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Complete Blood Count and Retinal Vessel Diameters

Barbara E. K. Klein, MD, MPH, **Ronald Klein, MD, MPH**, **Chelsea E. Myers, MS**, and **Kristine E. Lee, MS**
Department of Ophthalmology and Visual Sciences, School of Medicine and Public Health, University of Wisconsin, Madison, Wisconsin, USA

Abstract

Objective—To examine the cross-sectional associations of components of the complete blood count with retinal vessel diameters.

Methods—The data are from the 1988–1990 baseline examination of the Beaver Dam Eye Study cohort (n=4730). Blood pressure was measured, a medical history including questions on smoking was obtained, and fundus photographs centered on the optic disc were taken and digitized. Retinal arteriole and venule diameters were measured using computer-assisted software. The central retinal arteriole equivalent (CRAE) and central retinal venule equivalent (CRVE) were computed. A complete blood count was done.

Results—In age and sex adjusted analyses, red blood cell count (RBC), hemoglobin, hematocrit, and white blood cell (WBC) count were all statistically significantly associated with CRVE and CRAE, while platelet count was associated only with CRVE. These relationships persisted in more fully adjusted models, except platelet count became statistically significantly associated with both CRAE and CRVE.

Conclusions—Blood components as measured in a complete blood count are significant correlates of retinal vessel diameters and should be considered in analyses where retinal blood vessel diameters are outcomes.

INTRODUCTION

Retinal vessel diameters are associated with a variety of systemic traits and diseases. For example, narrower retinal arterioles are associated with higher blood pressure,[1–4] myocardial perfusion,[5] left ventricular remodeling,[6] and stroke.[7] Ikram and colleagues have found that wider retinal arterioles are associated with impaired fasting glucose and diabetes.[8] Wider retinal venules are associated with severity of diabetic retinopathy[9] and relatively smaller retinal venular diameter was found in persons with diabetes compared to those of similar age without type 2 diabetes[9] and with incident proteinuria in persons with type 2 diabetes.[10] Larger retinal venule diameters were associated with a variety of atherosclerosis indicators, such as higher carotid plaques scores and greater aortic calcifications, and risk factors such as body mass index and lower HDL cholesterol in the Rotterdam Study.[11,12]

Correspondence to: Barbara E. K. Klein, MD, MPH, University of Wisconsin-Madison, School of Medicine and Public Health, Department of Ophthalmology and Visual Sciences, 610 North Walnut St., 4th Floor WARF, Madison, WI 53726-2336, Phone: (608) 263-0276, Fax: (608) 263-0279, kleinb@epi.ophth.wisc.edu.

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Author contributions
Conception and design (BK, RK), acquisition of data (BK, RK), analysis and interpretation of data (BK, CM, KL), drafting of the manuscript (BK), critical revision of the manuscript for important intellectual content (RK, CM, KL), statistical expertise (CM, KL), obtaining funding (BK, RK), administrative/technical/material support (BK, CM, KL), supervision (BK).

It has been reported that hematocrit is significantly associated with retinal venular diameter13 although in the few studies that have investigated this, relationships are not consistent.[14] Also, white blood cell (WBC) count has been found to be associated with retinal venular diameters in a large population based study.[15] High WBC count, as is characteristic of leukemia,16 can alter the microvessel diameters due to the high concentration of cells. Furthermore, it has been demonstrated that leukocytosis in the peripheral and retinal circulation is associated with dilation of retinal arterioles and retinal venules in an experimental setting.17 When retinal arterioles are embolized with glass microspheres in a laboratory setting, the diameters of the embolized vessels are clearly dilated to accommodate the particulate emboli.18

Since retinal vessels (arterioles and venules) are parts of dynamic microvascular beds that may reflect many physiologic factors as well as the substances within them, we hypothesize that these structures may be influenced by the cells that are measured in the complete blood count in addition to other physiologic factors. We examine this hypothesis in population based data collected as part of the Beaver Dam Eye Study.

