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ORIGINAL ARTICLE

Association Between Retinal Vessel Caliber and Arterial Stiffness in a Population Comprised of Normotensive To Early-Stage Hypertensive Individuals

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BACKGROUND
Although impairment of the micro- and macrocirculation is considered inherent to sustained hypertension, there is a substantial lack of studies investigating whether an association exists between micro- and macrovascular damage, especially in early-stage hypertension.

METHODS
We studied a meticulously selected population, free of diabetes and cardiovascular disease, of 223 individuals: 137 never-treated, newly diagnosed patients with recent onset of hypertension and 86 normotensive individuals. Nonmydriatic retinal photography was used to assess retinal microvascular diameters, including central retinal arteriolar (CRAE) and venular equivalent and arteriovenous ratio (AVR). Arterial stiffness was evaluated by measurement of pulse wave velocity (PWV) and aortic augmentation index (AIx).

RESULTS
Compared with normotensive subjects, hypertensive patients exhibited significantly increased PWV (8.1 vs. 7.1 m/sec; $P < 0.001$) and AIx (23.86% vs. 18.8%; $P = 0.01$) and decreased CRAE (86.47 vs. 91.44 μm; $P = 0.001$) and AVR (0.74 vs. 0.78; $P = 0.007$). A significant inverse association was demonstrated between PWV and CRAE ($r = -0.205$; $P = 0.002$), which remained significant after multivariable analysis. Likewise, CRAE ($P = 0.04$) and AVR ($P = 0.02$) were independent predictors of AIx.

CONCLUSIONS
This study shows for the first time an association between quantitatively assessed retinal abnormalities and increased arterial stiffness in a sample of early-stage hypertensive and normotensive individuals, suggesting that micro- and macrocirculation impairment in hypertension is a dynamic, mutual, interdependent process present from its very early stages. Given the predictive value of both retinal arteriolar narrowing and arterial stiffness in terms of cardiovascular mortality and morbidity, identification of combined micro- and macrovascular damage might be helpful in cardiovascular risk stratification of hypertensive patients.

Keywords: arterial stiffness; arteriovenous ratio; blood pressure; hypertension; hypertensive retinopathy; macrocirculation; microcirculation; pulse wave velocity.

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Assessment of microcirculation in the arterial conduit has received increasing attention over the previous years. Microcirculation has been recognized as a major site of damage in the organs targeted by cardiovascular disease, including the heart, the brain, the kidney, and the retina. Of all of these organs, the retina represents an open and easily accessible window for the *in vivo* study of human microcirculation. This unique characteristic, combined with the introduction of advanced retinal imaging techniques, has rendered the study of the retinal microvasculature a part of both large-scale epidemiological studies and clinical practice in the field of cardiovascular disease.

The predictive value of mild hypertensive retinopathy in terms of cardiovascular mortality and morbidity has not only been demonstrated in a recent multitudinal study among hypertensive and normotensive individuals[1] but also further verified in a recently published meta-analysis that identified both retinal arteriolar narrowing and venular widening as independent predictors of future development of hypertension.[2] In addition, we recently showed for the first time that retinal arterioral narrowing is observed even in the very early stages of essential hypertension, confirmed by 24-hour blood pressure (BP) monitoring.[3]

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While the significance of blunted microvascular function under the continuous effect of high BP is beginning to unfold, loss of elasticity and subsequent arterial stiffness of the large conduit arteries has been considered intrinsic to hypertension. Decreased arterial compliance is one of the earliest detectable markers of morphological and functional changes of the arterial wall in hypertension.[4] Several measurements of vascular stiffness are now available, with pulse wave velocity (PWV) emerging as the gold standard for the evaluation of aortic stiffening, independently associated with an increased risk of cardiovascular morbidity and mortality.[5,6] A growing body of evidence suggests that arterial stiffness is associated with microvascular disease in target organs, including the heart, the kidney, and the brain,[7,8] reinforcing the concept of a cross-talk between large and small arteries in hypertension.[9]

