

Association of Retinal Vessel Caliber to Optic Disc and Cup Diameters

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PURPOSE. To investigate whether optic disc size is related to retinal venule and arteriole diameters.

METHODS. The population of Beaver Dam, Wisconsin, aged 43 to 86 years were invited to participate in a baseline examination from 1988 to 1990. During this examination, photographs, centered on the optic discs, were taken after pupil dilation. Optic discs and cups were measured from stereoscopic photographs, whereas retinal vessel measurements were taken from a single digitized photograph. Central retinal vein and central retinal arterial equivalents were subsequently calculated. Data for 3887 right eyes are included in the analyses.

RESULTS. Narrower retinal venules and arterioles were found in the smaller optic discs controlling for optic cup diameter as well as age, systolic and diastolic blood pressure, refraction, and sex. Central retinal artery equivalents ranged from $156.04 \pm 16.82 \mu\text{m}$ in the smallest optic disc category to $165.93 \pm 15.17 \mu\text{m}$ in the larger disc category ($P < 0.001$). Central retinal vein equivalents ranged from $228.93 \pm 21.26 \mu\text{m}$ in the smallest to $243.18 \pm 22.32 \mu\text{m}$ in the larger disc categories ($P < 0.001$). The significant reduction in retinal vessel diameters was only apparent for the smallest optic disc sizes. A reduction in retinal vessel diameters was less consistent and not significant for small optic cup sizes.

CONCLUSIONS. Smallest optic discs were associated with smaller central retinal artery and central retinal vein diameters. This anatomic relationship may be useful as an additional associated indicator for nonarteritic anterior ischemic optic neuropathy as well as for retinal vascular events. (*Invest Ophthalmol Vis Sci.* 2007;48:63–67) DOI:10.1167/iovs.05-1203

Small optic discs and cups have been suggested to be associated with increased risk for nonarteritic anterior ischemic optic neuropathy.¹ The mechanism proposed for the association is that the small discs and cups result from a small scleral canal,^{1,2} leading to crowding at the lamina cribrosa.^{2–4} It has been suggested that even mild ischemia^{3–7} and swelling of the optic nerve⁵ further compresses vessels at the disc, leading to further ischemia, swelling, hemorrhage, and infarction.

The retinal vessels pass through the lamina cribrosa and optic disc when entering and leaving the globe. It is our hypothesis that smaller optic discs are associated with smaller retinal vessels by virtue of crowding as the nerve traverses the lamina. We sought to evaluate this possibility in data from the Beaver Dam Eye Study.

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MATERIALS AND METHODS

A private census of the population of Beaver Dam, Wisconsin, was performed from September 15, 1987, to May 4, 1988, to identify all eligible residents in the city or township of Beaver Dam, Wisconsin.⁸ Of the 5924 eligible individuals, 4926 (83%) persons 43 to 86 years of age participated in the baseline examination between March 1, 1988, and September 14, 1990. Differences between participants and non-participants have been published.⁸ Ninety-nine percent of the population was white. All data were collected with Institutional Review Board approval in conformity with all federal and state laws, and the study was in compliance with the tenets of the Declaration of Helsinki as revised in 1983. A standardized examination including refraction, and medical history was obtained.⁸ Intraocular pressure was measured with a Goldmann applanation tonometer according to a standard protocol.⁹ Blood pressures were measured with the Hypertension Detection and Follow-up Program protocol.¹⁰ Pupils were dilated pharmacologically. Stereoscopic 30° color fundus photographs centered on the disc (Diabetic Retinopathy Study [DRS] standard field 1),¹¹ were taken.

Optic disc and cup measurements were taken from the stereoscopic pairs of photographs centered on the optic disc (DRS field 1) taken with a 30° fundus camera (FF2-4; Carl Zeiss Meditec, Dublin, CA), after pupil dilation according to a detailed standardized protocol. In brief, the stereoscopic pairs were examined, and both vertical and horizontal disc and cup diameters were measured with a template of graded circles.^{12,13} The magnification of the images from the fundus camera was 2.5.