METHODS

Population

There were 4926 persons 43–86 years of age who participated in the baseline examination of the Beaver Dam Eye Study in 1988–2000. Ninety-nine percent of the population was of European ancestry.[19] Informed consent was obtained from participants, and all examinations followed a similar protocol that was approved by the institutional Human Subjects Committee of the University of Wisconsin and conformed to the tenets of the Declaration of Helsinki.

Medical History

A history was obtained during the study evaluation during which questions were asked about smoking.

Laboratory and Examination Methods

A complete blood count (Coulter counter method) as well as a standardized medical history, measurements of blood pressure by standard protocol[20] and ocular examination with retinal photographs were obtained.20 Photographs of Early Treatment Diabetic Retinopathy Study field 1 were digitized and retinal vessel diameters were measured with a computer assisted standardized grading protocol from these images.21,22

Measurement of retinal vessel diameters

Stereoscopic 30° color retinal photographs were converted to digital images by a high-resolution scanner (Nikon LS2000, Nikon Inc, Japan) using standard settings for all photographs. Images were displayed on 21-inch monitors set to 1600 × 1200 pixels. The diameters of all arterioles and venules coursing through a standard area 0.5 to 1.0 disc diameters from the optic disc margin (Zone B) were measured using a custom computer program (Retinal Analysis, University of Wisconsin-Madison), according to a standard protocol. Each vessel was identified as an arteriole or venule by a trained grader, using the original color photograph for reference. The grader selected a segment of the vessel in Zone B for measurement and used various tools to determine the validity of the measurement. A measurement was considered invalid if the grader could not get an accurate measurement after three attempts. The entire image was rejected if more than one arteriole or venule larger than 40 microns (μm) in diameter could not be measured accurately. This cut-off was

based on preliminary data that showed vessels smaller than this diameter had no substantial impact on the summary values.[21]

Definitions

Cigarette smoking status was determined according to the following criteria: a never smoker had smoked fewer than 100 cigarettes in his/her lifetime; a past smoker had smoked 100 or more cigarettes in his/her lifetime but reported that he/she was no longer smoking; a current smoker had smoked more than 100 cigarettes in his/her lifetime and reported that he/she was still smoking. Pack years was calculated by first dividing the average number of cigarettes smoked per day by 20 and then multiplying by the number of years smoked.

Statistical Methods

Statistical analyses were conducted in SAS, version 9 (SAS Institute Inc., Cary, NC). Means were compared for statistically significant differences by the t-test and analysis of variance when two or more than two groups, respectively, were involved. Because the distributions of the blood elements were highly skewed and differed by sex, each blood element was analyzed using sex-specific quintiles. We computed the quintiles for blood elements for each sex separately but analyzed the data with both sexes together (i.e., Q1 for men and Q1 for women were grouped together as Q1 for the entire group). Central retinal arteriolar equivalents and central retinal venule equivalents are computed based on the diameters of the six largest of each vessel type in standardized digitized photographs of the optic discs.[21] Univariate analyses between each variable and central retinal arteriole equivalent (CRAE) and central retinal venule equivalent (CRVE) were conducted using simple linear regression. In additional analyses, age, sex, smoking status, diabetes status, and the other vessel measurement were added into a model sequentially to determine the impact on model fit. A final model for each blood element was developed using stepwise model selection.

RESULTS

Of the 4926 individuals who were interviewed and examined at the baseline exam, individuals were excluded from the analyses if there was no measurement for CRAE or CRVE in either eye (N=114), if data were missing for any of the laboratory values used in the analysis (N=14), or if the individual had a condition or disease such as leukemia, thrombocythemia or polycythemia (N=68), leaving 4730 individuals eligible for analysis.

Individuals who were excluded were more likely to be older, female, hypertensive, and more likely to have lower diastolic blood pressure, higher levels of glycosylated hemoglobin and all other blood elements except platelet count than those included. There were no differences in systolic blood pressure, pack-years smoked, platelet count, or current smoking between the two groups (Table 1).

An increase of one sex-specific quintile of WBC, red blood cell (RBC) count, hemoglobin, and hematocrit is significantly associated with larger CRAE and CRVE (Table 2). An increase of one sex-specific quintile of platelet count was also significantly associated with larger CRVE. Additional adjustment for age does not change the significance of these relationships. When the elements are considered as continuous variables the relationships are unchanged from when they are considered as quintiles.

