Original Article

The Association of Central Corneal Thickness with Ocular and General Parameters in a Community Setting: The Yazd Eye Study

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Abstract

Purpose: To assess central corneal thickness (CCT) and its associations in an adult Iranian population.
Methods: This was a population-based cross-sectional study of adults aged 40–80 years. Eyes with corneal disorders, previous ocular surgery, or trauma were excluded. All subjects underwent complete ophthalmic examination, general health assessment, laboratory tests, and a detailed interview. CCT was measured with an ultrasonic pachymeter. Intraocular pressure (IOP) was measured with Goldmann applanation tonometry. Except for the report on interocular differences in CCT, only one eye of each subject was used for the rest of statistical analyses.
Results: The mean age (±SD) of the 1203 participants, who had CCT measurements and met inclusion criteria, was 51.8 ± 8.5 years. The mean CCT was 544 ± 35, 564 ± 28, and 544 ± 36 µm in the eyes of the normal, ocular hypertension, and glaucoma groups, respectively ($P = 0.025$). In participants without glaucoma, the mean interocular difference in CCT was 9 ± 12 µm. CCT was not significantly associated with age, sex, or some select systemic factors (body mass index, diabetes, hypertension, and renal failure). While controlling for age and sex, CCT was greater in individuals with higher IOPs ($P < 0.001$), larger vertical or horizontal cup-to-disc ratios ($P = 0.044$, and $P = 0.025$, respectively), and hyperopia ($P = 0.009$).
Conclusion: In this adult Iranian population, CCT was significantly associated with IOP, cup-to-disc ratio, and the refractive status of eye. CCT outside the normal range of 475–613 µm or with interocular asymmetry greater than 33 µm (6%) should prompt evaluation for potential ocular disorders.

Keywords: Corneal Pachymetry; Cross Sectional Survey; Iran

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INTRODUCTION

The measurement of the central corneal thickness (CCT) is an essential component of a complete ophthalmic

examination. CCT correlates with the corneal barrier and endothelial pump function, and hence, is an indicator of the corneal health. An accurate measurement of CCT is also a crucial part of the preoperative assessment in refractive surgery candidates.[1] A low CCT has been recognized as an independent risk factor for both the onset and progression of glaucoma.[2,3] In addition, CCT can affect the accuracy of intraocular pressure (IOP) measurements by applanation tonometry.[4-6]

Several ocular, systemic, anthropological, and environmental factors have been reported to influence CCT.[2,5] Specifically, ethnic differences in CCT distribution have been well recognized. For example, compared to Caucasians, Hispanics, or Asians, African Americans consistently tended to have lower CCT measurements.[7,8] With respect to the possible variation in CCT of different ethnic populations, and considering that CCT is an important parameter in the diagnosis and treatment planning of many ocular conditions, it is necessary to study CCT in different populations in order to determine its normal range and distribution.

Such studies are limited in the Middle East. Only two population-based studies have evaluated CCT in Iranian adults; however, the measurements were made using optical devices.[9,10] In addition, their methodologies and studied parameters were not based on data from the Yazd Eye Study, which is a population-based prevalence survey of ocular diseases conducted on an Iranian population aged 40–80 years old.[11] Therefore, we conducted a study based on data from the Yazd Eye Study and, as a part of the complete ophthalmic examination, we obtained measurements of IOP in order to assess the distribution of CCT and the factors that correlated with this parameter.

METHODS

Study Population

The Yazd Eye Study is a population-based cross-sectional study of 2320 Iranian subjects, aged 40 to 80 years old, from the non-institutionalized urban and rural population of the Yazd district, which has an estimated population of 526,000 based on the 2006 national census. This study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

The detailed study methodology has been previously described.[11-13] In brief, subjects were selected through a multistage, random cluster sampling. The final sample size was 2320.

After obtaining written informed consents from all eligible participants, a trained interviewer administered a standard questionnaire to collect information on age, sex, level of education, and ocular, medical, and drug histories. All subjects were referred to an equipped eye clinic within 1 week for further evaluation. Eyes with corneal disorders and/or a history of previous ocular surgery or trauma were excluded from our analysis.