Although specific reliable tools have been developed that can easily, promptly, and noninvasively quantify both arterial stiffness and retinal arterioral narrowing and have been widely applied in large populations, there is a remarkable lack of studies investigating the relationship between aortic stiffness and retinal microvascular alterations in the very early stages of essential hypertension. We thus aimed at investigating the interface between micro- and macrovascular alterations, measured by specifically designed retinal evaluation software and PWV, respectively, in a meticulously selected group of newly diagnosed, never-treated, otherwise healthy patients with recent duration of hypertension, compared with their normotensive counterparts. To further evaluate vascular function, we calculated aortic augmentation Index (Aix), another measure of arterial stiffness and wave reflection.[6]

METHODS

The study population consisted of consecutive patients who attended the Hypertension Unit of the 2nd Propedeutic Department of Internal Medicine, Aristotle University, Thessaloniki, Greece. The study was conducted in accordance with the principles of the Helsinki Declaration and was approved by the Ethics Committee of Aristotle University of Thessaloniki. All participants were Caucasians and gave their written informed consent. Patients had never been previously treated with antihypertensive agents, received no other medication, and had no other known health problems. To ensure recent onset of hypertension, only patients with reported normal office and/or home BP measurements during the previous 12 months were included. Patients with secondary causes of hypertension and other comorbidities (including diabetes mellitus and cardiovascular diseases) verified through history, medical examination, and laboratory tests were excluded from the study. Anthropometric characteristics and alcohol and smoking habits were recorded, and body mass index was calculated as weight in kilograms divided by height in meters squared (kg/m^2). Blood samples were derived from all patients after overnight fasting, and serum total cholesterol, high- and low-density lipoprotein cholesterol, and triglyceride levels were estimated.

Essential hypertension was defined as BP >140/90 mm Hg according to guidelines (Seventh Report of the Joint National Committee[10] and European Society of Hypertension–European Society of Cardiology).[11] Blood pressure was measured with a mercury sphygmomanometer in the beginning of the study and with an automatic one (Microlife BP3MD1-3, Microlife AG, Switzerland) after mercury prohibition according to a standard methodology and was determined as the mean of the second and third value of 3 consecutive blood pressure recordings taken at a 2-minute interval after the subject was seated for 10 minutes. Mean arterial pressure was calculated by the formula (2 × diastolic BP) + systolic BP) / 3.

Estimation of aortic stiffness

Aortic stiffness was estimated by the measurement of both PWV and AIx. The Sphygmocor device (AtCor Medical, Sydney, Australia) was used for their assessment according to a standard protocol after overnight fasting. Regarding PWV, waveforms at the right common carotid and right femoral site were recorded sequentially after a 15-minute resting period in the supine position. Surface distance between the 2 recording sites was measured (sternal notch to carotid site and sternal notch to femoral site). Wave transit time was calculated using a simultaneously recorded electrocardiogram as a reference. Two successive measurements were recorded, and the mean was used. Measurements were performed by 2 different investigators, with intraclass correlation coefficients of 0.964 and 0.979, respectively, and interclass correlation coefficient of 0.960 calculated in a sample of 20 patients.

AIx was expressed as a percentage of the ratio of augmentation pressure to central pulse pressure (the difference between central systolic and diastolic pressure). Aortic augmentation pressure was calculated as the difference between the first and second systolic peaks of the ascending aortic waveform, obtained from applanation tonometry. For our analysis, we used AIx corrected for the mean heart rate of 75 bpm. Measurements were performed by 2 different investigators, with intraclass correlation coefficients of 0.957 and 0.960, respectively, and interclass correlation coefficient of 0.955 calculated in a sample of 20 patients.

Retinal vessels photography and analysis

All patients underwent bilateral, nonmydriatic digital fundus photography using a NIDEK AFC-230/210 camera (NIDEK, Fremont, CA). Two photographs were obtained from each eye, centered in the mid-fundus between the optic disc and the macula, and the best one was examined by a trained grader masked to the subject's identity and BP group assignment.

