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Original Article

Distribution and associated factors of optic disc diameter and cup-to-disc ratio in an elderly Chinese population☆

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Abstract

Background: Glaucoma is the second leading cause of blindness worldwide and East Asian people account for almost half of those affected. Vertical elongation of the optic cup is a characteristic feature of glaucoma. However, there is a significant overlap in the vertical cup-to-disc ratio (VCDR) between normal eyes and eyes affected by glaucoma. The purpose of this study was to determine the distribution of VCDR and vertical disc diameter (VDD) and their predictive factors in a population of elderly Chinese residents in Taiwan.
Methods: Four hundred and sixty elderly Chinese residents aged 72 years and older in the Shihpai district, Taipei, Taiwan participated in this study. Slit lamp biomicroscopic measurement of the VCDR and VDD after pupil dilation with a 78 diopter lens was performed by one glaucoma specialist. Multiple linear regression analyses were used to fit the best model for independent variables.
Results: The VCDR was recorded for 438 right eyes and 430 left eyes. After excluding participants with glaucoma, the mean ± SD VCDR was 0.44 ± 0.17 for both eyes, and the 97.5th percentile was 0.8. A greater VCDR was associated with a longer axial length [VCDR = −0.47 + 0.04(axial length)] under multiple regression analysis. The VDD was obtained for 420 right eyes and 406 left eyes. The mean ± SD VDD for all participants was 1.77 ± 0.22 mm for the right eye and 1.79 ± 0.22 mm for the left eye. A higher body mass index (BMI) and a longer axial length were significantly associated with a larger VDD under multiple regression analysis. [VDD = −0.05 + 0.07 (axial length) + 0.06 (obesity); if BMI <24, then obesity = 0; if BMI ≥24, then obesity = 1]. A larger VDD was associated with a larger VCDR ($p < 0.001$) and the VCDR could be predicted by the equation VCDR = −0.07 + 0.3VDD.
Conclusion: A greater VCDR was related to a longer axial length. A greater VDD was related to a higher BMI and a longer axial length.
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Keywords: Chinese population; elderly patients; vertical cup-to-disc ratio; vertical disc diameter

1. Introduction

Glaucoma is the second leading cause of blindness worldwide and East Asian people account for almost half of those affected.[1–3] Vertical elongation of the optic cup is a characteristic feature of glaucoma.[4,5] However, there is a significant overlap in the vertical cup-to-disc ratio (VCDR) between normal eyes and eyes affected by glaucoma.[6,7] In addition to glaucoma, there are physiological factors that may influence the VCDR.

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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Few studies have assessed the distribution of VCDR, the vertical disc diameter (VDD), and their potential predictive factors, especially in East Asia, and the results are controversial. For example, Garway-Heath et al[8] noted an increase in vertical optic cup diameter with age, whereas the Baltimore Eye Survey,[9] the Rotterdam Study,[10] and the Vellore Eye Study[11] refuted such findings.

The purpose of this survey was to investigate the distribution of VCDR and VDD and their associated systemic and ocular factors in a group of elderly Chinese residents recruited from the follow-up examination of the Shihpai Eye Study.[12,13]

2. Methods

The Shihpai Eye Study[12,13] was a community-based, cross-sectional survey of vision and eye diseases among residents aged at least 65 years in Shihpai district, Taipei, Taiwan who were not living in institutions. Residents 65 years of age and older were identified using the household registration system. This system officially registers personal information such as date of birth, sex, and home address, as well as family members and relations. According to the official household registration in 1999, the total number of residents aged at least 65 years in Shihpai was 4750; 3746 people were eligible for the study and 2045 were randomly selected to be invited to participate in the study.

