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Determinants of the Optic Cup to Disc Ratio in an Asian Population

The Singapore Malay Eye Study (SiMES)

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Objective: To describe the distribution and determinants of the optic cup to disc ratio (CDR) in Malay adults in Singapore.

Methods: This population-based, age-stratified study examined 3280 Malay people aged 40 to 80 years in Singapore. Participants underwent a standardized interview and an ocular examination. A slitlamp examination measured the vertical dimensions of the disc and cup, excluding areas of peripapillary atrophy and the Elschnig scleral ring.

Results: Vertical CDR was recorded for 3228 right eyes and 3237 left eyes. The mean (SD) CDR was 0.40 (0.15) in both eyes. The CDR in the right eye increased with age ($P<.001$) and was greater in men vs women (age-adjusted CDR, 0.42 vs 0.39; $P<.001$). In multiple linear regression, significant determinants of greater CDR were increasing age, male sex, higher intraocular pressure (IOP), lower diastolic blood pressure, lower body mass index, and previous cataract surgery. Of these, higher IOP was the most important determinant of the CDR. After excluding 149 persons with glaucoma, male sex, higher IOP, lower diastolic blood pressure, lower body mass index, and diabetes mellitus were significant predictors of greater CDR.

Conclusion: Greater vertical CDR was related to male sex, higher IOP, lower diastolic blood pressure, and lower body mass index.

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THE MORPHOLOGIC CHARACTERISTICS of the optic disc are routinely assessed to screen, diagnose, and monitor disease in conditions such as glaucoma and optic neuropathies. Of various optic disc features, the vertical cup to disc ratio (CDR) is the most commonly used clinical measurement, particularly for the diagnosis of glaucoma.[1]

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Systemic and ocular processes may affect the CDR, and understanding these factors may improve the clinical assessment of this sign. However, few population-based studies have assessed potential factors that may affect the CDR, and these have reported inconsistent results.[1-3] The Blue Mountains Eye Study[4] and the Barbados Eye Study[5] found an increase in mean CDR with age. However, the Baltimore Eye Study[1] and the Rotterdam Study[6] did not. Regarding sex, the evidence again has been conflicting. Quigley et al[7] found that males had a larger CDR, but the Vellore Eye Study[8] did not find a significant difference. The Baltimore Eye Study[1] and the Rotterdam Study[6] found that the mean optic disc area was significantly larger in men than in women, but they did not find a statistically significant association with vertical CDR. A major limitation of these studies is that participants with and without glaucoma were often analyzed together. However, because the prevalence of glaucoma varies among populations, it is unclear how this might have affected study findings.

This study aims to describe the distribution and determinants of vertical CDR in a population-based cohort of Malay adults in Singapore. In particular, we examine associations in the whole population and then after excluding persons with glaucoma.

METHODS

STUDY POPULATION

The Singapore Malay Eye Study was a population-based cross-sectional study of 3280 Malay

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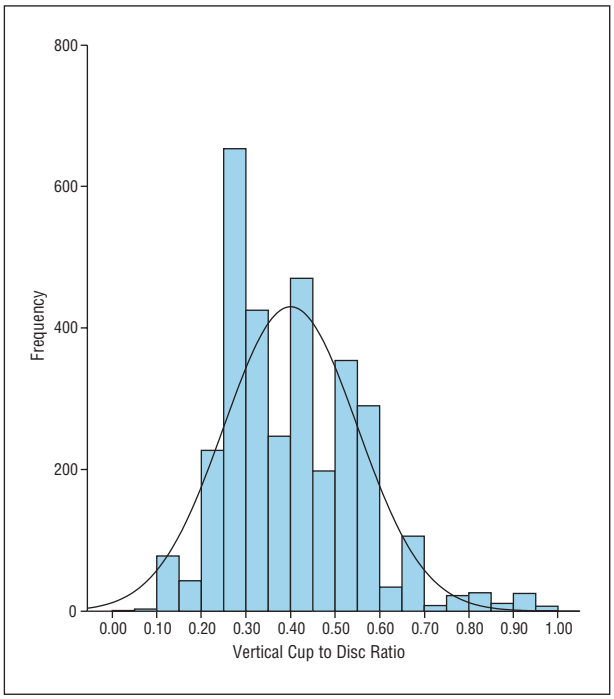

Figure 1. Distribution of the vertical cup to disc ratio in the right eye in the total population (n=3228). The mean (SD) vertical cup to disc ratio was 0.40 (0.15).