To achieve retinal vessel measurement and analysis, semiautomated computer software was developed by our Hypertension Unit in collaboration with the Institute of Computer Science, Foundation for Research and Technology–Hellas. Retinal photographs were assessed according to a standard protocol, which has been

described in detail elsewhere.[3,12,13] The software consisted of a measurement module that estimates vessel diameter in the input images and a graphical user interface module that facilitates user intervention at points of interest. The measurement area of the images was defined as the area from one half to 1 disc diameter from the optic disc margin. Parr and Hubbard formula, as modified in the Atherosclerosis Risk in Communities protocol,[14] was calculated automatically to summarize indices of the average retinal arterioral and venular diameters, referred to as the central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE), respectively,[14,15] as well as their ratio (arteriovenous ratio (AVR) = CRAE/CRVE).

Statistical analysis

Analysis was performed using the Statistical Package for Social Sciences version 19 (SPSS, Chicago, IL). Differences between mean values for continuous variables were estimated by Student *t* or Mann–Whitney test, whereas qualitative variables were compared by the χ^2 test. Continuous variables were described as mean ± SD or as median (minimum–maximum) according to the normality of their distribution. Correlation coefficients were calculated with Pearson and Spearman rank tests. To explore the relationship between arterial stiffness and retinal vessel diameters while controlling for other covariables, we applied models of multivariable linear regression analysis. Where needed to transform a non-normal distribution to a normal distribution, we used the logarithmic mean of the parameter. Intra- and inter-rater reliability were calculated by intraclass correlation coefficients. A probability value of $P \leq 0.05$ was considered statistically significant.

RESULTS

The study population consisted of 223 subjects aged 43.8 ± 11.7 years, of whom 142 (63.7%) were men and 81 were women (36.3%). According to their BP measurements, subjects were divided into hypertensive and normotensive groups (n = 137 and 86 individuals, respectively). All study participants reported alcohol intake of <5 units/week. Baseline characteristics of the study population are summarized in Table 1.

Arterial stiffness indices (PWV and AIx) were significantly increased in the hypertensive group compared with the normotensive group. Likewise, a significant difference was found in the retinal vascular calibers measured in the 2 groups, with hypertensive patients exhibiting lower CRAE and AVR compared with their normotensive counterparts (Table 2). CRVE did not differ significantly between the groups. No sex differences were observed concerning PWV and the retinal microcirculation indices. On the contrary, AIx significantly differed between men and women (19.5% vs. 32%, respectively; $P < 0.001$).

In the univariable analysis, both PWV and AIx were significantly correlated with age ($r = 0.511$ and $r = 0.536$; both $P < 0.001$), systolic BP ($r = 0.433$, $P < 0.001$; $r = 0.156$, $P = 0.022$), diastolic BP ($r = 0.362$, $P < 0.001$; $r = 0.195$; $P = 0.004$), total cholesterol ($r = 0.511$ and $r = 0.536$; both $P < 0.001$), and low-density lipoprotein cholesterol ($r = 0.282$ and $r = 0.260$; both $P < 0.001$). Moreover, PWV also correlated with triglycerides ($r = 0.206$; $P = 0.003$) and body mass index ($r = 0.236$; $P < 0.001$). Regarding micro- and macrocirculation associations, a significant inverse association was demonstrated between PWV and CRAE in our study population ($r = -0.205$; $P = 0.002$). PWV was identified as the only predictor of CRAE (beta = −0.189; $P = 0.04$) even after adjustment for aortic pulse pressure (beta = 0.049; $P = 0.12$) and other parameters (age, smoking, body mass index,

