0) for each 10-mm Hg increase in mean arterial BP. The association of narrowed retinal arterioles and higher BP was stronger in younger persons. For each 10-mm Hg increase in mean arterial BP, arteriolar diameters decreased by 7.0 μm in persons aged 43 to 54 years but by only 2.5 μm in persons aged 75 to 84 years. In contrast, retinal venular diameters narrowed with increasing age but not with increasing BP.

Conclusions. Retinal arteriolar diameters are narrower in older persons and in persons with higher BP, independent of other factors. The weaker association of retinal arteriolar diameters and BP in older people may reflect greater sclerosis of the retinal arterioles, preventing a degree of narrowing with higher BP similar to that seen in younger persons. (*Invest Ophthalmol Vis Sci.* 2003;44:4644–4650) DOI:10.1167/iovs.03-0079

Narrowing of the retinal arterioles has long been regarded as an early feature of hypertensive retinopathy[1–4] and has been suggested to predict cardiovascular mortality.[5–7] However, the available data have been limited by the imprecision of defining the severity of retinal arteriolar narrowing based on a clinical ophthalmoscopic examination.[8,9] In the Atherosclerosis Risk in Communities (ARIC) study, we developed a computer-based method to measure retinal arteriolar and venular diameters from digitized photographic images.[10] Using this approach, we have shown that retinal arteriolar narrowing can be measured reliably,[11] and is strongly associated with hypertension,[12] and, independent of BP and other risk factors, with incident coronary heart disease in women[13] and incident stroke and diabetes in men and women.[14,15] These findings therefore raise the possibility that an objective assessment of retinal arteriolar narrowing determined from examining photographs may provide unique cardiovascular risk information in the general population. However, the clinical utility of retinal photography for cardiovascular risk stratification depends not only on replication of these findings in other populations and settings, but also on a greater understanding of the distribution of retinal arteriolar diameters and their independent association with age and BP.

Several researchers have observed a weaker association between elevated BP and retinal arteriolar narrowing with increasing age.[3,4] This has been suggested to be due to greater severity of arteriolosclerosis (e.g., intimal thickening and medial hyperplasia, hyalinization, and sclerosis) in older people, preventing a degree of vasoconstriction similar to that in younger persons. However, data to support this hypothesis are limited.[1]

In the current report, we describe the distribution of retinal arteriolar and venular diameters and their cross-sectional associations with age, hypertension, and BP in the Beaver Dam Eye Study, a population-based cohort investigation of ocular diseases in adult white persons living in Wisconsin. We also examine whether age modifies the association between retinal vessel diameters and BP. Data for this study were based on the baseline examination.

Methods

Study Population

The study population and research methodology of the Beaver Dam Eye Study have been described in detail in other reports.[16–18] In brief, a private census of the population of Beaver Dam, Wisconsin, was performed from fall 1987 to spring 1988. Of 5924 individuals eligible, 4926 participated in the baseline examination between 1988 and 1990. Comparisons between participants and nonparticipants have been presented.[16] Informed consent was obtained from each participant at the beginning of the examination.

Retinal Vessel Grading

All participants had stereoscopic 30° color retinal photographs taken of two eyes, centered on the disc (Diabetic Retinopathy Study [DRS] standard field 1) and macula (field 2), and a nonstereoscopic photograph temporal to but including the fovea.[19,20] Retinal photographs of field 1 of right eyes were converted to digital images by a high-resolution scanner (LS2000; Nikon, Inc., Tokyo, Japan) using standard settings for all photographs.[21]

The diameters of all arterioles and venules coursing through a specified area (zone B) one-half to one disc diameter from the optic

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disc were measured with a computer program (OptiMate; Nematron, Milwaukee, WI), according to a standard protocol.[10,21] The procedure was performed as follows. A grader, masked to the participant's characteristics, retrieved an image from the network and identified each vessel as an arteriole or venule, using the original color photographs for reference. The grader selected a segment of the vessel within zone B for measurement, and the software program calculated the central and average width of five equidistant measures of that vessel segment (in micrometers). The grader then assessed the validity of each measurement by evaluating the consistency of the histogram and visual image, and the correlation between the average and central widths. The grader had the option of (1) accepting the average width, (2) accepting the central width, (3) declining both and remeasuring the vessel, or (4) manually adjusting the central width after remeasurement. The branches of arterioles were also measured if the trunk measures were 85 μm or more. Branch measurements were declined if either of the branches could not be measured accurately. On average, between 7 and 14 arterioles and an equal number of venules were measured per eye.

