Taiwan Journal of Ophthalmology 6 (2016) 15–20

Contents lists available at ScienceDirect

Taiwan Journal of Ophthalmology

journal homepage: www.e-tjo.com

Original article

Comparison of glaucoma diagnostic accuracy of macular ganglion cell complex thickness based on nonhighly myopic and highly myopic normative database

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ARTICLE INFO

Article history:
Received 21 December 2015
Received in revised form
6 January 2016
Accepted 11 January 2016
Available online 13 February 2016

Keywords:
glaucoma
myopia
optical coherence
tomography

ABSTRACT

Background/Purpose: To evaluate and compare the diagnostic discriminative ability for detecting glaucoma in highly myopic eyes from a normative database of macular ganglion cell complex (mGCC) thickness based on nonhighly myopic and highly myopic normal eyes.
Methods: Forty-nine eyes of 49 participants with high myopia (axial length $\geq$ 26.0 mm) were enrolled. Spectral-domain optical coherence tomography scans were done using RS-3000, and the mGCC thickness/significance maps within a 9-mm diameter circle were generated using built-in software. We compared the difference of sensitivity, specificity, and diagnostic accuracy between the nonhighly myopic database and the highly myopic database for differentiating the early glaucomatous eyes from the nonglaucomatous eyes.
Results: This study enrolled 15 normal eyes and 34 eyes with glaucoma. The mean mGCC thickness of the glaucoma group was significantly less than that of the normal group ($p < 0.001$). Sensitivity was 96.3%, and the specificity was 50.0% when using the nonhighly myopic normative database. When the highly myopic normative database was used, the sensitivity was 88.9%, and the specificity was 90.0%. The false positive rate was significantly lower when using the highly myopic normative database ($p < 0.05$).
Conclusion: The evaluations of glaucoma in eyes with high myopia using a nonhighly myopic normative database may lead to a frequent misdiagnosis. When evaluating glaucoma in high myopic eyes, the mGCC thickness determined by the long axial length high myopic normative database should be applied.

1. Introduction

Glaucoma is a multifactorial optic neuropathy characterized by a progressive loss of retinal ganglion cells, retinal nerve fiber layer (RNFL) thinning, and leading to irreversible visual impairment. Myopia is a refractive error and affects a significant proportion of the population, especially in East Asian countries. Most of the population-based studies and clinical trials have showed that moderate to high myopia is associated with increased risk of primary open-angle glaucoma, normal tension glaucoma, and ocular hypertension.[1,2] However, a myopic optic nerve can pose significant challenges with regard to making the correct diagnosis of glaucoma. They may have considerable morphological variations, e.g., larger disc sizes, tilted disc, shallower optic cups, and peripapillary atrophy.[3] The opportunity and risk of falsely diagnosing a glaucomatous individual as normal or a normal individual as glaucomatous may be high, especially in early glaucomatous damage.

Myopic eyes have longer axial lengths (ALs) and vitreous chamber depths.[4,5] Von Graefe[6], in an anatomical and ophthalmoscopic investigation, first postulated the relationship between long axial length and high myopia. Elongated axial length of the globe leads to various changes in the topography of the posterior pole, with concomitant decreased thickness of the retina, and development of macular pathologic features,[7] which usually affects specificity and sensitivity on glaucoma evaluation.[8,9]

Spectral-domain optical coherence tomography (SD-OCT) is currently the most advanced commercially available application of imaging technology, and it can offer more accurate and reproducible results.[10,11] Glaucoma damage affects retinal ganglion cells, which are

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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http://dx.doi.org/10.1016/j.tjo.2016.01.001

densely present in the macular region. Several researchers have suggested that macular thickness measurement could be a valuable parameter of glaucomatous structural change, and SD-OCT has enabled automatic assessments of macular ganglion cell complex (mGCC) thickness.[12] This combined inner retinal layers includes retinal nerve fiber layer, ganglion cell layer, and inner plexiform layer.