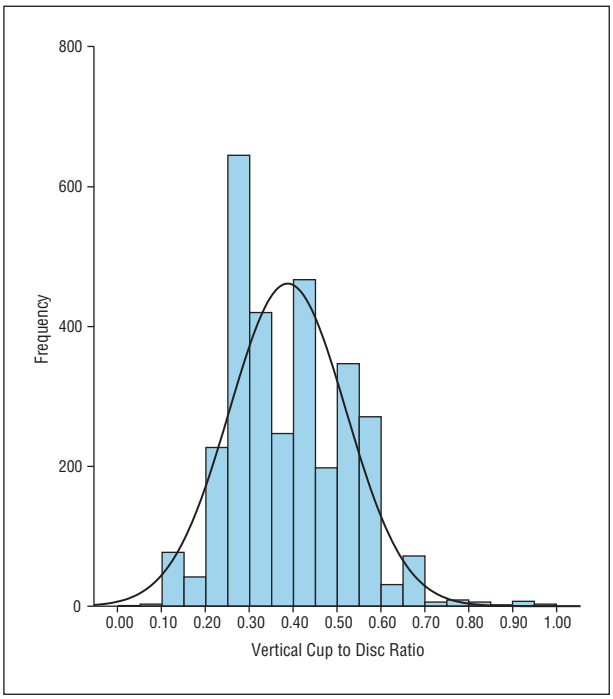

Figure 2. Distribution of the vertical cup to disc ratio in the right eye in persons without glaucoma (n=3081). The mean (SD) vertical cup to disc ratio was 0.39 (0.13).

residents of Singapore conducted between August 16, 2004, and July 10, 2006, and described previously.[9] In brief, an age-stratified random sampling procedure was used to select Malay people aged 40 to 80 years living in the southwestern part of Singapore.[9] Of 4168 persons eligible to participate, 3280 were examined (response rate, 78.7%). Nonparticipants were older but did not differ by sex or possession of a telephone in their homes (data not shown). This study was conducted in accordance with the World Medical Association Declaration of Helsinki. Ethics approval was obtained from the Singapore Eye Research Institute institutional review board.

STUDY MEASUREMENTS

Participants underwent a standardized interview, an ocular examination, and laboratory investigations at the Singapore Eye Research Institute Clinic. Slitlamp examination (Haag-Streit BQ 900; Haag-Streit AG, Koeniz, Switzerland) was performed before and after pupil dilation. Intraocular pressure (IOP) was measured using Goldmann applanation tonometry (Haag-Streit AG) and a standardized protocol.[9] Pupils were dilated with tropicamide, 1%, and phenylephrine hydrochloride, 2.5%.[9]

The optic disc was examined through a 78-diopter lens at ×10 magnification using the same technique as used in a population-based study of Chinese people in Singapore (Tanjong Pagar Survey).[10,11] The vertical dimensions of the disc and cup were measured using an eyepiece graticule, etched in 0.1 U. Measurements of vertical disc diameter excluded areas of peripapillary atrophy and the Elschnig scleral ring. The margins of the cup were defined by means of stereoscopic examination as the point of maximal inflexion of the contour. The vertical diameter of the cup was measured as the vertical distance between the points of maximal centrifugal extension of the cup between 11 to 1 o'clock and 5 to 7 o'clock. For small discs with no visible cup, the measurement was taken as the diameter of the emerging retinal vessel.[10,11]