Of the 2045 invited residents, 1361 (66.6%) participated in both the questionnaire and the eye examination. The baseline examination was conducted between July 1, 1999 and December 31, 2000. We planned to invite the 1361 residents who participated in the baseline examination to the follow-up study of the fixed cohort, which was conducted from March 25, 2006 to December 31, 2007. This study was conducted as a part of the follow-up survey. After excluding 205 (15.1%) residents who died before they were interviewed, 301 (22.1%) residents who moved away, and 31 (2.3%) residents by then living in institutions, 824 (60.5%) residents were eligible for the study.

A total of 725 (87.4%) residents agreed to be interviewed for the questionnaire. Those who were interviewed were invited to participate in a comprehensive ophthalmic examination conducted in Taipei Veterans General Hospital. Informed consent was obtained from each resident after explaining the purpose and procedure of the study. The survey followed the tenets of the Declaration of Helsinki. Ophthalmologists conducted the eye examinations according to a standardized protocol. This study was approved by the Institutional Review Board of Taipei Veterans General Hospital.

2.1. Eye examination protocol

The optic disc was evaluated under stereoscopic view with a 78 D lens (×16 magnification) after pupil dilatation. One glaucoma specialist (T.M.K.) examined all the participants. The lens was held with the thumb and index finger while the fourth finger rested on the plastic headband of the slit lamp to maintain a constant length between the lens and the patient's eye and to prevent lens tilt so precise measurements could be made. The margins of the cup were defined as the point of maximum inflexion of the contour of the optic disc surface. The VCDR was recorded in units of 0.05. The vertical diameter of the optic disc was measured with a 78 D lens, with the slit beam adjusted to the narrowest beam width and then focused on the surface of the disc. The height of the slit beam was then adjusted to coincide with the diameter of the optic disc. The beam height was then recorded to the nearest 0.05 mm.

It is not possible to measure the dimension of the optic disc directly *in vivo*, except during vitreoretinal surgery, therefore correction of the disc size is required for any indirect measurement. The size of the image as measured with the beam length on the slit lamp is dependent on the magnification due to the patient's eye. It is a variable dependent on the optical dimensions of the patient's eye and not the fundus imaging system (correction factor q mm/degree). The size of the image is also dependent on the magnification due to the condensing lens used to obtain the image (correction factor p degrees/mm), and the position of the condensing lens with respect to the eye. Thus to calculate the absolute dimensions of this image, the total magnification of the system must be known.[14]

The true size of the optic disc was calculated by a modified Littmann's formula,[14,15] as follows: $t = pqs$, where t = the true size of the optic disc, p = the fundus lens correction factor, q = the ocular factor, and s = the optic disc diameter measured at the slit lamp biomicroscope.

The intraocular pressure was measured by Goldmann applanation tonometry by one glaucoma specialist. Two measurements were taken for each eye and the mean value was used. If the two measurements differed by more than 2 mmHg, a third measurement was taken and the mean of the three measurements was used. The central corneal thickness was measured by specular microscopy (SP-9000, Konan, Hyogo, Japan) with three measurements taken for each eye and the median value was used for analysis. Axial length, lens thickness, and anterior chamber depth were measured using A-scan ultrasound biometry (AL-1000, Tomey, Aichi, Japan). The lens condition was assessed by slit lamp and graded according to the Lens Opacities Classification System III (LOCS III) by one ophthalmologist.[16,17]

Spherical equivalent (sphere + 1/2 cylinder) was calculated from the best refractive correction. A spherical equivalent between −1.0 D and +1.0 D was defined as emmetropia, less than −1.0 D as myopia, and greater than +1.0 D as hyperopia.

Glaucoma was diagnosed using the International Society of Geographic and Epidemiological Ophthalmology classification.[18] Category 1 was defined by structural and functional evidence: VCDR ≥0.8, VCDR asymmetry ≥0.35, or neuroretinal rim width ≤0.1, associated with reliable and compatible glaucomatous visual field defect not explained by other diseases. Category 2 was defined by advanced structural damage with unproved visual field loss: VCDR ≥0.85, or VCDR asymmetry ≥0.45. Category 3 was defined as when the optic disc was not seen and a visual field test was impossible: corrected visual acuity <3/60, and intraocular

pressure ≥23.9 mm Hg, or corrected visual acuity <3/60 and evidence of glaucoma surgery.