In order to investigate the relative strengths of the relationships of the blood elements to the vessel diameters, we developed models in which we sequentially included other known correlates of those diameters (Table 3). For all models, each element except platelet count was significantly associated with CRAE. The models indicate that including more of the additional variables increases the informativeness of the model measured by the change in

R^2. For all models, each blood element was significantly associated with CRVE. Additional adjustments for additional variables increased the R^2 of the model. The presence of diabetes has a small incremental effect on the fit of the models.

We next performed the modeling use a stepwise approach including as possible variables all those considered in model 4 of Table 3 (Tables 4 and 5). For CRAE, systolic blood pressure had the highest partial R^2, followed by smoking, the blood element, and diabetes for each blood element. In the model assessing the contribution of platelets to the other variables associated with CRAE, platelets no longer contributed a significant amount of information. For CRVE, smoking history has the greatest partial R^2, followed by the blood element and then sex and systolic blood pressure. Because of the importance of relative diameter, we repeated the analyses in table 4, this time including CRVE in the models for CRAE and CRAE in models for CRVE (Table 5). These additions markedly improved the R^2 of all models. In all models, the relative importance of smoking was diminished. The blood elements are the third most informative variable for CRVE or fourth most informative variable for CRAE when controlling for the other vessel measurement.

While the previous analyses consider each blood element individually, we next developed models when they are included together. We chose only one of the three measures of red blood cell status (RBC, hemoglobin and hematocrit) for the purposes of these analyses. We modeled the outcomes as was done in Tables 4 and 5. In models where CRAE is the outcome, and CRVE is not included, each of the blood element components adds significantly to the models with the red blood cell variable being most informative and WBC and platelet count adding less information. When CRVE is included the WBC is no longer significant in the models. In models where CRVE is the outcome, and CRAE is not included, each of the blood element components adds significantly to the models and, again, the red blood cell variables being most informative and WBC and platelets adding less information. When we add CRAE, all of the three different blood components remain significant in most models. The relative importance of most of the other variables that were used in the models in Tables 4 and 5 remain unchanged.

DISCUSSION

We have found that hematocrit, hemoglobin, RBC count, WBC count and platelet count are significantly associated with retinal vessel diameters. In addition, in our population these factors outweigh the relative importance of age, sex and diabetes status in all models for both CRAE and CRVE. The effects related to RBC are greater than those for WBC. There are relatively smaller effects of platelet count. The associations are direct, i.e., higher values are associated with wider diameters. While these data may indicate that these effects are related to that actual burden imposed by more particulate matter in the blood, it may be more informative to consider the physiologic factors related to the blood elements (counts). It is possible that relative systemic factors such as chronic hypoxia due to systemic diseases or exposures may be associated with relatively higher RBC count (and hemoglobin, hematocrit). An obvious exposure that is compatible with this notion is smoking, which we found to be associated with both CRAE and CRVE in analyses not adjusting for the diameter of either. Smoking, aside from potential effects on systemic hypoxia, is also associated with systemic inflammation. This mechanism has been invoked to explain previously described associations of WBC counts to CRVE. In the Atherosclerosis Risk in Communities Study, higher WBC count was also associated with larger CRAE.[13] Diabetes status, while significant in its effect, had a relatively small contribution compared to cigarette smoking for both CRAE and CRVE in our study.

Microvascular diameters undergo structural adaptation related to the local metabolic conditions.[23] Hematocrit influences local hemodynamics.[23] Vessel diameters are thought to change shear stress on vessel walls, dependent in part upon oxygen deficit and RBC signaling.[23] In the Rotterdam Study, retinal venule diameter was greater in persons with decreased cerebral blood flow and with decreased arteriolar oxygen saturation.[11,24] Oxygen stimulation is associated with decreased flow mediated diameters in large vessels.[25] While this may have implications for cardiovascular events, it is uncertain what the health impact of changes in the microvascular beds may be.