The thickness of mGCC can be used for early detection of glaucoma,[10] and the study conducted by Kim and colleagues[13] suggested that mGCC thickness measurements may be a good alternative or a complementary measurement to RNFL thickness assessment in the clinical evaluation of glaucoma in patients with high myopia. However, we need to know the mGCC thickness of the normative database in normal eyes, and this database should be obtained from an effective number of normal eyes and include the mGCC thicknesses of various areas around the fovea. Although the normative database is based on statistics, high myopes are usually not included, and therefore the normative database might not represent all patient populations. Thus, myopia can be a confounding factor in the assessment of RNFL thickness attributed to its influence on the RNFL thickness and leads to misdiagnoses.[14]

As AL increases, average mGCC thickness of both high myopic and glaucomatous eyes is relatively less than that in healthy emmetropic eyes. This suggests that axial length should be taken into account when assessing the reliability of OCT data.[14] It is also difficult to differentiate whether lower mGCC thickness is due to myopic changes or because of glaucomatous damage in eyes with both myopia and glaucoma. Even with these new imaging modalities with improved accuracy and precision for detecting glaucoma, OCT technology presents some challenges when evaluating myopic eyes.[15] Development and assessment of other diagnostic parameters of highly myopic globes is necessary to detect glaucoma.

It is known that ocular magnification of retinal images is affected by AL, refractive error, corneal curvature, and anterior chamber depth.[16,17] We should also consider AL-associated ocular magnification when evaluating mGCC thickness in high myopic eyes, as the difference in scanned area can lead to a misdiagnosis.[14]

The RS-3000 SD-OCT (Nidek, Gamagori, Aichi, Japan) may solve these two problems. There are two kinds of normative databases for this SD-OCT device: the original installed age-adjusted reference regular database for eyes with ALs < 26 mm, and an optional database for eyes with ALs between 26 mm and 29 mm for highly myopic eyes.[18,19] This normative database was developed based with data from normal eyes with long AL. Data were collected from Asian individuals by measuring the macular area in three dimensions to obtain retinal thickness.

High or pathologic myopia is typically defined as a refractive correction of −6.00 D or more and an AL > 26.0 mm.[20,21] The purpose of this research was to evaluate the various measurements of diagnostic ability of these two different databases in the RS-3000 SD-OCT device to diagnose glaucoma in Taiwanese eyes with high myopia.

2. Methods

2.1. Participants

This is an observational cross-sectional study and the participants were informed of the purpose and procedures of the measurements. Medical records of patients with high myopia (AL ≥ 26.0 mm) who were examined at the Glaucoma Clinic of the Department of Ophthalmology, Chang Gung Memorial Hospital, Taoyuan, Taiwan, were reviewed. All of the procedures conformed to the tenets of the Declaration of Helsinki.

All participants had comprehensive ophthalmic evaluation including slit-lamp biomicroscopy, intraocular pressure measurements by Goldmann applanation tonometry, central corneal thickness, gonioscopic examination by a Goldmann three-mirror lens, optic nerve head evaluation and fundus examination, digital color fundus photography (Digital Non-Mydriatic Retinal Camera, Canon, Tokyo, Japan), AL measurements by Optical Biometer AL-Scan (Nidek), central 30-2 Swedish Interactive Threshold Algorithm standard automated perimetry using a Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, CA, USA), measurements of the best-corrected visual acuity, automatic objective determination of the refractive errors, and SD-OCT examinations (RS-3000; Nidek).

The inclusion criteria were AL ≥ 26.0 mm, best-corrected visual acuity ≥ 20/20 in Snellen equivalents, normal anterior segment, normal and open angle by gonioscopy, presence of RNFL defects on color fundus photographs consistent with the glaucomatous appearances of the optic disc, and the presence of normal or glaucomatous visual field (VF) defects by automated perimetric test.