The procedure for measuring the retinal vessels has been described.¹⁴ Diameters of retinal vessels were measured after converting the field-1 photographs to digital images. All arterioles and venules were measured in the area between 0.5 and 1 disc diameter from the optic disc margin with a computer-assisted program. The measurements of individual arterioles and venules were combined according to the formulas developed by Parr et al.^{15,16} and Hubbard et al.¹⁷ and modified by Knudtson et al.,¹⁴ to provide central retinal artery (CRAE) and central retinal vein equivalents (CRVE). The measurements of the optic discs were performed at a different time than the measurements of the retinal vessels, and the graders were also different.

Refraction was measured with an automated refractor (Humphrey; Carl Zeiss Meditec) in 97% of study subjects; the Early Treatment of Diabetic Retinopathy protocol was used in the remaining 3%.¹⁸ Diabetes was defined as a history of diabetes or fasting blood sugar or glycated hemoglobin exceeding age-specific levels.¹⁹

Although measures were taken from photographs of both eyes, data presented are from the right eye. Optic disc, cup, and vessel measurements were available for 4039 right eyes. Optic discs and cups were not measured in eyes with drusen of the optic disc, proliferative retinopathy at the disc, vascular occlusions, or other disc abnormalities or irregularities. The measurements were not analyzed in eyes with probable or definite glaucoma at baseline. In addition, we excluded 152 right eyes of persons without data on age, refraction, or blood pressure. Relevant measures were available for 3887 right eyes.

Because our interest was in small optic discs and cups, we categorized the measures into three groups. The smallest possible optic cup measure was 0 and defined the first category. The next smallest measure was more than 0 but less than the smallest circle on the template (<0.031) and defined the second category. All remaining

TABLE 1. Characteristics of Those Excluded and Included in Analyses

	Excluded		Included			<i>P</i> *	
	<i>n</i>	%	<i>n</i>	%			
Categorical variable							
Men	1039	39.08	3887	45.23		0.06	
Hypertensive	1030	46.99	3883	34.61		0.03	
Diabetes	1027	15.68	3872	8.88		0.001	
Any cataract	690	51.88	3827	17.79		<0.001	
	<i>n</i>	Mean	SD	<i>n</i>	Mean	SD	<i>P</i> *
Continuous variable							
Age (years)	1039	68.90	11.21	3887	60.20	10.45	<0.001
IOP (mm Hg)†	1000	16.06	4.03	3883	15.25	3.13	<0.001
CRVE (μ)‡	356	236.44	26.53	3875	242.60	22.42	0.004
CRAE (μ)§	359	161.75	16.68	3882	165.62	15.26	0.001
Horizontal cup (in.)	759	0.056	0.025	3836	0.054	0.023	0.21
Vertical cup (in.)	768	0.064	0.028	3848	0.060	0.025	0.02
Horizontal disc (in.)¶	871	0.156	0.018	3875	0.154	0.017	0.96
Vertical disc (in.)¶	875	0.168	0.019	3882	0.166	0.018	0.72

* All probabilities adjusted for age (except age).

† IOP, intraocular pressure, right eyes.

‡ CRVE, central retinal vein equivalent, right eyes.

§ CRAE, central retinal artery equivalent, right eyes.

|| Optic cup diameter, right eyes.

¶ Optic disc diameter, right eyes.

measures defined the third category. A similar approach was taken to define optic disc categories; however, due to such small numbers at the lowest values (0.109 and 0.117 in.) these were combined with 0.125 in. to create the smallest category. The next smallest measure was 0.133 in., and all other measures were combined for the third category.

Linear regression analysis was used to model retinal vessel size based on optic cup or disc size after adjustment for other factors such as age, gender, refraction, intraocular pressure, and blood pressure. Because the size of the cup relative to the disc (i.e., cup-to-disc ratio) may be important, we included both disc and cup measures in some models (SAS ver. 8; SAS, Cary, NC).