Table 1. Baseline characteristics of the study population

Characteristic	Hypertensive patients	Normotensive subjects	*P* value
Age, y	44.7 ± 11.5	42.5 ± 12.1	0.17
Male sex, %	70.6	52.3	0.009
Office SBP, mm Hg	150 ± 14	123 ± 10	<0.001
Office DBP, mm Hg	94 ± 10	78 ± 8	<0.001
Heart rate, pulses/min	71 ± 11	68 ± 9	0.03
Smokers, %	43.3	42.8	0.91
BMI, kg/m^2	27.8 ± 4.2	26.2 ± 4.2	0.007
eGFR, ml/min	117.1 ± 34.1	111.0 ± 31.5	0.20
Total cholesterol, mg/dl	209.9 ± 43.3	191.0 ± 34.8	0.001
LDL cholesterol, mg/dl	136.6 ± 36.7	118.6 ± 34.3	0.001
HDL cholesterol, mg/dl	47.19 ± 11.8	51.4 ± 12.0	0.04
Triglycerides, mg/dl	111.5 (31.0–375.0)	106.3 (13.0–314.0)	0.009

Continuous variables are given as mean ± SD or as median (minimum–maximum) according to the normality of their distribution.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.

mean arterial pressure, total cholesterol) in the multivariable multiple regression model. The correlations between PWV and retinal vascular calibers are depicted in Figure 1. PWV did not significantly correlate with retinal microcirculation indices when hypertensive and nonhypertensive individuals were studied separately.

To verify whether the above associations remained statistically significant independently of the other covariables, we developed 3 multivariabl regression models, one for each retinal vascular caliber studied (Table 3). Age and mean arterial pressure were found to be statistically significant in all models, whereas from the different measurements of retinal vascular calibers, only CRAE remained a significant predictor.

Regarding AIx, univariable analysis showed a significant negative association with CRAE ($r = -0.145$; $P = 0.03$) but not with CRVE ($r = -0.042$; $P = 0.55$) and AVR ($r = -0.096$; $P = 0.16$). However, in the multiple regression models (Table 4), apart from age, mean arterial pressure, and male sex, both CRAE and AVR were identified as significant, independent predictors of AIx, whereas CRVE did not correlate significantly with AIx in the multivariable model.

DISCUSSION

To our knowledge, this is the first study to demonstrate an association between retinal arteriolar narrowing and increased arterial stiffness, both assessed with quantitative measures, in a meticulously selected sample of naive, never-treated patients with early-stage (within only 1 year of its appearance) essential hypertension and normotensive individuals. This association was independent of age, BP levels, and other vascular risk factors. In addition, decreased CRAE and AVR were identified as independent predictors of PWV and AIx, respectively, in the multivariable multiple regression models. It should be noted that when hypertensive and nonhypertensive individuals were studied separately, PWV did not significantly correlate with retinal microcirculation indices, probably because of the relatively small size of these subgroups (n = 137 and 86 individuals, respectively). This study confirms previous findings that micro- and macrocirculation (shown by decreased retinal arteriolar diameters and increased arterial stiffness, respectively) are impaired in hypertensive patients compared with normotensive subjects[3,16,17] Most important, this study moves one step further from the above observation, showing that not only do both quantitative measures denote presence of micro- and macrovascular impairment but they also significantly correlate with each other soon after the development of essential hypertension and long before the establishment of cardiovascular complications induced by sustained hypertension.

The micro- and macrovascular interplay in hypertension is currently the subject of intense investigation. This study adds to the accumulating data of concomitant micro- and macrocirculation impairment in the retina, the skin, the

Table 2. Arterial stiffness indices and retinal vascular calibers of the study population

Vascular parameter	Hypertensive patients	Normotensive subjects	*P* value
PWV, m/s	8.1 (5.4–14.6)	7.1 (4.3–10.9)	<0.001
Aortic index, %	23.86 ± 12.37	18.80 ± 14.68	0.01
CRAE, μm	86.47 ± 10.02	91.44 ± 10.61	0.001
CRVE, μm	118.61 ± 15.41	118.88 ± 14.12	0.90
AVR	0.74 ± 0.11	0.78 ± 0.12	0.007

Continuous variables were described as mean ± SD or as median (minimum–maximum) according to the normality of their distribution.
Abbreviations: AVR, arteriovenous ratio; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; PWV: pulse wave velocity.