Measurement of Systemic Factors

Height was measured with the subject standing without shoes. Weight was recorded while the subject wore indoor clothing, using a standard calibrated scale. BMI was calculated as the weight (kg) divided by the height squared (m^2).[14] Subjects were classified as either underweight (BMI <18.5), normal (BMI: 18.5–24.9), overweight (BMI 25–29.9), or obese (BMI ≥30).

During the same session, blood pressure was measured twice in the right arm while the subject was in sitting position, after 5 minutes of rest, using a standard mercury sphygmomanometer (nova-presameter®– Riester's, Germany). The average of the two measurements was recorded. Hypertension was defined as a systolic blood pressure ≥140 mmHg, a diastolic blood pressure ≥90 mmHg, or having a history of hypertension or use of antihypertensive medications. Individuals were considered to have diabetes if they had a fasting blood sugar (FBS) of ≥126 mg/dl (7 mmol/L) in two separate tests (on different days). They were also regarded as having diabetes if they were a known case of diabetes as determined by a physician and/or used insulin or oral anti-diabetic medications.[11] Albuminuria was used as a proxy for kidney dysfunction, which was defined as an albumin/creatinine ratio greater than 30 mg/g in one random sample of urine.

Measurement of Ocular Factors

Refraction was performed using a Topcon KR 8000 automated refractometer (Topcon Co., Tokyo, Japan). If autorefraction was not possible, manual retinoscopic refraction was tried. Spherical equivalent refraction (SE, sphere power plus half cylinder power) was used to classify refractive errors. Myopia and hyperopia were defined as a SE worse than –0.5 D and +0.5 D, respectively.[13]

The anterior segment was examined by trained ophthalmologists using slit-lamp biomicroscopy (BD 900, Haag-Streit, Bern, Switzerland). The anterior chamber angle was estimated on the basis of Van Herick's technique.[15] After administering one drop of 0.5% tetracaine hydrochloride (Anestocaine, Sinadaru, Iran) for topical anesthesia and fluorescein staining of the tear film, intraocular pressure was measured using a Goldmann applanation tonometer (AT 900, Haag-Streit, Bern, Switzerland). IOP was measured three times in each eye and the mean value was calculated and recorded. Gonioscopy was performed in all subjects using a Goldmann type goniolens (Ocular Instruments, Inc, Bellevue, WA, USA). Participants with occludable angles were referred for laser peripheral iridotomy.[11]

Subsequently, CCT was measured by a trained optometrist using an ultrasonic pachymeter (UP-1000; Nidek Technologies, Gamagori, Japan). Tetracaine hydrochloride eye drops were used for topical anesthesia. With the pachymetry probe positioned perpendicular to the cornea at the center of the pupil, five CCT measurements were obtained from each eye and the average value was calculated and recorded. To avoid a possible confounding effect from previous measurements on CCT readings, CCT values were obtained at least 30 minutes after any previous corneal manipulation.

After pupil dilation with 1% tropicamide drops, administered twice within a 5 minutes interval, the eyes were examined again using the slit-lamp, and the retina and optic disc were evaluated using a 78 D aspheric wide-field lens. The vertical (VCDR) and horizontal (HCDR) cup-to-disc ratios and neuroretinal rim (NRR) were carefully recorded. Glaucoma and ocular hypertension were diagnosed and classified according to the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) criteria.[12,16]

Statistical Analysis

Statistical analysis was performed using the STATA 12.0 software package (StataCorp LP, College Station, TX, USA). Except for the study on interocular differences in CCT, only one eye of each participant was used for statistical analyses. If both eyes were normal, hypertensive, or newly diagnosed with untreated glaucoma, a random eye was selected. If only one eye had either condition, then that eye was selected for statistical analysis. Analysis of covariance (ANCOVA) models was used to assess the effects of potential systemic and ocular determinants on CCT after adjusting for age and sex. The distribution of CCT was calculated within the entire study population, as well as within subgroups (normal subgroup and different classes of glaucoma). The level of significance was set at 5%.

RESULTS

In the Yazd Eye Study, 2098 out of 2320 eligible subjects participated in ophthalmologic examinations (response rate of 90.4%), of which 1203 subjects had CCT measurements and met other inclusion criteria. The responders comprised 45.6% men (mean ± SD age = 51.8 ± 8.5 years). The characteristics of participants in this analysis, compared to the rest of participants in the Yazd Eye Study, are given in Table 1.