At the end of this process, the software combined the individual measurements into summary indices, the central retinal arteriolar equivalent (CRAE) and the central retinal venular equivalent (CRVE), based on formulas by Parr et al.[22,23] and Hubbard et al.[10] CRAE, which represented the average arteriolar diameters of the eye, was defined as

$$W_c = (0.87W_a^2 + 1.01W_b^2 - 0.22W_aW_b - 10.73)^{1/2}$$

where W_c was calculated as the trunk arteriole diameter, and included diameter from the smallest (W_a) to largest branches (W_b). A similar formula was used to calculate the CRVE, which represented the average venular diameters of the eye:

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

where W_c, W_a, W_b were corresponding venular diameter measurements. Finally, the summary indices of the arteriolar and venular diameters were expressed as an arteriole-to-venule ratio (AVR). As previously reported, the AVR compensated for possible magnification differences between eyes. An AVR of 1.0 suggested that arteriolar diameters were, on average, the same as venular diameters in that eye, whereas a smaller AVR suggested narrower arterioles.[10,12]

A retinal photograph was considered ungradable if more than one arteriole or venule larger than 40 μm in diameter (as measured by software) could not be measured precisely after three attempts. This cutoff was based on preliminary data that showed vessels smaller than this diameter had no measurable impact on the summary values. Reproducibility of the retinal grading was high, as previously reported.[21] Alternate sets of 20 photographs per set were regraded for retinal vessel diameters every 3 months (i.e., a total of 40 different photographs). The intra- and intergrader intraclass correlation coefficients ranged from 0.78 to 0.99.

Definitions of Hypertension and BP

A standardized interview and examination was performed at each examination.[19] BP was measured with a random-zero sphygmomanometer according to the hypertension detection and follow-up program protocol, and the average of two measurements was used for analysis.[24] Mean arterial BP was defined as two thirds of the diastolic BP plus one third of the systolic BP. Hypertension was defined as systolic BP of 140 mm Hg or higher, diastolic BP of 90 mm Hg or higher, or the combination of self-reported high BP diagnosis and use of antihypertensive medications. A person with hypertension was further classified into two mutually exclusive categories: (1) well-controlled hypertension (using antihypertensive medications plus systolic BP $<$ 140 mm Hg and diastolic BP $<$ 90 mm Hg) and (2) uncontrolled untreated hypertension (using or not using antihypertensive medications with systolic BP of 140 mm Hg or higher or diastolic BP of 90 mm Hg or higher).