RESULTS

Persons whose right eyes were excluded from these analyses were more likely to be hypertensive, be diabetic, have cataract, be older, have higher intraocular pressures, have narrower CRVE and CRAE, and have larger vertical cup diameters than those whose data were included in the subsequent analyses (Table 1). CRAE and CRVE increased for increasing category of optic disc diameters from ≤ 0.125 to 0.133 to ≥ 0.141 in. in vertical and horizontal axes (Table 2). The retinal vessel diameters (CRAE and CRVE) increased with each increasing cate-

TABLE 2. Retinal Arteriole (CRAE) and Venule (CRVE) Diameters by Optic Disc and Cup Diameters, Right Eyes

Optic Disc and Cup Diameters	Categories (in.)	<i>n</i>	Crude Mean		Adjusted Mean		<i>P</i> *	<i>n</i>	Crude Mean		Adjusted Mean		<i>P</i> *
			CRAE (μm)	SD	CRAE (μm)	<i>P</i> *			CRVE (μm)	SD	CRVE (μm)	<i>P</i> *	
Horizontal disc	0.102-0.125	217	161.53	15.36	164.70†		218	236.27	21.11	241.15†			
	0.133	360	162.94	15.00	163.91†		359	238.32	20.54	239.70†			
	0.141-0.227	3244	166.23	15.19	165.91†		3238	243.59	22.57	243.11†			
						0.04						0.02	
Vertical disc	0.109-0.125	49	156.04	16.82	160.34‡		50	228.93	21.26	235.34‡			
	0.133	109	159.55	15.31	162.49‡		109	231.29	20.78	235.67‡			
	0.141-0.234	3681	165.93	15.17	165.78‡		3675	243.18	22.31	242.96‡			
						<0.001						<0.001	
Horizontal cup	0.000	36	159.43	14.29	162.08§		36	238.34	25.24	242.17§			
	<0.031	211	163.28	16.69	164.01§		212	238.09	21.80	240.27§			
	0.031-0.164	3574	165.86	15.14	165.79§		3567	242.99	22.38	242.82§			
						0.02						0.16	
Vertical cup	0.000	32	160.81	14.26	163.43		32	241.05	23.15	244.91			
	<0.031	136	163.10	16.70	164.21		136	237.54	21.81	240.14			
	0.031-0.164	3671	165.76	15.21	165.69		3666	242.86	22.39	242.73			
						0.14						0.57	

* *P* from test of trend after adjustment.

† Adjusted for age, horizontal cup, systolic and diastolic blood pressure, refraction, and sex.

‡ Adjusted for age, vertical cup, systolic and diastolic blood pressure, refraction, and sex.

§ Adjusted for age, horizontal disc, systolic and diastolic blood pressure, refraction, and sex.

|| Adjusted for age, vertical disc, systolic and diastolic blood pressure, refraction, and sex.

TABLE 3. Change in Retinal Vessel Measure for Every 0.08-in. Change in Optic Disc or Cup Measure* among Eyes Already in the Highest Category for Disc or Cup Measure

Optic Disc and Cup Diameters	CRAE				CRVE			
	Change	P	Adjusted*		Change	P	Adjusted*	
			Change	P			Change	P
Horizontal disc	-0.06	0.67	-0.23	0.10	0.31	0.16	-0.17	0.43
Vertical disc	0.38	<0.001	0.12	0.29	0.62	<0.001	0.22	0.18
Horizontal cup	0.07	0.45	-0.10	0.26	0.00	0.99	-0.31	0.02
Vertical cup	0.07	0.39	-0.06	0.47	-0.01	0.95	-0.24	0.05

* Adjusted for age, gender, refraction, systolic and diastolic blood pressure.