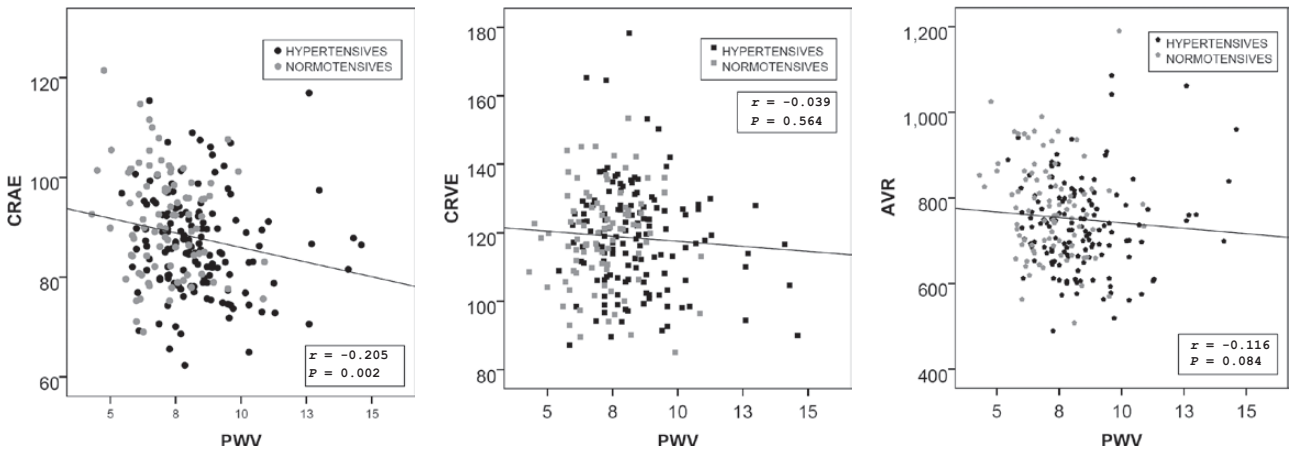

Figure 1. Correlations of PWV with retinal vessel diameters. Hypertensive patients are depicted in black, and normotensive subjects are depicted in gray. Abbreviations: AVR, arteriovenous ratio; CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; PWV, pulse wave velocity.

Table 3. Multivariable multiple regression models of pulse wave velocity determinants according to each retinal vascular caliber

Dependent variable	PWV (adjusted R^2 = 0.443; R^2 = 0.459; P < 0.001) (Retinal caliber: CRAE)				PWV (adjusted R^2 = 0.441; R^2 = 0.460; P < 0.001) (Retinal caliber: CRVE)				PWV (adjusted R^2 = 0.437; R^2 = 0.454; P < 0.001) (Retinal caliber: AVR)			
			95% CI				95% CI				95% CI	
	St. C	*P* value	LB	UB	St. C	*P* value	LB	UB	St. C	*P* value	LB	UB
Age	0.463	<0.001	0.003	0.004	0.469	<0.001	0.003	0.004	0.473	<0.001	0.003	0.004
Smoking	0.007	0.88	−0.016	0.018	0.002	0.97	−0.018	0.019	0.002	0.97	−0.017	0.017
BMI	0.086	0.09	0.000	0.004	0.078	0.16	−0.001	0.004	0.078	0.13	0.000	0.004
MAP	0.322	<0.001	0.001	0.003	0.348	<0.001	0.002	0.003	0.334	<0.001	0.002	0.003
Heart rate	0.164	0.001	0.001	0.002	0.171	0.001	0.001	0.002	0.167	0.001	0.001	0.002
Total cholesterol	0.019	0.72	0.000	0.000	0.025	0.67	0.000	0.000	0.014	0.79	0.000	0.000
Retinal caliber	−0.098	0.049	−0.002	0.000	−0.005	0.92	−0.001	0.001	−0.062	0.21	−0.129	0.029

Three different models are presented in the table. In each of them, pulse wave velocity is the predicted variable, and age, smoking, body mass index, mean arterial pressure, cholesterol, and retinal calibers (the arteriolar in the 1st, the venular in the 2nd, and their ratio in the 3rd) are the covariables used as predictors.