Definitions of Other Variables

Age was defined as the age at the time of the baseline examination. Nonfasting blood specimens were obtained, serum glucose was determined by the hexokinase method,[25,26] and serum total cholesterol and HDL-cholesterol were determined by enzymatic methods.[27,28] Persons were defined as having diabetes if they had a history of diabetes mellitus treated with insulin, oral hypoglycemic agents or diet or had diabetes newly diagnosed at the time of examination.[29] The latter was defined as no reported history of diabetes mellitus or use of hypoglycemic medications for diabetes mellitus with a casual blood sugar of higher than 11.1 mM and a glycosylated hemoglobin value that was greater than two standard deviations above the mean for a given age-sex group (for those 43–54 years of age, men >9.5% and women >9.6%; for those 55–64 years of age, men >9.4% and women >10.0%; for those 65–74 years of age, men >9.6% and women >9.6%; and for those 75 years of age or older, men >9.5% and women >9.6%). Primary care physicians of participants were also consulted about the patient's history of diabetes mellitus and treatment whenever the diagnosis was in doubt. The body mass index was defined as weight (in kilograms)/height (in square meters). Questions were asked relating to a history of cardiovascular disease (CVD; myocardial infarction, angina and/or stroke). For the evaluation of cataracts, photographs were taken of the lens after pupil dilation, using slit lamp and retroillumination cameras, as previously reported.[17] The photographs were subsequently graded for the presence and severity of cataract. Cigarette smoking and alcohol consumption status were determined. A subject was classified as a nonsmoker if he or she had smoked fewer than 100 cigarettes in his or her lifetime, as an ex-smoker if he or she had smoked more than 100 cigarettes in his or her lifetime but had stopped smoking before the baseline examination; and as a current smoker if he or she had not stopped smoking. A current heavy drinker was a person consuming four or more servings of alcoholic beverages daily, a former heavy drinker had consumed four or more servings daily in the past but not in the year before the baseline examination, and a nonheavy drinker had never consumed four or more servings daily on a regular basis.

Statistical Methods

Retinal vessel data (retinal arteriolar and venular diameter equivalents and the AVR) were analyzed as continuous variables. We compared mean retinal arteriolar and venular diameters and AVR by age-group (43–54; 55–64; 65–74; and 75–84 years), hypertension status (no; yes, controlled; yes, uncontrolled or untreated), and mean arterial BP (divided into six categories: 61.3–83.9; 84.0–89.9; 90.0–94.9; 95.0–99.9; 100.0–106.9; and 107.0–155.3 mm Hg) using analysis of covariance models. We used multiple linear regression models to examine further the independent relationships of retinal vessel diameters with age and BP (as continuous covariates). In the multivariate models, we adjusted for gender, hypertension, and diabetes status (yes, no), serum glucose, and total and HDL cholesterol levels (milligrams per decaliter), body mass index (kilograms per square meter), and cigarette smoking status (ever, never). Finally, we performed subsidiary analyses in subgroups stratified by age groups, gender, hypertension, diabetes, and cigarette smoking status.

Results

Photographs were ungradable for retinal vessel diameters in 679 (13.8%) eyes. Table 1 shows the baseline characteristics of participants with (n = 4247) and without (n = 679) gradable retinal photographs of right eyes. Participants without gradable photographs were older, and, after adjustment for age, were more likely to be women, to have hypertension, CVD, diabetes, and cataract and to have higher levels of serum glucose, gly-

TABLE 1. Comparison of Persons with and without Gradable Photographs for Retinal Vessel Measurements in the Beaver Dam Eye Study

	Gradable Photographs (n = 4247)	Ungradable Photographs (n = 679)	P*
Age (y)	61.0	68.2	<0.001
Men (%)	45.0	37.4	0.01
Hypertension (%)	50.0	54.2	0.04
History of CVD (%)	14.6	18.2	0.01
Diabetes (%)	9.6	14.6	<0.001
Any cataract (%)	13.6	35.0	<0.001
Current cigarette smoker (%)	55.4	54.0	0.49
Current heavy alcohol drinker (%)	17.1	17.2	0.95
Systolic BP (mm Hg)	132.2	132.0	0.86
Diastolic BP (mm Hg)	77.3	77.2	0.82
Serum glucose (mg/dL)	106.0	111.4	0.001
Glycosylated hemoglobin (%)	6.1	6.3	0.001
Proteinuria (mg/dL)	1.2	1.3	<0.001
Total serum cholesterol (mg/dL)	233.7	232.7	0.60
HDL cholesterol (ng/dL)	51.9	52.3	0.64
Body mass index (kg/m^2)	28.7	29.0	0.25

Data are age-adjusted and are means, unless marked %.
* Based on difference in means or proportions, adjusted for age in analysis of covariance models.

cosylated hemoglobin, and proteinuria. Systolic and diastolic BPs were similar in those with and without gradable photographs.