CCT measurements were normally distributed in normal eyes with a mean of 554 ± 35μm (95% CI: 542-546; the normal range including 95% of eyes: 475–613). The distribution of CCT in the normal subgroup compared to the glaucoma and ocular hypertension subgroups is

Table 1. Comparison of demographics and comorbidities between the participants of the CCT analysis and the rest of the participants of the Yazd eye study

	CCT analysis		P*
	-	+	
Sex			
Male	445 (49.7%)	549 (45.6)	0.064
Female	450 (50.3%)	654 (54.4)	
Age category (y)			
40-49	261 (29.2%)	545 (45.3%)	<0.001
50-59	274 (30.6%)	431 (35.8%)	
60-69	173 (19.3%)	166 (13.8%)	
70-80	187 (20.9%)	61 (5.1%)	
BMI (kg/m^2)			
Underweight	15 (2.0%)	20 (1.8)	0.003
Normal	251 (33.0%)	299 (26.9)	
Overweight	286 (37.6%)	498 (44.8)	
Obese	208 (27.4%)	295 (26.5)	
Hypertension			
No	496 (55.7%)	758 (63.7)	0.001
Yes	394 (44.3%)	432 (36.3)	
Diabetes			
No	628 (70.3%)	914 (77.2)	<0.001
Yes	265 (29.7%)	270 (22.8)	

*Based on Chi-squared test or Mann-Whitney U test, whichever was appropriate. CCT, central corneal thickness; y, year
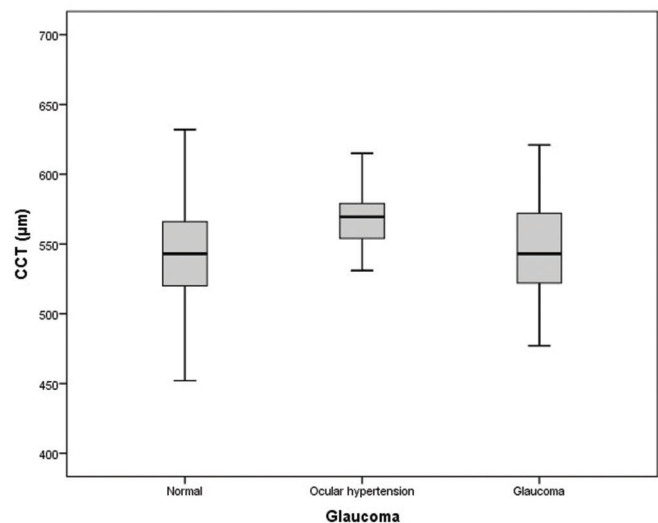
Figure 1. Box and whisker plot showing the distribution of central corneal thickness measurements in normal eyes versus eyes with glaucoma or ocular hypertension.

presented in Figure 1. Eyes with ocular hypertension had significantly higher CCT values compared to the normal eyes (564 ± 28 vs. 544 ± 35 μm, *P* = 0.025). The mean interocular difference of CCT was 9 ± 12 μm in subjects without glaucoma [Table 2].

There were no statistical differences in the mean CCT between male and female participants or between the different age groups [Table 3]. The relationship

Table 2. Interocular difference in central corneal thickness (CCT)					
	Number (%)	**Interocular difference (μm)†**		**Interocular difference (%)‡**	
		Mean±SD	**Median (Range)**	**Mean±SD**	**Median (Range)**
All Participants					
Total	1202				
Without glaucoma	1147 (95)	9±12	6 (0 to 164)	2±2	1 (0-30)
Ocular hypertension	22 (2)	7±5	6 (0 to 21)	1±1	1 (0-4)
Glaucoma	33 (3)	6±7	4 (0 to 31)	1±1	1 (0-6)
*P**		0.23		0.208	
Glaucoma					
POAG	14 (42)	6±6	5 (0 to 22)	1±1	1 (0-4)
NTG	16 (48)	6±8	3 (0 to 31)	1±2	1 (0-6)
PACG	3 (9)	4±1	4 (4 to 5)	1±0	1 (1-1)
*P**		0.836		0.848	