The exclusion criteria were: previous intraocular or refractive surgery; patients with diabetes mellitus; poorly controlled hypertension; other systemic disease; neurological diseases that might cause VF defects or RNFL damage; and other vitreous retinal disorders that can influence the retinal thickness, such as an epiretinal membrane, degenerative myopia with patchy chorioretinal atrophy or choroidal neovascularization, and low quality SD-OCT images were also excluded. When both of a patient's eyes were eligible, one eye was randomly selected for analysis.

2.2. Glaucoma diagnosis

Glaucomatous optic neuropathy was diagnosed when the optic disc had a glaucomatous appearance, for example, localized or diffuse neuro-rim thinning of the optic nerve head and/or RNFL defects corresponding to the glaucomatous VF defects. Glaucomatous visual filed defects were defined as those with one or more of the following criteria with reliable standard automated perimetry results: (1) a cluster of three points with probabilities of < 5% on the pattern deviation map in at least one hemifield, including one point or more with a probability of < 1%, or a cluster of two points with a probability of < 1%; (2) glaucomatous hemifield test results outside the normal limits; and (3) a pattern standard deviation (PSD) beyond 95% of normal limits as confirmed by at least two reliable examinations (false positive/negatives < 15%, fixation losses < 15%).[22]

Eyes were in the normal group if they did not have glaucomatous optic neuropathy appearance, visible RNFL defects, or glaucomatous VF defect on two reliable SAP tests. Participants with preperimetric glaucoma were excluded from this study.

2.3. SD-OCT measurement

All participants were imaged with the high-resolution scan procedure of the RS-3000 SD-OCT (Nidek) to obtain images of the mGCC. For wide-area three-dimensional imaging of the posterior pole, we performed OCT raster scanning over a 30 × 30 degree square area with a scan density of 512 A-scans vertically × 128 B-scans horizontally. Image quality was checked carefully and only good-quality scans, defined as scans with signal strength index < 6/10, and without any artifact were used for analysis. The mGCC thickness was calculated with the default software, Navis-EX version 1.4.1 (Nidek). Navis-EX is a viewing combines with image filing software that enables data from various Nidek diagnostic imaging devices to be stored and processed in a centralized database. This program can also correct the effect of the AL-related ocular magnification using a modified formula.[16]After correcting the ocular magnification, the mGCC thickness and significance maps were determined for a 9-mm diameter circle, which centered on the fovea. The mGCC thickness was measured from the internal

limiting membrane to the outer inner plexiform layer boundary, which supplements clinical work-up for the early detection of optic nerve fiber layer defects. Two types of thickness and significance maps of the mGCC—a superior/inferior (S/I) semicircle map and an eight-sector map or GChart (Figures 1 and 2)—were obtained. For GChart and S/I significance maps, there are three-level color coding to assess the thicknesses; the green (5–95% within the normal range), yellow (1–5% probability of being in the normal range), and red (< 1% probability of being within the normal range) color codes based on comparison with the internal normative database.

There are two sets of normative database of the RS-3000 system (Figures 1 and 2). The built-in regular nonhigh myopia normative database was collected from 130 healthy Asians and 90 healthy Caucasians. The average AL was 24.0 ± 0.9 mm and 23.4 ± 1.0 mm, respectively. The average refractive error was −1.0 ± 1.8 D and −0.6 ± 1.7 D, respectively.[19] The second highly myopic normative (optional) database consisted of data obtained from 112 healthy Asian eyes with an AL ≥ 26.0 mm; the average AL was 27.1 ± 0.8 mm and average refractive error of −8.1 ± 2.4 D.[20] All the SD-OCT images were evaluated by two masked investigators (H.S.L.C. and D.W.L.).

2.4. Statistical analysis

All statistical analyses were performed using GraphPad Prism5 (GraphPad Software Inc., La Jolla, CA, USA). The baseline characteristics and differences in the demographic features between the highly myopic normal group and the highly myopic early glaucoma group were compared for statistical significance using Fisher's exact test for dichotomous data or by the two-sample t test for continuous data. To evaluate the clinical usefulness of each database to distinguish highly myopic normal eyes from highly myopic early glaucoma based on the mGCC thickness, the sensitivity, specificity, diagnostic accuracy, and likelihood ratios of the SD-OCT significance maps when using both myopic normative databases in the same SD-OCT images were estimated. The mGCC scans were classified as abnormal thinning if at least one sector of the S/I or GChart significant maps was < 1%. Statistical significance was defined as $p < 0.05$.