Mean retinal arteriolar diameters were 202.5 ± 20.6 μm in men and 201.0 ± 20.6 μm in women, mean venular diameters were 232.4 ± 20.3 μm in men and 227.1 ± 20.2 μm in women, and mean AVRs were 0.874 ± 0.08 in men and 0.887 ± 0.08 in women.

Retinal arterioles and venules were narrower in older men and women (Table 2). Mean arteriolar diameters decreased from 204.4 μm in persons aged 43 to 54 years to 196.4 μm in persons aged 75 to 84 years. Similarly, mean venular diameters decreased from 231.2 μm in persons aged 43 to 54 years to 221.2 μm in persons aged 75 to 84 years.

Table 3 shows the relationship of retinal vessel diameters with hypertension status in the total population and in women and men separately. After we controlled for age and gender, the average arteriolar diameter was 196.2 μm in persons with uncontrolled or untreated hypertension, compared with 200.3 μm in persons with well-controlled hypertension and 205.8 μm in persons without hypertension ($P < 0.001$). In contrast, retinal venular diameters were not related to hypertension status. The AVR was significantly lower in people with hypertension, particularly those with untreated or uncontrolled hypertension. The pattern of association was generally similar in women and men.

Table 4 shows the results of multiple linear regression models of retinal vessel measurements with age and BP, adjusting for potential confounders. After controlling for gender, we saw significant and independent linear relationships of retinal arteriolar diameters with age and BP. When we controlled for gender, retinal arteriolar diameters were narrower by 2.3 μm ($P < 0.001$) in persons who were 10 years older, and by 4.9 μm ($P < 0.001$) in persons who had 10 mm Hg higher mean arterial BP. In contrast, venular diameters were related to increasing age, but not to increasing BP. Venular diameters were narrower by 2.3 μm ($P < 0.001$) for each decade increase in age but only by 0.5 μm ($P = 0.06$) for each 10-mm Hg increase in mean arterial BP. Reflecting the similar magnitude of decrease in retinal arteriolar and venular diameters with age but the relatively greater decrease in arteriolar diameters with BP, the retinal AVR decreased by 0.0007 ($P = 0.53$) for each decade increase in age and 0.020 ($P < 0.001$) for each 10-mm Hg increase in mean arterial BP. Figures 1 and 2 depict the associations for mean arterial BP. In the multivariate models, with adjustment for hypertension, diabetes, serum glucose, total and HDL-cholesterol, cigarette smoking, and body mass index, these associations were not substantially altered (Table

TABLE 2. Relationship of Retinal Vessel Diameters with Age

			Retinal Arteriolar Diameter			Retinal Venular Diameter			Retinal AVR		
	Age (y)	n	Mean (μm)	SD	P*	Mean (μm)	SD	P*	Mean	SD	P*
All	43–54	1404	204.4	(21.1)	< 0.001	231.2	(19.3)	< 0.001	0.89	(0.08)	0.60
	55–64	1205	202.4	(19.6)		231.5	(20.1)		0.88	(0.08)	
	65–74	1072	200.1	(20.5)		229.4	(20.4)		0.87	(0.08)	
	75–84	566	196.4	(20.7)		221.2	(20.9)		0.89	(0.09)	
Women	43–54	736	204.2	(21.3)	< 0.001	228.9	(19.0)	< 0.001	0.89	(0.08)	0.36
	55–64	641	202.6	(19.9)		230.3	(20.4)		0.88	(0.08)	
	65–74	613	199.2	(20.1)		226.7	(20.1)		0.88	(0.07)	
	75–84	347	194.5	(19.7)		218.2	(20.1)		0.89	(0.08)	
Men	43–54	668	204.7	(20.8)	< 0.001	233.7	(19.3)	< 0.001	0.88	(0.08)	0.81
	55–64	564	202.1	(19.2)		232.9	(19.8)		0.87	(0.08)	
	65–74	459	201.3	(21.0)		233.0	(20.2)		0.87	(0.08)	
	75–84	219	199.4	(21.8)		225.9	(21.3)		0.89	(0.09)	

* Based on linear regression models of retinal arteriolar diameters, venular diameters, and AVR with age.