Hypertension, diabetes, cardiovascular disease, and stroke were defined as positive if one of these conditions had previously been diagnosed by a doctor.

2.2. Statistical analysis

The dependent variables in the analysis were VCDR and VDD. The systemic independent variables tested were age, gender, education, weight, height, body mass index (BMI), waist-to-hip ratio, diastolic blood pressure, systolic blood pressure, pulse pressure, history of hypertension, diabetes, cardiovascular disease and stroke, smoking history, alcohol drinking history, and exercise habit. The ocular-independent variables tested were intraocular pressure, ocular perfusion pressure, central cornea thickness, anterior chamber depth, axial length, lens thickness, nuclear opacity, history of cataract surgery, and spherical equivalent. Analysis using the *t* test and ANOVA were performed to look for an association between each independent variable and dependent variables under univariate analysis.

Generalized estimating equations were used to fit the best model for independent variables. Independent variables with $p \leq 0.2$ under univariate analysis were analyzed using multiple regression analysis. A value of $p < 0.05$ was considered to be statistically significant. The parameter estimate was the slope coefficient of various independent variables in the generalized estimating equation. The analysis for VCDR was based on the participants after excluding those with glaucoma and on all participants for VDD.

Statistical analysis was performed using Statistical Analysis System software (SAS 6.12, SAS Institute, Cary, NC, USA).

3. Results

Of the 1361 participants who attended the baseline examination, 205 (15.1%) residents died before they were interviewed, 301 (22.1%) moved away, and 31 (2.3%) moved into institutions. Thus 824 (60.5%) participants were eligible for the study, 725 (87.4%) of whom agreed to be interviewed for the questionnaire. Among those interviewed, 460 (55.8% of those eligible or 39.8% of the remaining participants) took part in the ophthalmic examination. A comparison of the demographics and some of the variables in the participants with and without the eye examination showed that the participants were younger (78.1 ± 4.1 years vs. 80.4 ± 5.4 years, $p < 0.001$), more likely to be men ($p < 0.01$), married and living with a spouse ($p < 0.001$), and were more highly educated ($p < 0.001$). Participants were less likely to have a history of stroke ($p = 0.03$) and more likely to be current smokers ($p = 0.03$).

Among the participants, the men were significantly more highly educated ($p < 0.001$) and married and living with their spouse ($p < 0.001$) than the women. There was no significant difference among the other demographic variables for the participants (Table 1).

Table 1
Characteristics of study participants in Shihpai, Taipei, Taiwan, 2006–2007.

Characteristic	Men ($n = 301$)	Women ($n = 159$)	p
Age (y)			
72–79	214 (71.1)	113 (71.1)	0.99
80–93	87 (28.9)	46 (28.9)	
Education			
Secondary school and below	142 (47.3)	105 (66.0)	<0.001*
High school and above	158 (52.7)	54 (34.0)	
Body mass index (kg/m^2)			
<25	183 (60.8)	92 (59.0)	0.71
≥25	118 (39.2)	64 (41.0)	
Marital status			
With spouse	270 (90.3)	89 (57.1)	<0.001*
Without spouse	29 (9.7)	67 (42.9)	
History of hypertension			
Yes	149 (51.0)	78 (50.7)	0.94
No	143 (49.0)	76 (49.3)	
History of diabetes			
Yes	57 (19.8%)	34(22.2)	0.55
No	231 (80.2)	119 (77.8)	
History of cardiovascular disease			
Yes	112 (38.8)	65 (42.8)	0.42
No	177 (61.3)	87 (57.2)	
History of stroke			
Yes	10 (3.4)	4 (2.5)	0.61
No	284 (96.6)	154 (97.5)	

Data are presented as *n* (%).
*$p < 0.05$.