Another possible effect (or correlate) of hematocrit is to increase blood viscosity.[26] This increase in viscosity has been shown to be associated with risk factors for cardiovascular disease such as blood lipids and blood pressure27 and may also be a pathway whereby the blood factors we examined influence retinal vessel diameters.

Our study is limited in that it is a cross-sectional analysis and these findings may not be applicable to longitudinal data. Also, while we have controlled for the most important confounders, there may be others that we did not measure or that were not important in our analyses but may be important in other studies. Lastly, variability of our outcome (as well as our covariate) measurements may have influenced our findings, although we suspect that these would have led to our underestimate of the relationships we report.

In summary, we have found that blood cell counts (and related measures of hematocrit and hemoglobin) are significant correlates of retinal vessel diameters with greater effects than have been reported for some other correlates of these measures. We suggest that in research where retinal vessel diameters are the outcomes of interest, blood counts should be included as important determinants or correlates.

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Table 1

Characteristics of Those Included and Excluded from Analysis.

	Included			Excluded			
Risk factor	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**P value**
Age (years)	4730	61.74	11.07	196	69.14	11.74	<0.001
Systolic BP (mmHg)	4729	132.03	20.38	194	134.76	22.86	0.07
Diastolic BP (mmHg)	4729	77.39	10.99	194	75.69	11.42	0.04
Pack years smoked	4702	17.62	26.83	192	18.97	30.69	0.50
Glycosylated hemoglobin (%)	4727	6.08	1.56	176	6.94	2.63	<0.001
Hematocrit (%)	4730	43.04	3.73	177	44.64	6.63	<0.001
Hemoglobin (g/dL)	4730	14.48	1.37	177	15.04	2.35	<0.001
Platelet count (k/μL)	4727	288.51	73.53	177	298.43	151.96	0.10
White blood cell count (k/μL)	4729	7.35	2.08	177	8.48	3.61	<0.001
Red blood cell count (M/μL)	4730	4.66	0.44	177	4.82	0.78	<0.001
Sex (male)	2105	44.50		59	30.05		<0.001
Hypertension	2374	50.23		115	60.21		0.007
Diabetes	413	8.75		33	18.54		<0.001
Current smoker	926	19.59		44	23.68		0.29

SD = standard deviation; BP = blood pressure; CRAE = central retinal arteriole equivalent; CRVE = central retinal venule equivalent.

Table 2

Relationships of Blood Elements with Central Retinal Arteriole Equivalent and Central Retinal Venule Equivalent.

Blood Element		Sex	Range[a]	Central Retinal Arteriole Equivalent				Central Retinal Venule Equivalent			
				N[b]	Mean[b]	SD[b]	P value	N[b]	Mean[b]	SD[b]	P value
Hematocrit (%)	Q1	W	16.60–38.90	945	148.40	13.30	<0.001	948	223.79	19.76	<0.001
		M	26.50–42.60								
	Q2	W	39.00–40.60	943	149.13	13.74		944	226.51	21.03	
		M	42.70–44.40								
	Q3	W	40.70–42.10	945	149.22	13.79		943	229.78	20.95	
		M	44.50–46.00								
	Q4	W	42.20–43.90	952	149.75	13.87		952	232.36	21.41	
		M	46.10–47.90								
	Q5	W	44.00–49.90	938	151.22	14.16		940	237.32	23.83	
		M	48.00–56.30								
Platelet count (k/μL)	Q1	W	60.00–243.00	936	149.96	13.14	0.77	936	227.22	20.83	<0.001
		M	47.00–217.00								
	Q2	W	244.00–278.00	944	149.11	13.44		944	228.74	21.76	
		M	218.00–250.00								
	Q3	W	279.00–311.00	954	149.54	14.32		954	229.68	22.37	
		M	251.00–279.00								
	Q4	W	312.00–354.00	937	149.61	14.14		939	231.38	22.43	
		M	280.00–318.00								
	Q5	W	355.00–848.00	949	149.52	13.95		951	232.61	21.85	
		M	319.00–885.00								
Hemoglobin (g/dL)	Q1	W	4.90–12.90	895	148.25	13.54	<0.001	898	223.54	20.05	<0.001
		M	9.00–14.30								
	Q2	W	13.00–13.50	992	149.17	13.32		992	227.12	20.76	
		M	14.40–15.00								
	Q3	W	13.60–14.10	963	149.35	13.92		963	229.54	21.16	
		M	15.10–15.50								
	Q4	W	14.20–14.70	876	149.86	13.57		875	232.53	21.08	