Glaucoma was diagnosed using the International Society of Geographic and Epidemiological Ophthalmology classification.[11] Category 1 requires optic disc abnormality (vertical CDR or vertical CDR asymmetry ≥97.5th percentile or neuroretinal width between 11 to 1 o'clock and 5 to 7 o'clock <0.1 vertical CDR) and glaucomatous visual field defect. Category 2 requires a severely damaged optic disc (vertical CDR or vertical CDR asymmetry ≥99.5th percentile) in the absence of a satisfactory visual field test. Category 3 glaucoma is defined as blindness (corrected visual acuity <3/60), previous glaucoma surgery, or IOP greater than the 99.5th percentile if the optic discs cannot be examined.[11]

Height and weight were measured to calculate the body mass index (BMI), which is weight in kilograms divided by height in meters squared. Systolic and diastolic blood pressures (BPs) were measured with the participants seated after 5 minutes of rest using an automatic BP monitor and a standardized protocol.[9] *Pulse pressure* was defined as systolic minus diastolic BP and *ocular perfusion pressure* as two-thirds of the mean arterial BP minus the IOP, where mean arterial BP is two-thirds of the diastolic plus one-third of the systolic value.

Axial length, anterior chamber depth (ACD), and corneal curvature in the horizontal and vertical meridians were measured using noncontact partial-coherence laser inferometry (IOLMaster; Carl Zeiss Meditec, Jena, Germany). Cataract was graded clinically using the Lens Opacities Classification System III.[12] Levels of nonfasting serum glucose, lipids (total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol), hemoglobin A_{1c}, and creatinine were measured from venous blood collected from participants. *Diabetes mellitus* was defined as nonfasting glucose levels of 200 mg/dL or greater (to convert to millimoles per liter, multiply by 0.0555), self-report of diabetic medication use, or physician-diagnosed diabetes mellitus.

STATISTICAL ANALYSIS

Statistical analysis was performed using a software program (SPSS version 11.5; SPSS Inc, Chicago, Illinois). Proportions were com-

Table 1. Distribution of Vertical CDR in Right Eyes by Age Group and Sex

Age, y	Men and Women		Men		Women	
	No. of Right Eyes	CDR, Mean (SD)	No. of Right Eyes	CDR, Mean (SD)	No. of Right Eyes	CDR, Mean (SD)
			All Persons			
40-49	**807**	0.39 (0.13)	378	0.40 (0.13)	429	0.38 (0.14)
50-59	**952**	0.39 (0.14)	429	0.40 (0.13)	523	0.37 (0.14)
60-69	**766**	0.41 (0.17)	373	0.43 (0.17)	393	0.39 (0.18)
70-80	**703**	0.43 (0.17)	380	0.44 (0.19)	323	0.42 (0.16)
All ages	**3228**	0.40 (0.15)	**1560**	0.42 (0.15)	**1668**	0.39 (0.15)
P value for trend	NA	<.001	NA	.001	NA	.001
			Persons Without Glaucoma			
40-49	**793**	0.39 (0.13)	372	0.40 (0.12)	421	0.38 (0.13)
50-59	**927**	0.38 (0.13)	417	0.39 (0.12)	510	0.37 (0.13)
60-69	**725**	0.39 (0.14)	345	0.40 (0.14)	380	0.37 (0.13)
70-80	**636**	0.39 (0.13)	343	0.40 (0.16)	293	0.39 (0.13)
All ages	**3081**	0.39 (0.13)	**1477**	0.40 (0.14)	**1604**	0.38 (0.13)
P value for trend	NA	.04	NA	.69	NA	.07

Abbreviations: CDR, cup to disc ratio; NA, not applicable.

pared using the χ^2 test. Analysis of covariance models were initially used to estimate the mean vertical CDR, adjusted for age and sex. Multiple linear regression models were used to assess the independent association between CDR and risk factors. Final models are provided for right eyes only because the results for left eyes were largely similar. To test the normality and appropriateness of linear regression, we constructed Q-Q plots of vertical CDR that showed that vertical CDR was normally distributed between 0.1 and 0.7, which represented 99.2% (3203 of 3228 right eyes) of participants.