Table 3. Relationship of Retinal Vessel Diameters with Hypertension Status

	Hypertension	n	Retinal Arteriolar Diameter Mean (μm)	SE	P*	Retinal Venular Diameter Mean (μm)	SE	P	Retinal AVR Mean	SE	P
All	No	2166	205.8	(0.4)	< 0.001	230.1	(0.4)	0.16	0.90	(0.002)	< 0.001
	Yes, controlled	601	200.3	(0.7)		229.2	(0.7)		0.88	(0.003)	
	Yes, uncontrolled or untreated	1470	196.2	(0.5)		228.8	(0.5)		0.86	(0.002)	
Women	No	1194	205.5	(0.6)	< 0.001	228.3	(0.6)	0.03	0.90	(0.002)	< 0.001
	Yes, controlled	357	199.3	(1.1)		227.0	(1.1)		0.88	(0.004)	
	Yes, uncontrolled or untreated	781	194.8	(0.7)		225.6	(0.7)		0.87	(0.003)	
Men	No	972	206.3	(0.6)	< 0.001	232.4	(0.6)	0.82	0.89	(0.002)	< 0.001
	Yes, controlled	244	201.2	(1.3)		231.8	(1.3)		0.87	(0.005)	
	Yes, uncontrolled or untreated	689	197.8	(0.8)		232.7	(0.8)		0.85	(0.003)	

* Based on difference in mean values between hypertension categories, adjusted for age and gender (except for women and men, adjusted for age only) in analysis of covariance models.

4). The associations for systolic and diastolic BP were similar (data not shown).

Finally, we evaluated the effect of age on the retinal vessel diameter and BP associations. Figure 3 shows the multivariate adjusted association of retinal arteriolar diameters and mean arterial BP by age. The association of narrower retinal arteriolar diameters with higher BP was stronger in younger persons. Retinal arteriolar diameters were narrower by 7.0 μm in persons aged 43 to 54 years, by 3.3 μm in persons aged 55 to 64 years, by 4.0 μm in persons aged 65 to 74 years, and by 2.5 μm in persons aged 75 to 84 years, for each 10-mm Hg increase in mean arterial BP. Venular diameters were not related to BP in younger or older people (data not shown).

We found no interaction in analyses stratified by gender, hypertension, diabetes, and cigarette smoking status (data not shown).

Discussion

The present study provides population-based data on the distribution of retinal arteriolar and venular diameters—measured by using a quantitative, computer-based technique on digitized retinal photographs—and their cross-sectional associations with age and BP in adult white men and women aged 43 to 86 years. First, we showed that both retinal arteriolar and venular diameters are narrower in older than in younger people, independent of BP and other factors. Because arteriolar and venular diameters appear to narrow by a similar magnitude with age (approximately 2 μm for each decade of increase in age), the ratio of their diameters, the AVR, was relatively constant and independent of age. Second, independent of age and other risk factors, we showed that retinal arteriolar diameters are narrower in persons with higher BP. In contrast, venular diameters were not significantly related to BP. Thus, the AVR, as an indicator of relative arteriolar to venular diameters, also showed a strong and inverse relationship with increasing BP. Finally, we showed that the association of narrower retinal arteriolar diameters and higher BP was weaker in older persons.