*Calculated using analysis of covariance test (ANCOVA), controlled for age and sex, †Calculated as a modulus of the right eye CCT subtracted from the left eye CCT, ‡Calculated as a modulus of the right eye CCT subtracted from the left eye CCT, divided by the mean CCTs of both eyes; NTG, normal tension glaucoma; PACG, primary angle closure glaucoma; POAG, primary open angle glaucoma; SD, standard deviation

Table 3. Association of age and sex with central corneal thickness					
	All Participants			**Subjects without glaucoma**	
	***N* (%)**	**Mean±SD**	**Median (range)**	***N* (%)**	**Mean±SD**	**Median (range)**
Sex					
Male	549 (45.6)	543±35	543 (416-682)	526 (45.8)	542±35	543 (416-682)
Female	654 (54.4)	545±35	544 (424-678)	622 (54.2)	545±35	544 (424-678)
*P**		0.233			0.256	
Age category					
40-49	545 (45.3)	543±35	543 (424-678)	529 (46.1)	543±35	543 (424-678)
50-59	431 (35.8)	545±36	546 (416-630)	413 (36)	544±35	545 (416-630)
60-69	166 (13.8)	547±34	544 (437-682)	154 (13.4)	547±35	544 (437-682)
70-80	61 (5.1)	540±30	543 (478-618)	52 (4.5)	541±30	543 (478-618)
*P***		0.531			0.642	

*Calculated using *t*-test, **Calculated using analysis of variance; SD, standard deviation; N, number

between selected ocular factors with CCT is shown in Table 4. Analysis of covariance, adjusted for age and sex, showed that a greater CCT was associated with a higher IOP ($P < 0.001$), greater VCDR ($P = 0.044$) and HCDR ($P = 0.025$), and hyperopia ($P = 0.009$). The Van Herick score was not associated with CCT. The association between IOP and CCT is shown in Figure 2.

The relationship between selected systemic factors and CCT is shown in Table 5. We did not find any statistically significant association between BMI, diabetes, hypertension, or albuminuria and CCT.

DISCUSSION

According to the results of the present study, the mean CCT in this Iranian population without glaucoma or ocular hypertension (as measured using an ultrasound pachymeter) was 544 ± 35 μm. The normal range, which is expected to contain 95% of the population, was 475 to 613 μm. Two population-based studies on CCT have been conducted in Iran.[9,10] In contrast to the

present study in which the gold standard ultrasonic method was used, both the previous studies used optical devices to measure CCT. In the Shahroud Cohort Eye Study,[9] CCT was evaluated with Pentacam HR in 3820 participants 40 years of age or older and the reported mean CCT is 528 μm (normal range: 455–601). The Tehran Eye Study,[10] which included 410 subjects (≥14 years old) used the Orbscan II and reported that the mean CCT is 556 μm (normal range: 478–634) [Table 6]. Differences in the reported CCTs in Iranian populations may be due to the different methodologies used or age groups studied. In contrast to our study that did not find any significant association between age and CCT, both the Tehran and Shahroud studies report an inverse association. All three CCT studies of the Iranian population did not reveal any significant associations between sex or BMI and CCT.

The mean CCT and its normal range from various large-scale population-based studies throughout the world are presented in Table 6.[5,7,9,10,17-31] Since distinct measurement methods were used in the different