For linear regression, we provide the β coefficient and the partial R^2. The β coefficient depends on the unit of measurement of the independent variable and cannot be directly compared with other independent variables in the model. The incremental partial R^2 allows assessment of the relative importance of the independent variables in the model. We conducted 2 subsidiary analyses. First, we repeated the analysis excluding glaucoma cases. Second, we repeated the analysis excluding patients with nuclear cataract (Lens Opacities Classification System III nuclear opacification or color ≥5.0).

RESULTS

The mean age of participants was 58.7 years. Vertical CDR was recorded for 3228 right eyes and 3237 left eyes. There were 149 patients with glaucoma, giving an overall prevalence of 4.5% in the population.

The mean (SD) vertical CDR was 0.40 (0.15) for both eyes. **Figure 1** shows the distribution of vertical CDR in the right eye in the entire study population, and **Figure 2** shows the distribution of vertical CDR in the right eye in persons without glaucoma. **Table 1** gives the distribution of vertical CDR by age group and sex for all persons (n=3228) and after excluding patients with glaucoma (n=3081). Vertical CDR increased with age in both groups ($P<.001$ and $P=.04$, respectively).

Table 2 summarizes systemic predictors of vertical CDR in the right eye in the total population (n=3228) and after excluding glaucoma cases (n=3081). After controlling for age, the CDR was greater in men than in women ($P<.001$). Lower weight and BMI were associated with greater vertical CDR. Results were largely similar when patients with glaucoma were excluded (Table 2). In the analysis of eyes in which patients with nuclear cataract were excluded, vertical CDR remained greater in men than in women (0.41 vs 0.38; $P<.001$). Lower weight and BMI were still associated with greater vertical CDR (data not shown).

Ocular predictors of vertical CDR are summarized in **Table 3**. Vertical CDR was significantly larger with higher levels of IOP and lower levels of ocular perfusion pressure in the total population and in persons without glaucoma. Shallower ACD and previous cataract were associated with larger vertical CDR, but these associations were not significant after excluding patients with glaucoma (Table 3). Because ACD is associated with pseudophakia and aphakia, further multiple linear analyses were conducted using models containing only 1 of the 2 variables: ACD or previous cataract surgery. These analyses showed that ACD was not a significant determinant of vertical CDR in all persons and in those with glaucoma once cataract surgery was not in the model (data not shown). Cataract surgery, however, remained a significant determinant in all persons ($P=.003$) but not in models when persons with glaucoma were excluded ($P=.16$). In the final multiple linear regression, only cataract surgery was included in models for all persons.

Results were largely similar in analyses of eyes in which patients with nuclear cataract were excluded, in which higher levels of IOP and lower levels of ocular perfusion pressure were significantly associated with larger CDR (data not shown).

Table 4 provides the final multiple linear regression models of vertical CDR in the total population and after excluding patients with glaucoma. In all persons, significant independent determinants of greater CDR were increasing age ($P<.001$), male sex ($P<.001$), lower dia-