Blood Element		Sex	Range[a]	Central Retinal Arteriole Equivalent N[b]	Mean[b]	SD[b]	P value	Central Retinal Venule Equivalent N[b]	Mean[b]	SD[b]	P value
		M	15.60–16.20								
	Q5	W	14.80–16.50	997	151.02	14.46		999	236.64	23.92	
		M	16.30–18.50								
Red blood cell	Q1	W	2.28–4.18	945	149.10	13.56	0.004	949	224.35	19.98	<0.001
count (M/μL)		M	2.88–4.55								
	Q2	W	4.19–4.40	953	149.70	13.41		954	227.98	20.76	
		M	4.56–4.77								
	Q3	W	4.41–4.59	942	148.70	14.53		940	229.63	21.44	
		M	4.78–4.97								
	Q4	W	4.60–4.79	934	149.22	13.24		935	232.01	22.44	
		M	4.98–5.20								
	Q5	W	4.80–6.68	949	151.01	14.14		949	235.78	23.24	
		M	5.21–6.43								
White blood cell	Q1	W	2.20–5.50	914	148.68	12.97	<0.001	913	224.57	19.48	<0.001
count (k/μL)		M	2.50–5.70								
	Q2	W	5.60–6.50	946	149.35	13.43		948	227.82	20.91	
		M	5.80–6.70								
	Q3	W	6.60–7.50	983	148.63	13.69		984	228.62	21.42	
		M	6.80–7.60								
	Q4	W	7.60–8.80	915	149.41	14.27		915	232.08	21.36	
		M	7.70–8.70								
	Q5	W	8.90–43.70	964	151.60	14.40		969	236.45	24.25	
		M	8.80–24.10								

Q = quintile; W = women; M = men; SD = standard deviation.

[a] Range of blood values for women and men included in each quintile.

[b] For women and men combined in each quintile.

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Table 3

Multivariate Relationships Between Blood Elements and Central Retinal Arteriole and Venule Equivalents

	Central Retinal Arteriole Equivalent														
	Model 1 [a]			Model 2			Model 3			Model 4			Model 5		
Blood Element	Est [b]	P value[c]	R^2[d]	Est	P value	R^2	Est	P value	R^2	Est	P value	R^2	Est	P value	R^2
Hematocrit	0.65	<0.001	0.013	0.44	0.002	0.037	0.73	<0.001	0.094	0.70	<0.001	0.096	−0.44	<0.001	0.435
Hemoglobin	0.61	<0.001	0.012	0.39	0.006	0.036	0.71	<0.001	0.094	0.68	<0.001	0.096	−0.39	<0.001	0.434
Platelet count	0.34	0.02	0.009	0.31	0.03	0.036	0.50	<0.001	0.091	0.40	0.007	0.092	0.04	0.72	0.432
White blood cell count	−0.14	0.34	0.008	−0.24	0.09	0.035	−0.16	0.24	0.089	−0.15	0.28	0.091	−0.56	<0.001	0.436
Red blood cell count	0.59	<0.001	0.012	0.22	0.12	0.035	0.52	<0.001	0.092	0.49	<0.001	0.093	−0.31	0.006	0.434
	Central Retinal Venule Equivalent														
	Model 1 [e]			Model 2			Model 3			Model 4			Model 5		
Blood Element	Est	P value	R^2	Est	P value	R^2	Est	P value	R^2	Est	P value	R^2	Est	P value	R^2
Hematocrit	3.31	<0.001	0.076	2.82	<0.001	0.130	2.93	<0.001	0.133	2.90	<0.001	0.134	2.24	<0.001	0.459
Hemoglobin	3.16	<0.001	0.072	2.63	<0.001	0.126	2.76	<0.001	0.129	2.72	<0.001	0.130	2.07	<0.001	0.456
Platelet count	1.01	<0.001	0.035	0.96	<0.001	0.101	1.01	<0.001	0.102	0.89	<0.001	0.103	0.52	0.005	0.439
White blood cell count	1.22	<0.001	0.037	0.98	<0.001	0.101	1.00	<0.001	0.103	1.01	<0.001	0.104	1.18	<0.001	0.445
Red blood cell count	2.80	<0.001	0.063	1.96	<0.001	0.113	2.06	<0.001	0.115	2.03	<0.001	0.116	1.56	<0.001	0.448