Table 4. Association of selected ocular features with central corneal thickness

	All Participants			Subjects without glaucoma		
	Number (%)	Mean±SD (μm)	Median (range)	Number (%)	Mean±SD (μm)	Median (range)
IOP (Quartile)						
≤ 12	310 (26.1)	535±36	534 (434-682)	305 (26.6)	535±36	533 (434-682)
13-14	418 (35.1)	542±34	542 (416-632)	412 (35.9)	542±34	543 (416-632)
15-16	282 (23.7)	548±32	549 (450-627)	276 (24)	549±32	549 (450-627)
≥ 17	180 (15.1)	557±34	559 (424-678)	155 (13.5)	556±35	557 (424-678)
P*		<0.001[†]			<0.001[†]	
VCDR (Quartile)						
≤ 0.20	300 (30.9)	542±36	540 (424-682)	295 (31.4)	541±36	540 (424-682)
0.21-0.30	236 (24.3)	544±32	544 (469-624)	230 (24.5)	544±32	543 (469-624)
0.31-0.45	260 (26.8)	545±34	544 (434-632)	257 (27.4)	545±34	544 (434-632)
≥0.46	174 (17.9)	547±36	549 (416-678)	156 (16.6)	547±36	549 (416-678)
P*		0.044			0.076	
HCDR (Quartile)						
≤ 0.25	212 (31.2)	542±34	541 (456-629)	206 (31.5)	542±33	540 (456-629)
0.26-0.30	134 (19.7)	544±33	542 (477-620)	131 (20)	544±33	541 (477-620)
0.31-0.45	195 (28.7)	545±33	545 (434-630)	192 (29.3)	545±33	544 (434-630)
≥ 0.46	139 (20.4)	550±35	551 (416-678)	126 (19.2)	550±35	551 (416-678)
P*		0.025			0.025	
Van Herick score						
closed	5 (0.4)	549±11	547 (536-562)	3 (0.3)	548±13	547 (536-562)
1	17 (1.4)	542±41	529 (478-613)	15 (1.3)	547±42	538 (478-613)
2	34 (2.9)	542±28	545 (488-597)	33 (2.9)	541±27	544 (488-596)
3	76 (6.4)	544±32	541 (472-618)	73 (6.4)	544±32	540 (472-618)
4	1055 (88.9)	544±35	543 (416-682)	1022 (89.2)	544±35	543 (416-682)
P*		0.997			0.998	
Refractive error						
Myopia	389 (32.9)	540±37	540 (416-629)	370 (32.4)	540±37	540 (416-629)
Emmetropia	615 (51.9)	545±34	546 (434-682)	596 (52.2)	544±34	545 (434-682)
Hyperopia	180 (15.2)	549±33	548 (469-622)	176 (15.4)	548±33	548 (469-622)
P*		0.009			0.026	

*Calculated using analysis of covariance test (ANCOVA), controlled for age and sex, [†]Remained statistically significant as assessed via ANCOVA after adjustment for all significant variable in addition to age and sex, HCDR, horizontal cup-to-disc ratio; IOP, intraocular pressure; VCDR, vertical cup-to-disc ratio; SD, standard deviation

studies, they should be compared with caution. Considering those studies that used the standard ultrasonic method, it was found that Indians[25,26] (511 and 514 μm), Burmese[22] (522 μm), Africans[7] (530 μm), and Koreans[30] (531 μm) had thinner corneas than other populations did. Iranians, with a Middle Eastern ethnicity, showed comparable CCT distributions with Caucasians[17,24] (537 and 540 μm), Latinos[18] (547 μm), Singaporean Chinese[23,27] (541 and 542), and Nepalese[29] (539 μm); all displayed CCT values of approximately 540 μm, with a difference of a few microns. These differences have important clinical implications, particularly in countries with multi-ethnic populations. For example, a CCT of 450 μm is probably normal in an Indian subject, while it may herald corneal ectasia in an Iranian patient and thus merits further evaluation.

The association of CCT with different demographic, ocular, and systemic factors from various studies is summarized in Table 7. Based on previous studies, the independent association between age and CCT is controversial; some studies report an inverse association, while others (including our study) found no significant association [Table 7]. The inconsistent conclusions regarding age with CCT in various studies may stem from the different age ranges of the study populations [Table 6]. In addition, the greater prevalence of diseases such as diabetes (which is associated with thicker corneas) in the older population, may be a reasonable cause for the possible masking of a true inverse association between age and CCT in our study, which included patients with and without systemic disorders. The aforementioned studies also had inconsistent conclusions about the independent association of sex with CCT. The studies that demonstrated an association report an invariably greater CCT in men than in women. The possible effect of sex hormones on the corneal anatomy and biomechanics

is biologically plausible and should be addressed in future studies.