Table 2. Systemic Predictors of Vertical CDR in Right Eyes

Characteristics	All Persons (n=3228)			Persons Without Glaucoma (n=3081)		
	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value
Sex						
Male	1560	0.42 (0.004)	<.001	1477	0.40 (0.003)	<.001
Female	1668	0.39 (0.004)		1604	0.38 (0.003)	
Place of birth						
Singapore	2436	0.40 (0.003)	.99	2331	0.39 (0.003)	.63
Malaysia	705	0.40 (0.006)		666	0.39 (0.005)	
Indonesia or other	84	0.40 (0.017)		81	0.40 (0.015)	
Race						
Malay	2111	0.40 (0.003)	.84	2006	0.39 (0.003)	.09
Boyanese	394	0.40 (0.008)		389	0.40 (0.007)	
Javanese or other	720	0.40 (0.006)		683	0.39 (0.005)	
Educational level						
No formal education	659	0.41 (0.007)	.13	613	0.39 (0.006)	.02
Less than elementary school	296	0.41 (0.009)		284	0.40 (0.008)	
Elementary school	1462	0.39 (0.004)		1405	0.38 (0.004)	
High school or higher	804	0.41 (0.006)		773	0.39 (0.005)	
Smoking status						
Current smoker	658	0.40 (0.007)	.95	632	0.39 (0.006)	.94
Past smoker	584	0.40 (0.007)		547	0.39 (0.006)	
Never smoker	1986	0.40 (0.004)		1902	0.39 (0.004)	
Alcohol intake						
Never	3159	0.40 (0.003)	.44	3017	0.39 (0.002)	.95
Current or past	53	0.42 (0.021)		49	0.39 (0.019)	
Hypertension						
No	1025	0.41 (0.005)	.12	988	0.39 (0.005)	.45
Yes	2203	0.40 (0.003)		2093	0.39 (0.003)	
Diabetes mellitus						
No	2482	0.40 (0.003)	.24	2370	0.38 (0.003)	.01
Yes	745	0.41 (0.006)		710	0.40 (0.005)	
Systolic BP						
First quartile	832	0.41 (0.006)	.62	806	0.39 (0.005)	.93
Second quartile	813	0.40 (0.005)		779	0.39 (0.005)	
Third quartile	796	0.40 (0.005)		761	0.39 (0.005)	
Fourth quartile	784	0.40 (0.006)		732	0.39 (0.005)	
Diastolic BP						
First quartile	843	0.41 (0.005)	.12	793	0.39 (0.005)	.31
Second quartile	773	0.41 (0.006)		743	0.39 (0.005)	
Third quartile	811	0.40 (0.005)		778	0.39 (0.005)	
Fourth quartile	798	0.39 (0.005)		764	0.38 (0.005)	
Pulse pressure						
First quartile	834	0.41 (0.006)	.16	809	0.39 (0.005)	.28
Second quartile	788	0.39 (0.005)		761	0.38 (0.005)	
Third quartile	801	0.40 (0.005)		764	0.39 (0.005)	
Fourth quartile	802	0.41 (0.006)		744	0.39 (0.005)	
Height						
First quartile	803	0.40 (0.007)	.30	769	0.39 (0.006)	.17
Second quartile	821	0.41 (0.006)		778	0.39 (0.005)	
Third quartile	785	0.39 (0.006)		749	0.38 (0.005)	
Fourth quartile	797	0.41 (0.007)		765	0.40 (0.006)	
Weight						
First quartile	800	0.41 (0.005)	.01	758	0.39 (0.005)	.004
Second quartile	810	0.41 (0.005)		777	0.39 (0.005)	
Third quartile	796	0.40 (0.005)		753	0.39 (0.005)	
Fourth quartile	800	0.39 (0.005)		773	0.37 (0.005)	

(continued)

stolic BP ($P=.002$), lower BMI ($P=.001$), higher IOP ($P<.001$), and past cataract surgery ($P<.004$). Of these factors, IOP was the most important determinant of CDR, with the largest partial R^2 of 0.013. Factors in this model accounted for only 3.7% of all variation in CDR (adjusted $R^2=0.037$).