[a] Model 1 adjusted for age and sex; Model 2 adjusted for Model 1 and smoking status; Model 3 adjusted for Model 2 and systolic blood pressure; Model 4 adjusted for Model 3 and diabetes status; Model 5 adjusted for Model 4 and central retinal venule equivalent.

[b] Beta estimate for an increase in 1 sex-specific quintile of risk factor

[c] For risk factor in model

[d] For model fit

[e] Models are same as in [a] above, except Model 5 adjusted for Model 4 and central retinal arteriole equivalent.

Table 4

Stepwise Selection for Variables with Central Retinal Arteriole Equivalent and Central Retinal Venule Equivalent.

Central Retinal Arteriole Equivalent					
Risk Factor	**Model Terms Selected**	**Est (SE)** [a]	**P value**	**Partial R^2**	**Model R^2**
Hematocrit	Systolic BP, per 10 mmHg	−1.72 (0.09)	<0.001	0.0611	0.10
	Smoking history, current vs past/never	6.73 (0.49)	<0.001	0.0269	
	Hematocrit, per sex-specific quintile	0.58 (0.14)	<0.001	0.0056	
	Diabetes, present vs absent	2.25 (0.68)	0.004	0.0017	
Hemoglobin	Systolic BP, per 10 mmHg	−1.71 (0.09)	<0.001	0.0611	0.10
	Smoking history, current vs past/never	6.73 (0.49)	<0.001	0.0269	
	Hemoglobin, per sex-specific quintile	0.55 (0.14)	<0.001	0.0054	
	Diabetes, present vs absent	2.24 (0.68)	0.005	0.0016	
Red blood cells	Systolic BP, per 10 mmHg	−1.72 (0.10)	<0.001	0.0611	0.09
	Smoking history, current vs past/never	7.04 (0.48)	<0.001	0.0269	
	Red blood cells, per sex-specific quintile	0.58 (0.14)	<0.001	0.0048	
	Diabetes, present vs absent	2.17 (0.68)	0.003	0.0017	
White blood cells	Systolic BP, per 10 mmHg	−1.70 (0.09)	<0.001	0.0611	0.09
	Smoking history, current vs past/never	6.77 (0.50)	<0.001	0.0269	
	White blood cells, per sex-specific quintile	0.39 (0.14)	<0.001	0.0029	
	Diabetes, present vs absent	2.32 (0.68)	0.003	0.0018	
Platelet count	Systolic BP, per 10 mmHg	−1.68 (0.09)	<0.001	0.0610	0.09
	Smoking history, current vs past/never	2.99 (0.25)	<0.001	0.0269	
	Diabetes, present vs absent	2.25 (0.68)	0.001	0.0021	
	Sex, women vs men	−1.23 (0.40)	0.002	0.002	
Hematocrit	Smoking history, current vs past/never	13.67 (0.78)	<0.001	0.0889	0.13
	Hematocrit, per sex-specific quintile	2.69 (0.22)	<0.001	0.0304	
	Sex, women vs men	6.02 (0.60)	<0.001	0.0081	
	Systolic BP, per 10 mmHg	−0.62 (0.15)	<0.001	0.0045	
	Age, per year	−0.95 (0.30)	0.006	0.0017	
	Diabetes, present vs absent	2.47 (1.07)	0.05	0.0007	
Hemoglobin	Smoking history, current vs past/never	13.71 (0.79)	<0.001	0.0889	0.13