The most consistent conclusion made by previous studies is related to the association between IOP and CCT [Table 7]. For every 100 µm change in CCT, the IOP changed from 1.03 to 3.0 mmHg. The association of IOP with CCT could be bidirectional; the CCT affects the apparent measurement of IOP and the IOP may affect CCT through the modification of the corneal endothelial pump function.
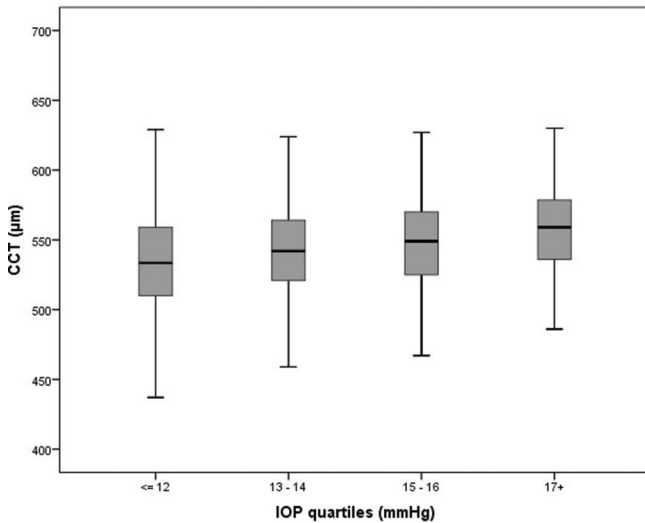
Figure 2. Box and whisker plot showing the distribution of central corneal thickness measurements, categorized based on intraocular pressure.

Most of previous studies reported either a greater CCT in hyperopes (including ours) or no association. Hyperopic eyes are known to have a thicker eye wall compared to myopic eyes. Documenting the type of ametropia (refractive vs. axial) may help in exploring the true association between refractive error and CCT.

In the studies that report a significant association, a greater BMI and the presence of diabetes mellitus were found to be related with a greater CCT. Hypertension did not show any association in seven studies (including this study) and only one publication reports an inverse association [Table 7]. Overall, it is unlikely that the mentioned systemic factors could affect CCT in a clinically relevant manner.

Renal failure has a direct association with CCT in the Singapore Malay Eye Study,[23] while we found no association between albuminuria and CCT. Taken together, the results of the previous studies suggest that the CCT may have an inverse association with age and direct association with IOP. The inconsistent conclusions between various investigations regarding the links between CCT and other parameters may be due to the different populations studied, dissimilar covariates, or statistical approaches.

Our study showed that 95% of the participants without glaucoma or ocular hypertension had an interocular difference of 33 µm (6%) or less in CCT measurements. An increased difference between contralateral eyes may necessitate more attention to exclude corneal disorders. In Latinos,[18] the calculated normal range for interocular

Table 5. Association of selected systemic features with central corneal thickness among participants of the Yazd Eye Study

	All Participants			Subjects without glaucoma		
	Number (%)	Mean±SD (µm)	Median (range)	Number (%)	Mean±SD (µm)	Median (range)
BMI (kg/m²)						
Under weight	20 (1.8)	536±35	528 (469-608)	19 (1.8)	532±31	526 (469-599)
Normal	299 (26.9)	543±34	543 (438-632)	289 (27)	544±34	543 (438-632)
Over weight	498 (44.8)	545±37	545 (424-682)	483 (45.1)	545±37	544 (424-682)
Obese	295 (26.5)	542±33	543 (416-678)	281 (26.2)	542±34	543 (416-678)
*P**		0.851			0.802	
Diabetes						
No	914 (77.2)	543±35	543 (416-682)	892 (78.1)	543±35	543 (416-682)
Yes	270 (22.8)	546±35	546 (424-630)	250 (21.9)	546±35	545 (424-630)
*P**		0.233			0.347	
Hypertension						
No	758 (63.7)	543±35	543 (425-682)	741 (64.5)	543±35	543 (425-682)
Yes	432 (36.3)	545±34	543 (416-630)	407 (35.5)	545±34	544 (416-630)
*P**		0.483			0.42	
Renal failure						
Yes	32 (2.7)	544±37	543 (468-603)	30 (2.6)	544±38	543 (468-603)
No	1157 (97.3)	544±35	543 (416-682)	1117 (97.4)	544±35	543 (416-682)
*P**		0.956			0.996	