Our study supports some of the findings in studies in other populations and settings (the ARIC study, the Cardiovascular Health Study [CHS] and the Blue Mountains Eye Study [BMES] in Australia), in which similar approaches were used to measure retinal vessel diameters. Although all three studies used a computer-assisted imaging approach and the Parr-Hubbard formula to quantify retinal vessel diameters from digitized photographs, these studies are not directly comparable, as the sampling methodologies and sociodemographic characteristics of the study populations are different. In the ARIC study and the CHS, we used the AVR as a measure of retinal arteriolar narrowing.[10–14,30–32] This was based on the assumption that potential magnification differences between photographs could

Table 4. Relationship of Retinal Vessel Diameters with Age and Mean Arterial Blood Pressure

	Retinal Arteriolar Diameter Mean Change (μm)* (95% CI)	P	Retinal Venular Diameter Mean Change (μm)* (95% CI)	P	Retinal AVR Mean Change* (95% CI)	P
Age and Gender Adjusted Model†						
Age, 10 years	−2.3 (−1.7 to −2.8)	< 0.001	−2.3 (−1.8 to −2.9)	< 0.001	−0.0007 (0.000 to 0.000)	0.53
Mean Arterial Blood Pressure, 10 mm Hg	−4.9 (−4.4 to −5.4)	< 0.001	−0.5 (0.02 to −1.0)	0.06	−0.020 (−0.018 to −0.021)	< 0.001
Multivariate-Adjusted‡						
Age, 10 years	−2.1 (−1.5 to −2.7)	< 0.001	−2.0 (−1.4 to −2.6)	< 0.001	−0.001 (0.000 to 0.000)	0.36
Mean Arterial Blood Pressure, 10 mm Hg	−4.4 (−3.8 to −5.0)	< 0.001	−0.4 (0.3 to −1.0)	0.28	−0.018 (−0.015 to −0.020)	< 0.001

* Regression coefficient of age and mean arterial blood pressure in linear regression models of retinal arteriolar diameters, venular diameters, and AVR.

† Linear regression models include the following covariates: age, mean arterial blood pressure, and gender.

‡ Linear regression models include the following covariates: age, mean arterial blood pressure, gender, hypertension status, diabetes status, serum glucose, total and HDL cholesterol levels, body mass index, and cigarette smoking status.

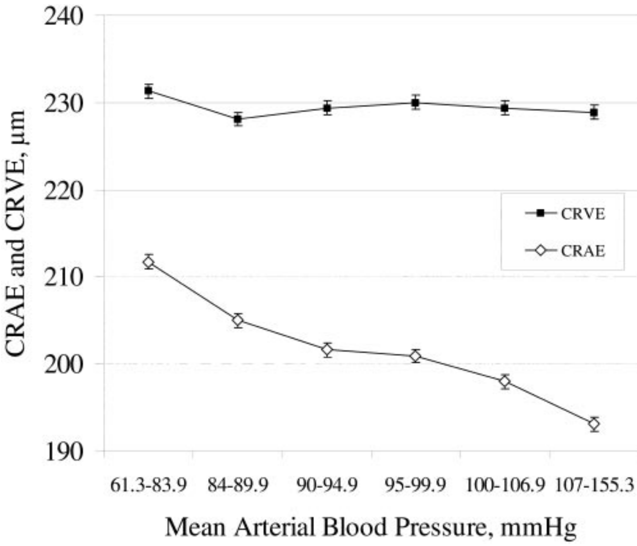

FIGURE 1. Retinal arteriolar and venular diameters (CRAE and CRVE), by mean arterial blood pressure, adjusted for age and gender.

result in measurement error (e.g., vessel caliber may be artificially magnified in photographs of myopic eyes), and that the AVR would minimize such an error, because retinas with artificially magnified arterioles could be expected to have similarly magnified venules. In the middle-aged ARIC study population (n = 8524, age 49–73 years), we reported a smaller AVR in older persons, suggesting that retinal arterioles narrow with increasing age.[30] In the older CHS population (n = 2050, age 69–97 years), however, we found no relationship between AVR and age.[31] Our present study now suggests that both retinal arteriolar and venular diameters decrease with age. Because the age-related decline was similar in magnitude for arterioles and venules, the AVR remained relatively stable over the entire age range in the study population. The BMES in Australia (n = 3654, age 49–98 years) also reported a similar age-related narrowing of both arterioles and venules.[33] However, the magnitude of the age-related narrowing was nearly twice that found in our population. Retinal arteriolar diameters decreased by 4.8 μm and venular diameters by a 4.1-μm per decade increase with age (after similar adjustment for gender and mean arterial BP). One possible explanation for this difference is that the sample population in the BMES was older, and it is possible that vessel narrowing was greatest in the oldest people, thus skewing the average decline for the total sample.