Central Retinal Arteriole Equivalent					
Risk Factor	**Model Terms Selected**	**Est (SE)** [a]	**P value**	**Partial R^2**	**Model R^2**
	Hemoglobin, per sex-specific quintile	2.48 (0.22)	<0.001	0.0267	
	Sex, women vs men	6.06 (0.60)	<0.001	0.0083	
	Systolic BP, per 10 mmHg	−0.62 (0.16)	<0.001	0.0044	
	Age, per year	−0.84 (0.30)	0.01	0.0013	
	Diabetes, present vs absent	2.40 (1.08)	0.06	0.0007	
Red blood cells	Smoking history, current vs past/never	15.10 (0.77)	<0.001	0.0889	0.13
	Red blood cells, per sex-specific quintile	2.71 (0.21)	<0.001	0.0307	
	Sex, women vs men	6.05 (0.60)	<0.001	0.0071	
	Systolic BP, per 10 mmHg	−0.64 (0.16)	<0.001	0.0047	
White blood cells	Smoking history, current vs past/never	13.75 (0.80)	<0.001	0.0889	0.12
	White blood cells, per sex-specific quintile	1.91 (0.22)	<0.001	0.0133	
	Sex, women vs men	6.00 (0.61)	<0.001	0.0083	
	Systolic BP, per 10 mmHg	−0.55 (0.16)	<0.001	0.0035	
	Age, per year	−0.91 (0.30)	0.003	0.0016	
	Diabetes, present vs absent	2.70 (1.08)	0.03	0.0009	
Platelets	Smoking history, current vs past/never	8.24 (0.41)	<0.001	0.0885	0.11
	Sex, women vs men	3.38 (0.63)	<0.001	0.0070	
	Platelet count, per sex-specific quintile	0.98 (0.22)	<0.001	0.0045	
	Systolic BP, per 10 mmHg	−0.41 (0.16)	0.001	0.0021	
	Diabetes, present vs absent	3.12 (1.08)	0.01	0.0014	
	Age, per year	−0.81 (0.30)	0.01	0.0011	

[a] Beta estimate and standard error from linear regression model.

Table 5

Stepwise Selection for Variables with Central Retinal Arteriole Equivalent (CRAE) and Central Retinal Venule Equivalent (CRVE), with CRVE considered for CRAE models and CRAE considered for CRVE models.

Central Retinal Arteriole Equivalent					
Risk Factor	**Model Terms Selected**	**Est (SE)[a]**	**P value**	**Partial R^2**	**Model R^2**
Hematocrit	CRVE, per 25 μm	9.64 (0.18)	<0.001	0.3763	0.44
	Systolic BP, per 10 mmHg	−1.50 (0.08)	<0.001	0.0462	
	Sex women vs men	−2.77 (0.31)	<0.001	0.0096	
	Hematocrit, per sex-specific quintile	−0.39 (0.11)	<0.001	0.0014	
	Age, per year	0.40 (0.15)	0.01	0.0010	
	Diabetes, present vs absent	1.20 (0.55)	0.03	0.0006	
Hemoglobin	CRVE, per 25 μm	9.62 (1.97)	<0.001	0.3763	0.44
	Systolic BP, per 10 mmHg	−1.50 (0.08)	<0.001	0.0462	
	Sex, women vs men	−2.77 (0.31)	<0.001	0.0096	
	Age, per year	0.38 (0.15)	0.004	0.0010	
	Hemoglobin, per sex-specific quintile	−0.32 (0.11)	0.007	0.0009	
	Diabetes, present vs absent	1.21 (0.55)	0.03	0.0006	
Red blood cells	CRVE, per 25 μm	9.63 (0.18)	<0.001	0.3763	0.44
	Systolic BP, per 10 mmHg	−1.49 (0.08)	<0.001	0.0462	
	Sex, women vs men	−2.77 (0.31)	<0.001	0.0096	
	Red blood cells, per sex-specific quintile	−0.42 (0.11)	<0.001	0.0017	
	Age, per year	0.37 (0.15)	0.01	0.0008	
	Diabetes, present vs absent	1.30 (0.55)	0.02	0.0007	
White blood cells	CRVE, per 25 μm	9.58 (1.96)	<0.001	0.3763	0.43
	Systolic BP, per 10 mmHg	−1.51 (0.08)	<0.001	0.0463	
	Sex, women vs men	−2.75 (0.31)	<0.001	0.0096	
	Age, per year	0.39 (0.15)	0.005	0.0010	
	White blood cells, per sex-specific quintile	−0.23 (0.11)	0.04	0.0005	
	Diabetes, present vs absent	1.17 (0.55)	0.03	0.0006	
Platelet count	CRVE, per 25 μm	9.58 (0.18)	<0.001	0.38	0.44
	Systolic BP, per 10 mmHg	−1.51 (0.08)	<0.001	0.0460	