3. Results

This study included 15 normal high myopia individuals and 34 high myopic glaucomatous patients. Baseline demographics and perimetry parameters (mean deviation and PSD) of two groups are shown in Table 1. The average axial length was 28.00 ± 1.18 mm in the normal group and 27.38 ± 1.08 mm in the glaucoma group ($p = 0.079$). The mean refractive error was −5.68 ± 5.13 D in the normal group and −7.69 ± 3.66 D in the glaucoma group ($p = 0.521$). No statistically significant differences in age, spherical equivalent of refractive errors, axial length, intraocular pressure, or central corneal thickness were observed between the two groups. Visual field (SAP 30-2) mean deviation and PSD values did significantly different among the two groups ($p = 0.005$ and $p = 0.002$, respectively). Table 2 shows the mGCC thickness parameters of the

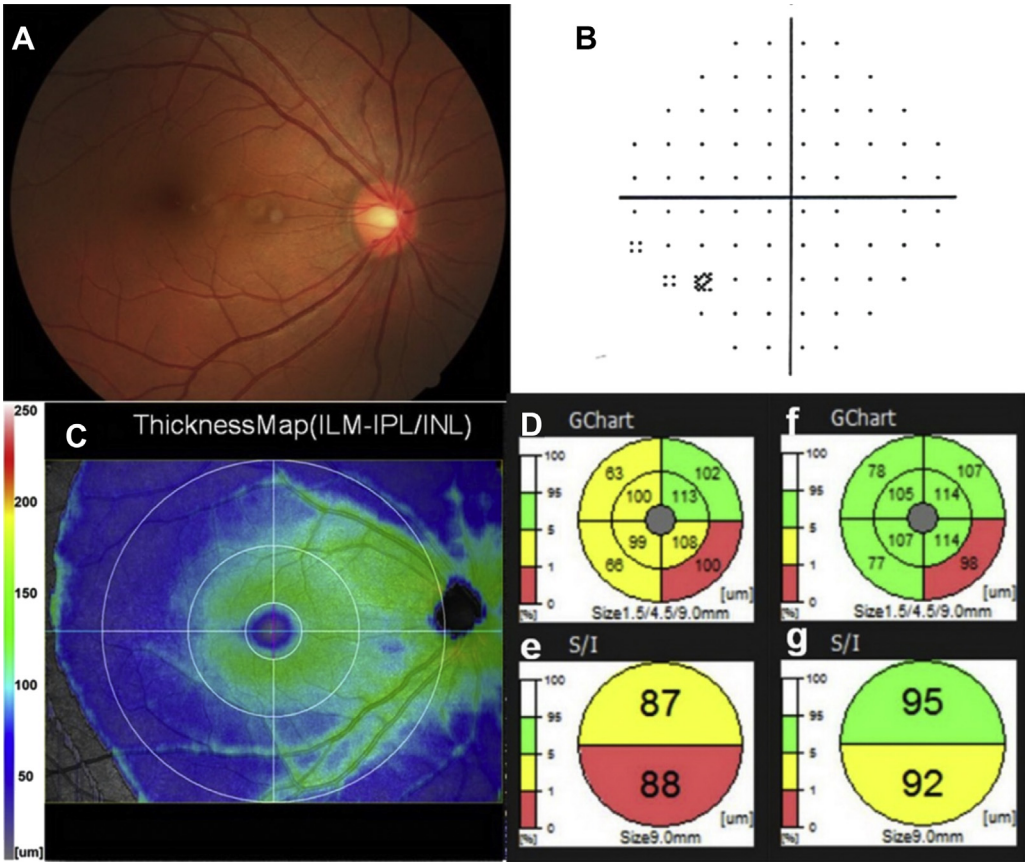

Figure 1. An example of fundus photograph, visual fields, and spectral-domain optical coherence tomography images of a 41-year-old highly myopic woman without glaucoma. The axial length of the eye is 26.14 mm and the refractive error (spherical equivalent) is −7.0 diopters. (A) Color fundus photograph. (B) Pattern deviation of the Humphrey perimeter showing relatively normal visual field. (C) 9 mm × 9 mm square area of the RS-3000 OCT macular ganglion cell complex thicknesses map (Nidek, Gamagori, Aichi, Japan) overlaid on scanning laser ophthalmoscopy image. (D) GChart (8-sectored map). (E) superior/inferior (S/I) semicircle map. (F, G) The macular ganglion cell complex thickness and significance maps correcting by the long axial length normative database, color coding is changed after switching the database.