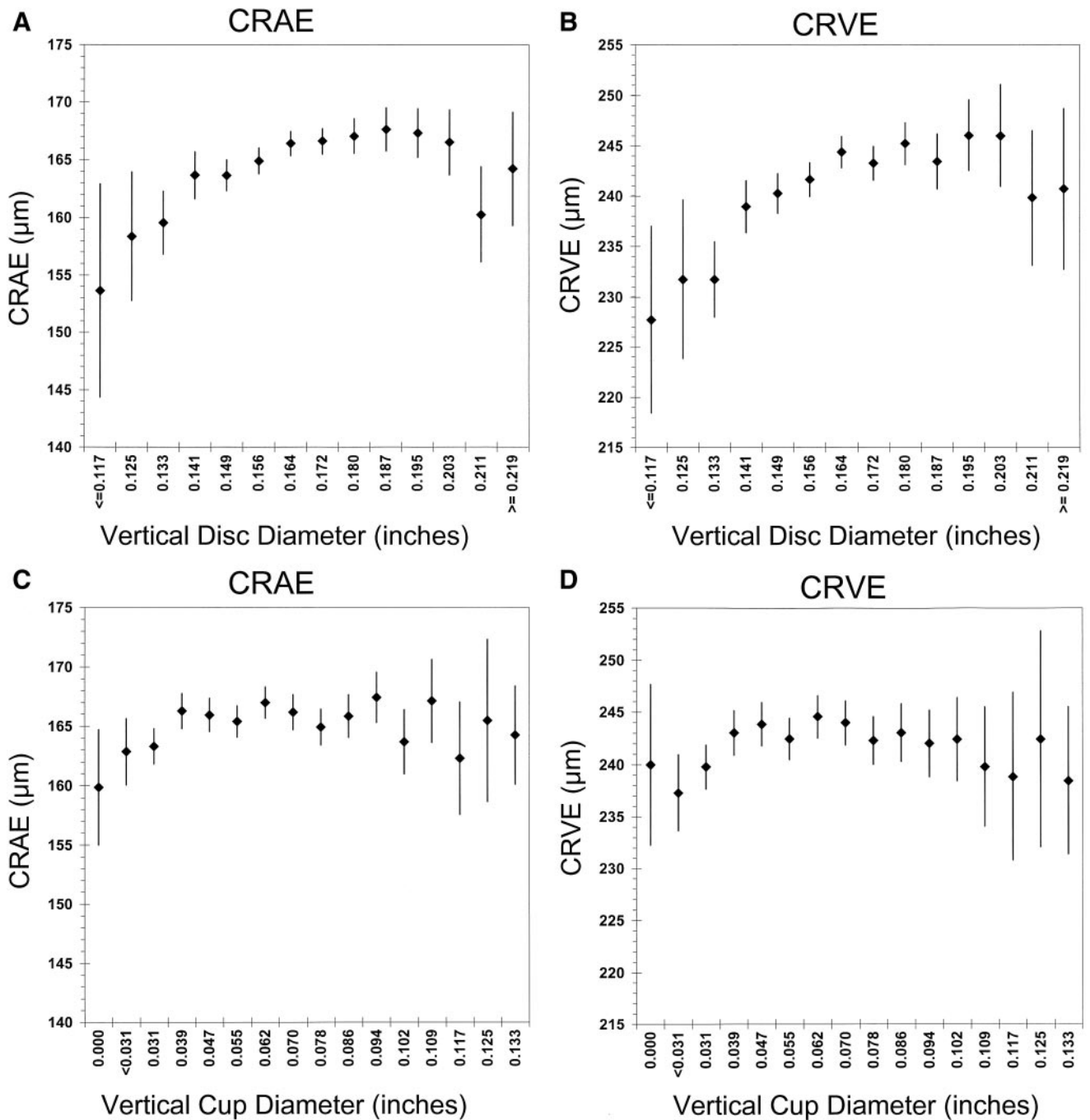


FIGURE 1. Mean retinal vessel diameters (CRAE, A, C; CRVE, B, D) for optic disc (A, B) and cup (C, D) as a continuous measure. Vertical bars represent the 95% confidence interval around the mean.

gory of cup diameters from 0 to <0.031 to ≥ 0.031 in., in vertical and horizontal axes (Table 2).