After excluding participants with media opacities, participants who could not cooperate for the examination, and participants who declined the assessment, VCDR was obtained in 438 (95.2%) right eyes and 430 (93.5%) left eyes. The mean ± SD VCDR for participants was 0.44 ± 0.17 for both eyes. Excluding participants with glaucoma had minimal impact on the distribution except for the 97.5th percentile (VCDR 0.9 vs. VCDR 0.8 after excluding participants with glaucoma) and the 99.5th percentile (VCDR 1.0 for right eye and 0.95 for left eye vs. 0.85 for the right eye and 0.9 for the left eye after excluding participants with glaucoma), in which both values became smaller.

Under univariate analysis, education ($p = 0.04$) was the only demographic characteristic that was significantly associated with VCDR. Among ocular predictors, axial length [axial length ≤23.0 mm vs. 23.0 mm < axial length ≤24.0 mm ($p = 0.001$) and axial length >24.0 mm vs. 23.0 mm < axial length ≤24.0 mm ($p = 0.001$)] and nuclear opacity (LOCS III grade >2 vs.≤2; $p = 0.04$) were significantly associated with VCDR. Intraocular pressure ($p = 0.46$), ocular perfusion pressure ($p = 0.45$), and central corneal thickness ($p = 0.74$) were not significantly associated with VCDR. Under multiple regression analysis, axial length ($p < 0.001$) was the only factor significantly associated with VCDR (Table 2) and their relation can be represented by the equation VCDR = −0.47 + 0.04 (axial length).

Table 2
Systemic and ocular predictors of vertical cup-to-disc ratio under multiple regression analysis in Shihpai, Taipei, Taiwan, 2006–2007.

Variable	Parameter estimate	p
Age (≥80 vs. <80 y)	0.03	0.19
Education (high vs. low)	0.04	0.07
Waist-to-hip ratio (≥0.90 vs. < 0.90)	0.004	0.85
History of hypertension (yes vs. no)	−0.001	0.95
History of cardiovascular disease (yes vs. no)	−0.04	0.08
Smoker (current vs. non-smoker)	−0.06	0.07
Smoker (previous smoker vs. non-smoker)	−0.003	0.91
Axial length (mean 23.46 ± 1.18 mm)	0.04	<0.001*
Nuclear opacity (>2 vs. ≤2)	0.04	0.06

*$p < 0.05$.

After excluding participants with media opacities, those who could not cooperate for the examination, and those who declined, the VDD was measured for 420 (91.3%) right eyes and 406 (88.3%) left eyes. The mean ± SD VDD was 1.77 ± 0.22 mm for the right eye and 1.79 ± 0.22 mm for the left eye. The mean ± SD horizontal disc diameter was 1.72 ± 0.23 mm for the right eye and 1.70 ± 0.23 mm for the left eye.

Under univariate analysis, a higher BMI (≥24 vs. <24; $p = 0.01$) was associated with a larger VDD. Among the ocular predictors, axial length (axial length ≤23.0 mm vs. 23.0 mm < axial length ≤24.0 mm; $p < 0.0001$ and axial length >24.0 mm vs. 23.0 mm < axial length ≤24.0 mm; $p < 0.0001$), nuclear opacity (>2 vs. ≤2; $p = 0.01$) and spherical equivalent (spherical equivalent <−1.0 vs. −1.0 ≤ spherical equivalent ≤ +1.0; $p < 0.01$ and spherical equivalent > +1.0 vs. −1.0 ≤ spherical equivalent ≤ +1.0; $p < 0.01$) were associated with VDD. Intraocular pressure and central corneal thickness were not associated with VDD. Under multiple regression analysis, a higher BMI (≥24 vs. <24; $p = 0.01$) and a longer axial length ($p < 0.0001$) were associated with a larger VDD (Table 3). Their relationship can be represented by the equation: VDD = −0.05 + 0.07(axial length) + 0.06(obesity); (if BMI <24, then obesity = 0, if BMI ≥24, then obesity = 1).