When these data were analyzed excluding patients with glaucoma, male sex, diastolic BP, BMI, and IOP all remained significant determinants. However, age did not remain significantly associated with vertical CDR when persons with glaucoma were excluded. Also, diabetes mellitus was significantly associated with vertical

Table 2. Systemic Predictors of Vertical CDR in Right Eyes (cont)

Characteristics	All Persons (n=3228)			Persons Without Glaucoma (n=3081)		
	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value
BMI						
First quartile	807	0.42 (0.005)	.008	756	0.40 (0.005)	.003
Second quartile	800	0.40 (0.005)		771	0.39 (0.005)	
Third quartile	793	0.40 (0.005)		764	0.38 (0.005)	
Fourth quartile	796	0.39 (0.006)		764	0.37 (0.005)	
Serum glucose						
First quartile	853	0.40 (0.005)	.61	811	0.38 (0.005)	.34
Second quartile	709	0.40 (0.006)		685	0.39 (0.005)	
Third quartile	779	0.40 (0.005)		743	0.39 (0.005)	
Fourth quartile	761	0.41 (0.006)		719	0.39 (0.005)	
Hemoglobin A_{1c}						
First quartile	898	0.40 (0.005)	.98	862	0.39 (0.005)	.82
Second quartile	688	0.40 (0.006)		660	0.39 (0.005)	
Third quartile	807	0.40 (0.005)		762	0.38 (0.005)	
Fourth quartile	764	0.40 (0.006)		728	0.39 (0.005)	
Total cholesterol						
First quartile	803	0.40 (0.005)	.16	764	0.39 (0.005)	.22
Second quartile	788	0.41 (0.005)		752	0.39 (0.005)	
Third quartile	795	0.39 (0.005)		754	0.38 (0.005)	
Fourth quartile	785	0.40 (0.005)		756	0.39 (0.005)	
LDL cholesterol						
First quartile	798	0.40 (0.005)	.49	757	0.39 (0.005)	.52
Second quartile	805	0.41 (0.005)		771	0.39 (0.005)	
Third quartile	780	0.40 (0.005)		744	0.38 (0.005)	
Fourth quartile	785	0.40 (0.005)		751	0.39 (0.005)	
Serum creatinine						
First quartile	821	0.41 (0.006)	.13	786	0.39 (0.005)	.06
Second quartile	778	0.41 (0.006)		743	0.39 (0.005)	
Third quartile	744	0.39 (0.006)		705	0.38 (0.005)	
Fourth quartile	759	0.40 (0.006)		726	0.39 (0.005)	

Abbreviations: BMI, body mass index; BP, blood pressure; CDR, cup to disc ratio; LDL, low-density lipoprotein.
[a] Some of the numbers do not sum to the total because of missing data.
[b] Adjusted for age and sex.

CDR in persons without glaucoma. In this model, IOP was again the most important determinant of CDR, with the largest partial R^2 of 0.012. Factors in this model accounted for even less of the variation in CDR (adjusted R^2=0.026).

In a subsidiary multiple regression analysis replacing diastolic BP with ocular perfusion pressure, significant independent determinants of greater CDR in all persons were increasing age, male sex, lower ocular perfusion pressure, lower BMI, higher IOP, and cataract surgery (data not shown). Of these factors, IOP was again the most important determinant of CDR, with the largest partial R^2 of 0.101. All factors accounted for only 3.5% of all variation in CDR (adjusted R^2=0.035).

COMMENT

This population-based study in Asian Malays demonstrated that sex, IOP, BMI, diastolic BP, and ocular perfusion pressure were significant determinants of vertical CDR. The pattern of associations was largely similar after excluding persons with glaucoma and nuclear cataract, suggesting that these findings were not simply reflecting associations with glaucoma and were not affected by difficulties in assessing CDR in eyes with significant media opacity. Axial length was not associated with vertical CDR, and age was not a significant predictor of CDR once glaucoma was excluded.

The ocular and systemic factors studied herein accounted for less than 4% of the variation in vertical CDR, suggesting that other factors affect vertical CDR, including possible genetic factors. In support of this, studies[13-15] suggest that the heritability of disc area and CDR is approximately 0.5.