Central Retinal Arteriole Equivalent					
Risk Factor	**Model Terms Selected**	**Est (SE)[a]**	**P value**	**Partial R^2**	**Model R^2**
	Sex, women vs men	−2.75 (0.31)	<0.001	0.0096	
	Platelet count, per age-specific quintile	−0.51 (0.11)	<0.001	0.003	
	Age, per year	0.33 (0.15)	0.02	0.0007	
	Diabetes, present vs absent	1.09 (0.55)	0.04	0.0005	
Hematocrit	CRAE, per 10 μm	9.46 (0.18)	<0.001	0.3763	0.45
	Hematocrit, per sex-specific quintile	2.17 (0.17)	<0.001	0.0294	
	Sex, women vs men	6.44 (0.47)	<0.001	0.0254	
(CRVE)	Smoking history, current vs past/never	7.10 (0.64)	<0.001	0.0158	
	Systolic BP, per 10 mmHg	1.02 (0.13)	<0.001	0.0060	
	Age, per year	−1.11 (0.24)	<0.001	0.0019	
Hemoglobin	CRAE, per 10 μm	9.48 (0.19)	<0.001	0.3763	0.45
	Hemoglobin, per sex-specific quintile	2.05 (0.17)	<0.001	0.0267	
	Sex, women vs men	6.48 (0.48)	<0.001	0.0256	
	Smoking history, current vs past/never	6.72 (0.63)	<0.001	0.0155	
	Systolic BP, per 10 mmHg	1.02 (0.13)	<0.001	0.0062	
	Age, per year	−1.02 (0.24)	<0.001	0.0016	
Red blood cells	CRAE, per 10 μm	9.46 (0.18)	<0.001	0.3763	0.46
	Smoking history, current vs past/never	8.36 (0.63)	<0.001	0.0387	
	Red blood cells, per sex-specific quintile	2.12 (0.17)	<0.001	0.0240	
	Sex, women vs men	6.42 (0.48)	<0.001	0.0133	
	Systolic BP, per 10 mmHg	0.98 (0.24)	<0.001	0.0057	
	Age, per year	−0.90 (0.24)	0.013	0.0012	
White blood cells	CRAE, per 10 μm	9.54 (0.19)	<0.001	0.3763	0.45
	Smoking history, current vs past/never	7.10 (0.65)	<0.001	0.0387	
	White blood cells, per sex-specific quintile	1.58 (0.18)	<0.001	0.0105	
	Sex, women vs men	6.44 (0.48)	<0.001	0.0119	
	Systolic BP, per 10 mmHg	1.09 (0.13)	<0.001	0.0072	
	Age, per year	−1.07 (0.24)	<0.001	0.0019	
Platelets	CRAE, per 10 μm	9.64 (0.19)	<0.001	0.3769	0.44

Central Retinal Arteriole Equivalent					
Risk Factor	**Model Terms Selected**	**Est (SE)[a]**	**P value**	**Partial R^2**	**Model R^2**
	Smoking history, current vs past/never	8.13 (0.64)	<0.001	0.0385	
	Sex, women vs men	6.38 (0.48)	<0.001	0.0132	
	Systolic BP, per 10 mmHg	1.20 (0.13)	<0.001	0.0095	
	Platelets, per sex-specific quintile	1.18 (0.17)	<0.001	0.0057	
	Age, per year	−0.90 (0.24)	<0.001	0.0013	

[a] Beta estimate and standard error from linear regression model.