The imaging and measurement of optic disc and cup diameters, as well as vessel diameters, were affected by refractive error and age. Vessel diameters were associated with systemic blood pressure and sex. Optic disc and cup diameters in the same axis correlated highly (0.56 for both horizontal and vertical measurements). Although highly correlated, small differences at the categories of interest may have important effects, and so we included all these characteristics in our multivariable analyses (Table 2). After adjustment, the same associations of increasing retinal vessel diameter with increasing category for disc and cup diameter remained. The associations between both horizontal and vertical disc diameters and CRAE and CRVE were significant. The association for trend of horizontal optic cup diameter with CRAE was significant, whereas that between vertical cup diameter and CRAE and horizontal cup diameter and CRVE was of borderline significance. The relationship of vertical cup diameters to CRVE was not significant. Replacing blood pressure with intraocular pressure in models had no significant effect on the relationships. Further adjustment for body height and diabetes status had no significant effect on the relationships.

Most of the eyes in the study had optic disc and cup diameters that fell in the largest (highest) category. Within this group, there were no significant differences in retinal vessel diameters with each increasing size of optic disc diameter treated continuously (Table 3). There was some increase for increasing vertical disc measure which was no longer significant after adjusting for other measures. The increase in retinal vessel diameters with increasing disc and cup diameters up to the third category and subsequent leveling off with further increases in vertical disc and cup diameters is shown in Figure 1. Similar results were found for horizontal disc and cup diameters.

DISCUSSION

Our population-based data indicate an association between small optic discs and cups and narrower retinal arterioles. Beyond the smallest categories of optic disc and cup diameter, there were no further relationships between retinal vessel size and optic disc and cup diameters. The finding is in keeping with the notion of an effect of crowding at the optic nerve head that would not occur when the disc is a threshold diameter.

An association between optic disc diameter and retinal vessels may be a reflection of disc and vessel diameters being proportionately related to each other and may not be a causal effect of crowding on vessel diameter. Such anatomic differences as well as magnification differences resulting from refraction would be expected to produce proportional changes. Although refraction was an important variable in our models, we found no proportional change in vessel diameter for disc diameters ≥ 0.141 in. To control for possible anatomic differences, we included body height in additional analyses. This adjustment had no effect on our finding. Therefore, the relationship we found is not explained by proportional changes.

Because diabetes has been shown to be associated with vessel size (although unrelated to magnification), we included this characteristic in the additional analyses. Diabetes status did not influence our results. Because diabetes and body height were not important, we presented the results of a more parsimonious model that does not include them.

The associations between vessel calibers and size of optic discs are more consistent than for optic cups. Whereas optic cup diameter may truly not be as strongly related to vessel diameters as disc diameter, it is also possible that the greater grader variability in measuring optic cup diameters¹² influ-

enced our estimate of the relationships. Also, variations in intraocular pressure may have added to the variability in optic cup size. In addition, associations between vessel calibers and horizontal disc diameters are less consistent than those with vertical disc diameters, perhaps because of the elliptical nature of the optic disc. Eyes with smaller vertical disc diameters will have smaller optic discs overall than those with small horizontal disc diameters. Analysis using similar categories for the average of the horizontal and vertical measures results in significantly smaller vessel calibers for the smallest categories (data not shown).

Our study was prompted by the clinical observation that eyes having an episode of nonarteritic ischemic optic neuropathy (NAION) appear to have smaller optic discs and cups in the fellow eye than other eyes. We have observed, in other studies, relationships of systemic markers of inflammation,^{20,21} diabetes, and hypertension^{22,23} to narrower retinal vessels. Some of these risk factors have also been found to be associated with NAION.²⁴⁻²⁸ Although it is possible that narrower retinal vessels are a reflection of these other systemic conditions and markers, it is also possible that retinal vessel diameters are independently related to disc measurements and that these all may be related to the development of nonarteritic ischemic optic neuropathy. The possible clinical utility of our observation awaits further research in the context of studies aimed at defining the prevalence and risk factors for this disease.

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