In the present study, the most important determinant of vertical CDR was IOP, with the largest absolute value of partial R^2. This was true even when patients with glaucoma were excluded. The importance of IOP is consistent with the Baltimore Eye Study[1] and the Blue Mountains Eye Study.[2] The Blue Mountains Eye Study[2] showed that for every 10–mm Hg increase in IOP, the CDR increased by 0.04. The Barbados Eye Study[5] also found that IOP was an important determinant in patients with open-angle glaucoma. The Beaver Dam Eye Study[16] assessed optic disc change during a 5-year interval and reported that change in IOP was significantly associated with change in vertical CDR.

Of the other ocular factors, past cataract surgery was associated with a greater vertical CDR, although this was not seen in persons without glaucoma. To our knowl-

Table 3. Ocular Predictors of Vertical CDR in Right Eyes

Characteristic	All Persons (n=3228)			Persons Without Glaucoma (n=3081)		
	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value	No. of Right Eyes[a]	CDR, Mean (SE)[b]	*P* Value
Intraocular pressure						
First quartile	940	0.39 (0.005)	<.001	900	0.38 (0.004)	<.001
Second quartile	791	0.39 (0.005)		760	0.38 (0.005)	
Third quartile	884	0.40 (0.005)		854	0.39 (0.005)	
Fourth quartile	607	0.43 (0.006)		561	0.41 (0.006)	
Ocular perfusion pressure						
First quartile	797	0.42 (0.005)	.003	757	0.40 (0.005)	.05
Second quartile	815	0.40 (0.005)		787	0.38 (0.005)	
Third quartile	782	0.40 (0.005)		743	0.39 (0.005)	
Fourth quartile	799	0.40 (0.004)		760	0.38 (0.005)	
Axial length						
First quartile	783	0.39 (0.006)	.17	754	0.38 (0.005)	.43
Second quartile	776	0.40 (0.005)		741	0.39 (0.005)	
Third quartile	775	0.41 (0.006)		731	0.39 (0.005)	
Fourth quartile	765	0.40 (0.006)		734	0.39 (0.005)	
Anterior chamber depth						
First quartile	818	0.40 (0.005)	.02	768	0.39 (0.005)	.07
Second quartile	788	0.41 (0.005)		747	0.39 (0.005)	
Third quartile	799	0.40 (0.005)		777	0.39 (0.005)	
Fourth quartile	802	0.39 (0.005)		773	0.38 (0.005)	
Refraction						
Myopia	816	0.39 (0.005)	.22	776	0.38 (0.005)	.05
Emmetropia	1303	0.41 (0.004)		1258	0.39 (0.004)	
Hypermetropia	1078	0.40 (0.005)		1025	0.39 (0.004)	
LOCS III nuclear opacity						
<1.0	20	0.33 (0.034)	.17	19	0.31 (0.030)	.06
1.0-1.9	82	0.37 (0.017)		82	0.36 (0.015)	
2.0-2.9	791	0.40 (0.006)		767	0.39 (0.005)	
3.0-3.9	1276	0.40 (0.004)		1244	0.39 (0.004)	
4.0-4.9	611	0.40 (0.007)		565	0.39 (0.006)	
≥5.0	186	0.40 (0.012)		172	0.40 (0.011)	
Cataract surgery						
No	2993	0.40 (0.003)	.02	2870	0.39 (0.002)	.44
Yes	228	0.42 (0.010)		205	0.39 (0.010)	

Abbreviations: CDR, cup to disc ratio; LOCS III, Lens Opacities Classification System III.
[a] Some of the numbers do not sum to the total because of missing data.
[b] Adjusted for age and sex.