Abbreviations: AVR, arteriovenous ratio; BMI, body mass index; CI, confidence interval; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; LB, lower boundary; MAP, mean arterial pressure; PWV, pulse wave velocity; St. C., standardized coefficient; UB, upper boundary.

Table 4. Multivariable multiple regression models of aortic index determinants according to each retinal vascular caliber

	AI (adjusted R^2 = 0.493; R^2 = 0.512; P < 0.001) (Retinal caliber: CRAE)				AI (adjusted R^2 = 0.481; R^2 = 0.500; P < 0.001) (Retinal caliber: CRVE)				AI (adjusted R^2 = 0.554; R^2 = 0.568; P < 0.001) (Retinal caliber: AVR)			
			95% CI				95% CI				95% CI	
	St. C	*P* value	LB	UB	St. C	*P* value	LB	UB	St. C	*P* value	LB	UB
Age	0.373	<0.001	0.029	0.054	0.375	<0.001	0.028	0.055	0.480	<0.001	**0.438**	**0.676**
Sex	0.482	<0.001	1.011	1.590	0.477	<0.001	0.993	1.579	0.427	<0.001	9.562	15.072
Smoking	−0.053	0.31	−1.010	0.314	−0.057	0.29	−0.432	0.129	−0.105	0.03	−5.560	−0.385
BMI	−0.015	0.78	−0.039	0.029	−0.025	0.66	−0.042	0.027	−0.051	0.30	−0.493	0.153
MAP	0.234	<0.001	0.012	0.035	0.260	<0.001	0.015	0.037	0.254	<0.001	0.168	0.374
Total cholesterol	0.017	0.77	−0.003	0.004	0.022	0.71	−0.003	0.004	0.025	0.63	−0.026	0.042
Retinal caliber	−0.113	0.04	−0.027	−0.001	−0.016	0.77	−0.011	0.008	−0.115	0.02	−26.213	−2.691

Three different models are presented in the table. In each of them, augmentation index is the predicted variable, and age, sex, smoking, body mass index, mean arterial pressure, cholesterol, and retinal calibers (the arteriolar in the 1st, the venular in the 2nd, and their ratio in the 3rd) are the covariables used as predictors.

Abbreviations: AI, augmentation index, AVR, arteriovenous ratio; BMI, body mass index; CI, confidence interval; CRAE, central retinal arteriolar equivalent; CRVE, central retinal venular equivalent; LB, lower boundary; MAP, mean arterial pressure; St. C., standardized coefficient; UB, upper boundary.

kidney, the brain, and the aorta of hypertensive patients, showing coexisting subclinical damage of both small (retinal) and large (aortic) vessels, even in the very early stages of essential hypertension. Several explanations have been proposed to support the pathophysiological background of the hypothesis of their mutual and interdependent development. Microcirculation impairment of the vasa vasorum in experimental models causes structural and functional dysfunction of the larger arterial vessels, reducing their elastic properties.[18,19] In addition, increased peripheral resistance owing to microvascular damage may account for an increase in mean arterial BP, which in turn promotes large artery stiffening.[9] Inversely, stiffened large arteries, possibly through increased pulse pressure, may aggravate impairment of the microvasculature.[7] In our study, however, PWV significantly predicted CRAE independent of pulse pressure, confirming the role of PWV as arterial stiffness index and suggesting that increased arterial stiffness might mediate changes in the retinal microcirculation. After all, both small and large vessels are subject to a series of pathophysiological changes induced by hypertension, including endothelial dysfunction[20–22] and inflammatory factors.[23,24]