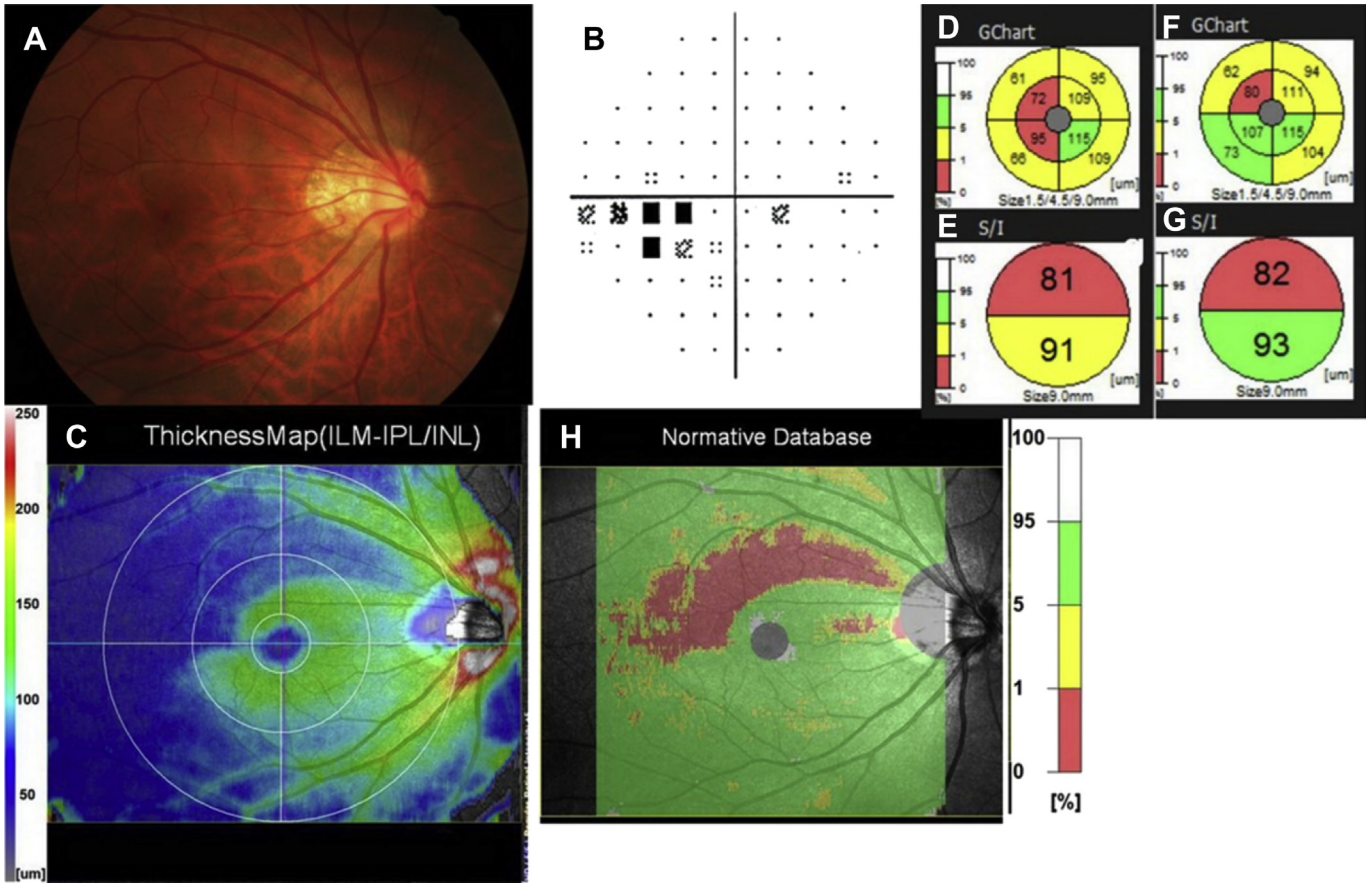

Figure 2. An example of fundus photograph, visual fields, and spectral-domain optical coherence tomography images of a 49-year-old highly myopic man with glaucoma. The axial length of the eye is 27.86 mm and the refractive error (spherical equivalent) is −8.00 diopters. (A) Color fundus photograph showing a superotemporal retinal nerve fiber layer defects. (B) Pattern deviation of the Humphrey perimeter showing an inferior glaucomatous defect in the visual field. (C) The macular ganglion cell complex (mGCC) thicknesses map showing a thinner superior arcuate shape area compared with inferior area. (D) GChart (8-sectored map) and (E) superior/inferior (S/I) semicircle map when using the built-in normative database. (F, G) The mGCC thickness and significance maps correcting by the long axial length normative database, and color codings of the inferior sectors are changed, however, color codings of the superior sectors are not changed. The superior mGCC thickness is still assigned to abnormally thinning after switching the database, which correspond with the inferior glaucomatous perimetric defect. (H) Color-coded map indicating distribution range of the patient's mGCC thickness in a population of normative eyes.

high myopia glaucoma group was significantly thinner than that of the normal high myopia group in all sectors for both the S/I maps and GChart maps.

3.1. Diagnostic ability of the two types of the normative databases