*Calculated using analysis of covariance test (ANCOVA), controlled for age and sex. BMI, body mass index; SD, standard deviation

Table 6. Comparison of central corneal thickness measurements between various ethnic groups

Study	Ethnicity	Participants, n (eye)	Age	CCT (μm)		
				Mean±SD	Normal range*	Method
Rotterdamm (Wolfs et al; 1997)[17]	White (The Netherlands)	352 (random eye)	55+	537±34†	470-604	Ultrasound
Mongolia (Foster et al; 1998)[5]	Mongolian	1127 (right eyes)	10+	495±32	432-558	Optical (Device I)
Barbados (Nemesure et al; 2003)[7]	Black	1064 (both eyes)	50+	530±38	456-604	Ultrasound
Los Angeles Latino (Hahn et al; 2003)[18]	Latino (The USA)	1699 (random eye)	40+	547±34	480-614	Ultrasound
Tajimi (Suzuki et al; 2005)[19]	East Asian (Japanese)	7313 (both eyes)	40+	518±30	459-577	Specular microscopy
Tajimi (Tomidokoro et al; 2007)[20]	East Asian (Japanese)	2868 (both eyes)	40+	521±32	458-584	Specular microscopy
Beijing (Zhang et al; 2008)[21]	East Asian (Chinese)	3100 (random eye)	45+	556 ± 33	491-621	AS-OCT
Meiktila (Casson et al; 2008)[22]	Myanmar	1909 (both eyes)	40+	522±33	457-587	Ultrasound
Singapore Malay (Su et al; 2009)[23]	East Asian (Singaporean Malay)	3239 (right eyes)	40+	541±34	474-608	Ultrasound
Tehran (Hashemi et al; 2009)[10]	Middle East (Iranian)	410 (right eyes)	14+	556±40	478-634	Optical (Orbscan II)
Blue Mountains (Rahman et al; 2010)[24]	White (Australian)	1346 (right eyes)	49+	540±34	473-607	Ultrasound
Chennai (Vijaya et al; 2010)[25]	Indian	6754 (right eyes)	40+	511±34	444-578	Ultrasound
Nagpur (Nangia et al; 2010)[26]	Indian	4685 (both eyes)	30+	514±33	449-579	Ultrasound
Liwan (Wang et al; 2011)[27]	East Asian (Chinese)	1205 (right eyes)	50+	542±31	481-603	Ultrasound
Shahroud (Hashemi et al; 2011)[9]	Middle East (Iranian)	3820 (right eyes)	40+	528±37	455-601	Optical (Pentacam HR)
Tanjong Pagar (Day et al; 2011)[28]	East Asian (Singaporean Chinese)	938 (right eyes)	40+	539±32	476-602	Optical (Device I)
Bhaktapur (Thapa et al; 2012)[29]	Nepalese	2330 (right eyes)	40+	539±34	472-606	Ultrasound
Namil-meon (Hwang et al; 2012)[30]	East Asian (Korean)	1259 (right eyes)	40+	531±32	468-594	Ultrasound
Gutenberg (Elflein et al; 2014)[31]	White (Germany)	4698 (both eyes)	35+	552±35	483-621	Optical (Pachycam)

AS-OCT, anterior segment optical coherence tomography; CCT, central corneal thickness; *n*, number; SD, standard deviation

difference in CCT was 0–25 μm. In addition, interocular difference of more than 15–20 μm may be associated with worse a prognosis of the eye with a thinner cornea in the context of glaucoma.[32,33]

Previous studies demonstrate a significant association between CCT and the parameters of the optic nerve head. Cankaya et al[34] and Pakravan et al[35] show that CCT was inversely correlated with the optic disc area in healthy and glaucomatous eyes, respectively. In the present study, we found that CCT was directly correlated to HCDR and VCDR. This observation is consistent with that of Cankaya et al,[34] who also report an inverse correlation between CCT and optic disc rim area. Overall, the present study further confirms a suggested association between optic disc structure and CCT. This implicate that certain eyes are susceptible to glaucoma.

In line with previous reports,[18,25] our study showed that subjects with ocular hypertension had a greater CCT than normal subjects did. This observation corroborates the positive association found between IOP and CCT. However, the analysis of CCT in the glaucoma subgroup was not properly powered; therefore, it is not reliable.