Table 3
Systemic and ocular predictors of vertical disc diameter under multiple regression analysis in Shihpai, Taipei, Taiwan, 2006–2007.

Variable	Parameter estimate	p
Age (≥80 vs. <80 y)	0.01	0.72
Education (high vs. low)	0.01	0.56
Body mass index (≥24 vs. <24)	0.06	<0.03*
History of alcohol intake (current vs. never)	0.01	0.78
History of alcohol intake (quit vs. never)	−0.02	0.77
Ocular perfusion pressure (>48 vs. ≤48)	0.01	0.55
Axial length (mean 23.46 ± 1.18 mm)	0.07	<0.001*
Nuclear opacity (>2 vs. ≤2)	0.07	0.31
Spherical equivalent (myopia vs. emmetropia)	−0.01	0.63
Spherical equivalent (hyperopia vs. emmetropia)	0.03	0.66

*$p < 0.05$.

On the analysis of the relationship between VCDR and VDD, a larger VCDR was significantly associated with a larger VDD. The VCDR could be predicted from VDD by the formula VCDR = −0.07 + 0.3VDD ($p < 0.0001$).

4. Discussion

This study of Chinese residents aged 72 years and older showed that BMI was associated with VDD and axial length was related to both VCDR and VDD.

The 97.5th percentile VCDR of our participants was 0.8, larger than the 0.7 found in other surveys[19,20] (Table 4). It should be noted that participants with glaucoma are included in some population-based studies. Moreover, measurements obtained by different methods are not interchangeable. With a very similar age group and measuring method, it was seen that the mean VCDR was larger in our study (0.44 ± 0.17) than in the Singapore Malay Eye Study[4] (0.39 ± 0.13) (Table 5). This discrepancy may be explained by ethnicity and inter-individual variations in measurement.

Our study found that gender was not a determinant of VCDR. This was in concordance with the Rotterdam Study[10] and the Vellore Eye Study,[11] but was in contrast with the findings of the Tanjong Pagar Study[21] and the Singapore Malay Eye Study,[4] where men were noted to have a larger VCDR.

Inconsistency has also been noted in whether VCDR increases with age. Garway-Heath et al[8] noted an age-related decline in the neuroretinal rim area of 0.28% per year by planimetry and 0.39% per year by scanning laser ophthalmoscopy, whereas Varma et al[9] noted no progressive age-related decline in neural rim area. The Blue Mountains Eye Study[22] found that each decade increase in age was associated with a 0.01 (1.9%) increase in the mean VCDR. Age did not remain significantly associated with VCDR in the Rotterdam Study,[10] or when patients with glaucoma were excluded in the Singapore Malay Eye Study.[4] Age was not related to VCDR in our elderly participants and another study of Asian adults.[23]

In the Rotterdam Study,[10] each diopter increase towards myopia was related to a 1.4% increase in rim area. The Tanjong Pagar Study[21] found that rim area was associated with axial length. As the refractive status of an eye was determined by a combination of axial length, lens thickness, density, and position as well as corneal curvature, these variables should be adjusted. Refractive error was not related to VCDR in our study. Instead, our study found that for every 1 mm increase in axial length, there was an increase of 0.04 in the VCDR.

Table 4
Values of 97.5th percentile and 99.5th percentile of vertical cup-to-disc ratio in different studies.

	97.5th percentile	99.5th percentile
Bangladesh Survey[19]	0.70	0.85
Mongolian Study[18]	0.70	0.70
Tanjong Pagar Survey[21]	0.71	0.81
Tanzania Survey[20]	0.7	0.8
Blue Mountains Eye Study[5]	0.68	0.73 (99th)
This study	0.80	0.85

Table 5
Distribution of vertical cup-to-disc ratio and vertical disc diameter in different studies.