When using the nonhighly myopic normative database for evaluating the S/I maps, the sensitivity and specificity were 0.824 and 0.600, respectively. The sensitivity decreased to 0.706 and the specificity increased to 0.933 when the long AL highly myopic normative database was used. However, the difference of the sensitivity was not statistically significant ($p = 0.21$). The change of specificity was significantly ($p = 0.024$) higher when the long AL highly myopic normative database was used. There was only one patient whose S/I significance map changed from within the normal range to abnormal thinning by using highly myopic normative database. The estimation of the positive and negative likelihood ratio for the S/I maps of the nonhighly myopic database were 2.059 and 0.294, respectively, and the value of both ratios increased to 10.588 and 0.315, respectively, when the long AL highly myopic normative database was used. The diagnostic accuracy of the S/I maps was 0.755 when using the nonhighly myopic normative database and was 0.776 when using the highly myopic normative database (Tables 3 and 4).

For the analysis results from GChart maps, when using the nonhighly myopic normative database, the sensitivity was 0.941 and the specificity 0.467. When the highly myopic normative database was used, the sensitivity of the GChart maps decreased to 0.853 and the specificity increased to 0.800. Comparing the two databases, the sensitivities were not significantly different ($p > 0.99$), but the specificity was significantly higher when using the highly myopic normative database ($p = 0.009$). The estimation of the positive and negative likelihood ratio for GChart maps of the nonhighly myopic database were 1.765 and 0.126, respectively, and the value of both ratios increased to 4.265 and 1.084, respectively,

Table 1
Demographic and ocular characteristics of study participants.