Table 7. Demographic, ocular, and systemic determinants of CCT in various population-based studies

Study	Demographics		Ocular factors		Systemic factors		
	Age	Sex (M/F)	IOP	Refraction	BMI	Diabetes	Hypertension
Rotterdam (Wolfs et al; 1997)[17]	No	No	+ (1.9 mmHg/100 μm)				
Mongolia (Foster et al; 1998)[5]	- (5-6 μm/decade)	No	+ (1.8-2.4 mmHg/100 μm)				No
Barbados (Nemesure et al; 2003)[7]	-	No	No	+ (SE)	No	+	No
Los Angeles Latino (Hahn et al; 2003)[18]	- (2.9 μm/decade)	+	+ (1.4 mmHg/100 μm)				
Tajimi (Suzuki et al; 2005)[19]	- (only men)	+	+ (1.2 mmHg/100 μm)	- (only men)	No		No (Systolic BP)
Tajimi (Tomidokoro et al; 2007)[20]	No	+	+	No			No
Beijing (Zhang et al; 2008)[21]	No	+	+ (3 mmHg/100 μm)	No	No		
Meiktila (Casson et al; 2008)[22]	No	No	+ (1.3 mmHg/100 μm)	+ (SE)	No		
Singapore Malay (Su et al; 2009)[23]	-(5.1 μm/decade)	No	+ (1.9 μm/1 mmHg)	No	+	+	No
Tehran (Hashemi et al; 2009)[10]	-	No	No	No	No		
Blue Mountains (Rahman et al; 2010)[24]	-		+				
Chennai (Vijaya et al; 2010)[25]	-(2.41 μm/decade; urban)	+	+ (2.45 mmHg/100 μm; urban)				
Nagpur (Nangia et al; 2010)[26]	-	+	+2 mmHg/100 μm	No	+		
Liwan (Wang et al; 2011)[27]	- (4 μm/decade)	No	+ (2.3 mmHg/100 μm)	No	No	+	No
Shahroud (Hashemi et al; 2011)[9]	-(2.1 μm/decade)	No		+ (SE; 0.72 μm/1D)	No		
Tanjong Pagar (Day et al; 2011)[28]	- (6.8 μm/decade)		+ (1.7 μm/1 mmHg)			No	
Bhaktapur (Thapa et al; 2012)[29]	- (2.7 μm/decade)	No	+ (1.03 mmHg/100 μm)				
Namil-meon (Hwang et al; 2012)[30]	- (2.6 μm/decade)	+	+ (1.9 mmHg/100 μm)			No	-

Table 7. Contd...

Study	Demographics		Ocular factors		Systemic factors		
	Age	Sex (M/F)	IOP	Refraction	BMI	Diabetes	Hypertension
Gutenberg (Elflein et al; 2014)[31]	No	+			+	No	No
Yazd (current study)	No	No	+	+ (Hyperopia *vs.* Myopia)	No	No	No

+, means statistically significant direct association; -, means statistically significant inverse association; No, means no statistically significant correlation; blank tabs: not tested in the study. BMI, body mass index; BP, blood pressure; F, female; IOP, intraocular pressure; M, male; SE, spherical equivalent

The present study is the first large-scale population-based study that evaluated CCT with the gold standard ultrasonic method in an Iranian population. The major limitation of this study was the small sample size of glaucoma patients, which precludes any in-depth statistical analysis for this subgroup. Therefore, the results of this study are mostly attributed to the subjects without glaucoma and should not be generalized to patients with glaucoma or other ocular abnormalities.

In summary, the outcomes of the present study suggest that the normal range (95% CI) of CCT for the Iranian population without glaucoma is 475–613 μm and the normal range (95% CI) for interocular difference is 0–31 μm. These findings will have implications for the diagnosis and management of glaucoma or corneal disorders in this population. We found a positive relationship between CCT and IOP, VCDR, HCDR, and hyperopic refractive error. This study did not show any association between CCT and age, sex, BMI, or the selected systemic disorders. Further studies are warranted to determine the CCT characteristics and its associations in glaucomatous Middle Eastern populations.

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Conflicts of Interest

There are no conflicts of interest.

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