	Age (y)	Method	Vertical cup-to-disc ratio	Vertical disc diameter/disc area
Rotterdam Eye Study[10]	≥55	Image analyzer system	0.49 ± 0.14	2.42 ± 0.47 mm^2
Baltimore Eye Study[9]	≥40	Image analyzer system	0.56 (blacks) 0.49 (whites)	2.94 ± 0.74 mm^2 (Blacks) 2.63 ± 0.46 mm^2 (Whites)
Blue Mountains Eye Study[5]	≥49	Photograph with stereo viewer	0.43 ± 0.14	1.50 mm (median)
Vellore Eye Study[11]	47.5 (mean)	Photograph with stereo viewer	0.56 ± 0.08	1.87 ± 0.24 mm 2.58 ± 0.65 mm^2
Tanjong Pagar Survey[21]	40–79	Fundus contact lens Planimetry	0.47 (median) 0.55 ± 0.01	1.73 ± 0.19 mm 2.17 ± 0.46 mm^2
Bangladesh Survey[19]	≥35	90 diopter lens	0.34 ± 0.14	—
Tanzania Survey[20]	≥40	78 diopter lens	0.41 ± 0.16	—
Singapore Malay Eye Study[4]	70–80	78 diopter lens	0.39 ± 0.13	—
Beijing Eye Study[25]	≥40	Planimetry	—	2.65 ± 0.57 mm^2
This study	≥72	78 diopter lens	0.44 ± 0.17	1.77 ± 0.22 mm, 2.39 ± 0.57 mm^2

The disc area increased by 0.02 mm^2 for each 10 cm increase in height in the Rotterdam Study.[10] The Tanjong Pagar Study[21] also noted similar findings. In our study, a higher BMI was related to a larger VDD. However, this view was not supported by the Singapore Malay Eye Study.[4] The relationship between disc size and BMI was investigated by only a few large-scale studies and this deserves further evaluation.

Longer axial length was associated with a larger VDD in our study. These results confirmed an anatomical study that found a larger optic disc in eyes with larger diameter.[24] In the Rotterdam Eye study,[10] disc area linearly increased slightly and significantly by 1.6% for each diopter increase towards myopia. The Tanjong Pagar Study[21] noted that for every millimeter increase in axial length, there was a 3.7% increase in disc area. Axial length was noted to be related to VDD in the Vellore Eye Study[11] and the Baltimore Eye Survey[9] (refractive error).

Despite the difference in the absolute value of optic disc size between the Beijing Eye Study[25] and our study (Table 5), the relationship that the larger the optic disc, the larger the optic cup was in concordance. This was also noted by the Vellore Eye Study[11] and the Blue Mountains Eye Study.[5] Hence knowing a patient's disc size is relevant when screening for glaucoma as the VCDR depends on disc area.[5]

The response rate in our study was relatively low (55.8%). Obtaining population-based prevalence estimates of eye disease among the elderly is challenging because this group is less likely to participate in research studies.[26] The inclusion rate in the Rotterdam Study[10] ranged from 59% in the 75–84 year age group to 28% in the group ≥85 years. Similarly, in the Baltimore Eye Survey,[9] inclusion rates were 48% in the 70–79 year age group and 21% in the group ≥80 years. Another potential reason for the low participation rate is that a lack of utilization of ophthalmological care for prevention and treatment has created the impression that loss of vision is expected in later life and the idea that nothing can be done to improve the situation among elderly people, particularly among less educated elderly people.

In our survey, the non-participating residents were older, more likely to be less educated, and women; nursing home residents from the original cohort were not examined. The unexamined residents remain a potential source of bias.

A potential source of error in this survey is interobserver variation in grading. Our VCDR and VDD were measured by one glaucoma specialist and the problem of interobserver grading should be eliminated. Moreover, our survey was conducted in a medical center by professionally trained ophthalmologists.

The VCDR in our elderly participants was independent of age, sex, and refractive error. The VCDR was larger in participants with a longer axial length. A larger VDD was related to a higher BMI and a longer axial length. In evaluating whether VCDR is large in a particular patient, the VDD must be taken into account.

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