Table 4. Multiple Linear Regression of Vertical CDR, Right Eyes

Characteristic	Adjusted Difference in CDR[a]					
	All Persons			Persons Without Glaucoma		
	β Coefficient	Partial R^2	*P* Value	β Coefficient	Partial R^2	*P* Value
Age, per 10 y	.009	0.008	<.001	.002	0.001	.49
Female vs male sex	−.029	0.008	<.001	−.024	0.007	<.001
BMI	−.002	0.003	.001	−.002	0.004	<.001
Intraocular pressure, per mm Hg	.005	0.013	<.001	.004	0.012	<.001
Diastolic BP, per 10 mm Hg	−.007	0.003	.002	−.005	0.002	.03
Cataract surgery, yes vs no	.030	0.002	.004			
Diabetes mellitus, yes vs no	NA	NA	NA	.015	0.002	.01

Abbreviations: BMI, body mass index; BP, blood pressure; CDR, cup to disc ratio; NA, not applicable.
[a] For all persons, the adjusted R^2=0.037; for persons without glaucoma, the adjusted R^2=0.026.

edge, no other study has examined this association in a population. The Barbados Eye Study[5] reported that cataract was associated with an increased risk of open-angle glaucoma, but the present study did not find a significant association between nuclear opacity and vertical CDR.

These data revealed other interesting associations. Lower BMI was associated with larger CDR, independent of IOP.

The Barbados Eye Study[5] found that a higher BMI had some protective effect on the risk of open-angle glaucoma. Gasser et al[17] found that there was a tendency for patients with glaucoma to have a lower BMI than controls. However, underlying reasons for this association are unclear. We also found lower diastolic BP and ocular perfusion pressure to be associated with larger CDR, independent of IOP and even when patients with glaucoma were excluded. The Barbados Eye Study[5] also found associations of low diastolic BP and low BP to IOP ratio with risk of open-angle glaucoma. These observations provide evidence of possible mechanisms of reduced optic nerve head perfusion in glaucoma pathogenesis.

Two factors associated with CDR have been well studied. Age was a significant determinant of CDR only in the total sample, but not after excluding persons with glaucoma. This pattern is similar to that in the Rotterdam Study.[6] However, in the Blue Mountains Study,[2] each decade increase in age was associated with a 1.9% increase in mean CDR, and this relationship was still present after excluding patients with glaucoma or known optic disc disease. Garway-Heath et al[4] also reported that CDR increases by approximately 0.1 between ages 30 and 70 years. Despite conflicting results from different populations, histologic studies have reported a loss of ganglion cell nerve fibers with age.[18-22] Jonas et al[22] estimated this loss to be approximately 0.36% per year, and Johnson et al[19] estimated it to be 0.625% per year. This may be an important area for further research.[2] Male sex was also a statistically significant determinant of larger CDR, consistent with other studies, reflecting possibly larger disc areas in men than in women.[7]

There are limitations of this study. First, the optic disc size of the participants was not measured, and optic disc size is known to affect CDR.[23] The Vellore Eye Study[8] found that high interindividual variability in optic disc and cup diameters results in variability in CDR. Therefore, CDR may have relatively low diagnostic power to differentiate between healthy eyes and those with early glaucoma. This power would increase significantly if the optic disc size is taken into account.[23] We collected Heidelberg Retina Tomograph II data on this population, and they are being analyzed to address these issues. Second, although the evaluation of CDR was quantified using an eyepiece graticule, it relied on subjective assessment of the disc and cup margins to perform the measurements. Training and agreement of CDR assessment with one of us (P.J.F.) using the Tanjong Pagar protocol was performed before the study commenced; however, the measurements were performed by multiple observers, and intergrader reproducibility was not assessed during the study. However, the effect of such measurement errors, likely to be random, is a dilution of strength of associations. Finally, myopic or tilted discs and media opacities could also have affected the optic disc evaluation and may have introduced unknown biases, although analyses excluding nuclear cataract had no effect on these associations.

In summary, in this population-based study, significant determinants of greater vertical CDR were male sex, higher IOP, lower diastolic BP, lower ocular perfusion pressure, lower BMI, past cataract surgery, and diabetes mellitus. Of these, higher IOP was the most important determinant of CDR. Nevertheless, the variables evaluated in this study accounted for less than 4% of the variation in vertical CDR, suggesting that other unknown factors may affect the CDR.

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