Previous studies have suggested that retinal arteriolar narrowing, assessed qualitatively through clinical ophthalmoscopy, is an early but characteristic sign in people with hypertension.[1–4,34] The strong association between elevated BP and narrowed retinal arteriolar diameters, assessed quantitatively in the present study, provides important data to support these early observations. We found venular diameters not to be related to BP. After multivariable adjustment, each 10-mm Hg increase in mean arterial BP was associated with a 4.4-μm ($P < 0.001$) decrease in arteriolar diameters but only a 0.4 μm ($P = 0.28$) decrease in venular diameters. Thus, our study suggests that the impact of BP on arterioles is much more prominent than on venules, supporting the concept that retinal venules have generally relatively constant caliber, except in specific circumstances (severe diabetic retinopathy or central retinal venous obstruction). We also found that the effect of BP on retinal arteriolar diameters is stronger in younger than in older people. Each 10-mm Hg increase in mean arterial BP was associated with a 7.0-μm decrease in arteriolar diameters in younger persons 43 to 54 years, but with only a 2.5-μm decrease in older persons 75 to 84 years. This finding provides new data to support previous observations by Leishman[3] and Scheie[4] that generalized retinal arteriolar narrowing results from a combination of hypertension and arteriolosclerosis. Thus, the weaker association of BP and arteriolar diameters in older people reflects an age-related increase in rigidity and sclerosis of retinal arterioles that prevents a similar severity of narrowing in younger persons.

In general, the associations between retinal vessel diameters and BP described herein are in keeping with results from the ARIC study, the CHS, and the BMES. All three studies showed that retinal arteriolar diameters are strongly and inversely associated with elevated BP,[12,32,33] but that venular diameters are not associated[12,32] (or only weakly associated[33]) with BP. For example, in the BMES, each 10-mm Hg increase in mean arterial BP was associated with a 3.5-μm decrease in arteriolar diameters but only a 0.96-μm decrease in venular diameters.[33] The weaker association of BP and arteriolar diameters in the BMES is again likely related to the older population in that study compared with that in Beaver Dam.

We also note that in hypertensive persons, those with uncontrolled BP despite treatment or those who were not receiving treatment had greater arteriolar narrowing than those with good BP control. This supports previous analyses in Beaver Dam and in the Blue Mountains that showed people with uncontrolled or untreated hypertension were significantly more likely to have focal retinal changes, including focal arteriolar narrowing, arteriovenous nicking and retinopathy than hypertensive people with adequate BP control.[35–37] Because both generalized retinal arteriolar narrowing and the focal retinopathy changes are correlated with end-organ damage elsewhere and independently predict stroke,[14] these data highlight the importance of appropriate BP control in reducing hypertension-associated complications.

Important limitations of this study should be noted. First, because these analyses were cross sectional, it is impossible to determine cause (e.g., increasing age and BP) and effect (e.g., narrowing of arteriolar diameters). Prospective data from the ARIC study suggest that retinal arteriolar narrowing may even precede the onset of hypertension (Wong TY, unpublished data, 2003). Second, selection bias may have masked or attenuated some associations, as a number of photographs were ungradable because of the presence of cataract (see Table 1).