Our study, excluding the effects of long-standing hypertension, suggests that micro- and macrocirculation impairment in hypertension is a dynamic, mutual, and interdependent process present from the very early stages of hypertension onset. Therefore, it appears that the true

challenge is not to determine whether micro- or macrovascular impairment precedes in this vicious circle but how identification of subclinical vascular damage can be useful in clinical terms. The clinical interpretation of our findings may be of major significance. Traditional risk scores may underestimate cardiovascular risk in specific population subgroups, especially those at low or intermediate risk, including asymptomatic hypertensive patients.[11] Reassessment of patients' cardiovascular risk using imaging biomarkers, including quantitative assessment of the retinal vasculature with retinal photography and the arterial stiffness with PWV, may enhance the accuracy of cardiovascular risk prediction. Both measures have been verified as significant predictors of cardiovascular mortality and morbidity in hypertensive patients.[25–27] Whether reversal of these alterations with appropriate medication may be accompanied by improvement of residual cardiovascular risk remains to be investigated in future studies.

Previous studies dealing with the association between retinal vascular calibers and arterial stiffness in hypertensive patients are scarce and do not always coincide. In a rural, community-dwelling Japanese population, higher branchial–ankle PWV was predicted by mild retinal changes, but the population was affected by other comorbidities and the retina was only qualitatively evaluated.[28] The Multi-Ethnic Study of Atherosclerosis revealed an association between retinal arteriolar narrowing and reduced aortic distensibility in a large population of 3,425 individuals.[29] However, the latter parameter was determined by chest magnetic resonance imaging, which is an expensive method that is hard to incorporate in the everyday clinical setting for the purpose of evaluating arterial stiffness and therefore lacking robust validation in clinical trials,[30] contrary to PWV, which is the gold standard for the evaluation of aortic stiffening according to the guidelines.[2] In addition, study participants were not free from other comorbidities, including diabetes mellitus, and retinal photographs were taken at a 2-year interval from the magnetic resonance imaging examination. PWV was used in a succeeding study that showed a significant association with the degree of hypertensive retinopathy.[31] However, hypertensive retinopathy was only qualitatively addressed and therefore subject to the inherent limitations of qualitative evaluation, and the vast majority of participants were already under antihypertensive treatment and not entirely free from other comorbidities, including diabetes mellitus. On the contrary, PWV was similar in all tertiles of retinal AVR in a population of hypertensive, diabetic, and healthy individuals, but the software used for the quantitative assessment of the retinal vasculature only assessed pairs of the main vessels, rejecting all other vessels.[32] Data on the association between pulse wave analysis and retinal microvascular diameters are even fewer, with 1 study failing to reveal any correlations of central, pulse, and augmentation pressures or AIx to AVR, CRAE, and CRVE in a subgroup analysis of 46 healthy male marathon runners.[33]

Although the prognostic role of retinal venular widening in terms of hypertension prediction is gaining recognition,[2] CRVE was similar between newly diagnosed hypertensive and normotensive individuals in our study. Previous studies suggest that CRVE is associated with stroke;[26] however, in our study, CRVE did not significantly correlate with PWV nor AIx. A relationship between PWV and CRAE, but not CRVE, which was consistent with our results, was demonstrated in a group of 145 Asian acute ischemic stroke patients.[34]

Using quick, easy, and reliable tools (quantitative measurement of retinal vascular diameters by retinal photography and arterial stiffness with PWV) that are well established and widely applied not only in the field of cardiovascular research but also in the everyday clinical setting, our study is the first to reveal an association between micro- and macrovascular impairment as an early and distinctive feature of hypertensive vascular disease. The main limitation was the cross-sectional nature of the study. Therefore, the causal and temporal relationships between retinal microvascular and hypertension cannot be examined. Whether regression of these alterations with appropriate treatment denotes improvement of patients' cardiovascular risk profile remains to be investigated in future studies.

DISCLOSURE

The authors declared no conflict of interest.

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