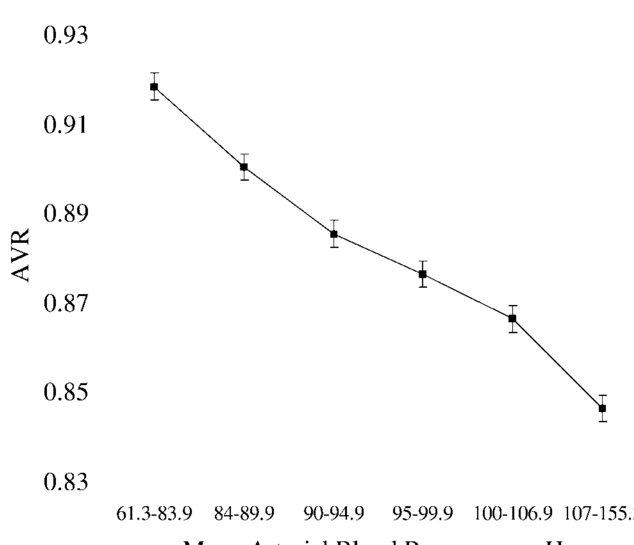

FIGURE 2. Retinal arteriole-to-venule ratio (AVR), by mean arterial blood pressure, adjusted for age and gender.

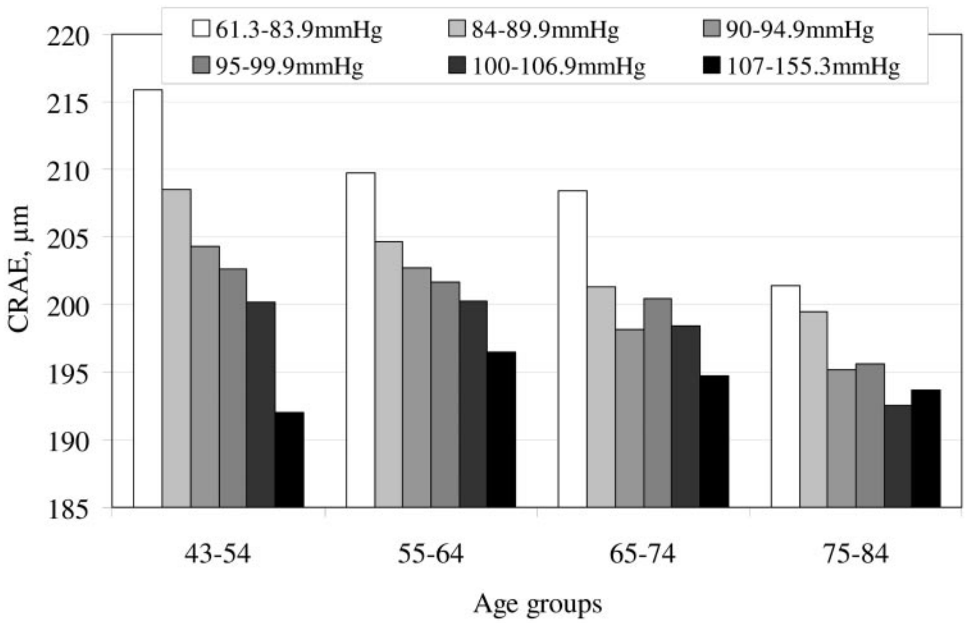

FIGURE 3. Retinal arteriolar diameters (CRAE), by mean arterial blood pressure, in persons of different age-groups.

Finally, despite the computer-based approaches used to measure retinal vessel diameters and the overall high reproducibility of the measurements, unknown sources of variability in these measurements cannot be excluded. Retinal vessel diameters may change in size in an individual, even over a short period. For example, the caliber of retinal vessel changes with the pulse cycle and taking photographs at untimed points in the pulse cycle may result in an unrecognized source of variation in the measurements of retinal vessel diameters.[38] This imprecision may have resulted in some attenuation of the BP association.

In conclusion, using a computer-assisted imaging method to measure retinal vessel calibers from photographs, we found that the diameters of retinal arterioles and venules narrow with increasing age. Independent of age, retinal arteriolar diameters narrow with increasing BP. The weaker association of BP and arteriolar diameters in older people provides evidence that increased arteriolosclerosis of retinal arterioles may prevent the degree of narrowing with higher BP that occurs in younger persons.

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