	Glaucoma	Normal	*p*
Participants (*n*)	34	15	
Age (y)	43.3 ± 11.9	37.3 ± 14.7	0.134
Axial length (mm)	27.38 ± 1.08	28.00 ± 1.18	0.079
Refractive error (Diopters)	−7.69 ± 3.66	−5.68 ± 5.13	0.521
Central corneal thickness (μm)	538.20 ± 29.60	530.00 ± 28.80	0.124
Intraocular pressure (mmHg)	18.20 ± 2.40	14.30 ± 2.10	0.315
Standard achromatic perimetry			
MD (dB)	−2.98 ± 1.46	−1.46 ± 1.24	0.005
PSD (dB)	−3.98 ± 1.73	−1.43 ± 0.72	0.002

Data are presented as mean ± standard deviation.
MD = mean deviation; PSD = pattern standard deviation.

Table 2
Comparison of the analysis chart[a] parameters of mGCC thickness between high myopic glaucoma group and high myopic normal group.

		Glaucoma ($n = 34$)	Normal ($n = 15$)	p	AROC (95% CI)
Total (μm)		77.40 ± 16.64	95.70 ± 9.24	< 0.001	0.810 (0.728–0.893)
S/I	Superior	79.91 ± 15.56	98.27 ± 10.09	< 0.001	0.835 (0.724–0.946)
	Inferior	74.88 ± 17.53	93.13 ± 7.82	< 0.001	0.790 (0.667–0.914)
GChart	Inner.TS	90.03 ± 19.43	111.3 ± 16.22	< 0.001	0.808 (0.688–0.927)
	Inner.TI	84.79 ± 21.66	105.3 ± 11.78	0.001	0.768 (0.637–0.899)
	Inner.NS	105.1 ± 20.08	121.6 ± 13.98	0.006	0.733 (0.589–0.877)
	Inner.NI	98.06 ± 20.98	114.3 ± 12.42	0.008	0.707 (0.559–0.854)
	Outer.TS	61.00 ± 10.96	76.60 ± 7.01	< 0.001	0.879 (0.787–0.972)
	Outer.TI	58.21 ± 12.10	71.00 ± 5.26	< 0.001	0.808 (0.689–0.927)
	Outer.NS	89.91 ± 21.27	111.9 ± 11.78	< 0.001	0.809 (0.690–0.928)
	Outer.NI	82.41 ± 23.70	106.0 ± 12.78	< 0.001	0.785 (0.659–0.912)

AROC = area under receiver operating characteristic curve; CI = confidence interval; mGCC = macular ganglion cell complex; NI = nasal inferior; NS = nasal superior; TI = temporal inferior; TS = temporal superior.
[a] Superior/inferior (S/I) pole and GChart: analysis charts of average thickness of each sector surrounding the macula with color code based on comparison to a normative database.

when the long AL highly myopic normative database was used. When using the nonhighly myopic normative database, the diagnostic accuracy of the GChart maps was 0.796 and it increased to 0.837 when the highly myopic normative database was used (Tables 3 and 4).

4. Discussion

Accurate glaucoma diagnostic examinations are important for improved patient management. However, the correlation between myopia and increased susceptibility to, or progression of, glaucoma remains controversial. Differentiating myopia and glaucoma is usually difficult, particularly between high myopes and early glaucoma. If the diagnostic instrument can be properly used, we may not only avoid failure to treat real glaucoma patients but also can avoid misdiagnosis and wasting medical resources on high myopic individuals who do not have glaucoma.

The mGCC algorithm is a relatively new potential glaucoma diagnostic tool of SD-OCT, and may represent a more sensitive method for early detection and monitoring of structural glaucomatous damage. Diagnosis of glaucoma using various imaging instruments is usually made by referencing built-in normative data with the diagnostic classification (within normal limits, borderline, abnormal). However, mGCC thickness measurements are frequently classified as abnormal or glaucoma in healthy myopic eyes when compared with the normative database.[23]

Sensitivity, specificity, and likelihood ratios are important aspects of a diagnostic test performance. Since both specificity and sensitivity are used to calculate the likelihood ratio (how many times more likely a particular test result is in individuals with the disease than in those without disease), it is clear that neither positive likelihood ratio nor negative likelihood ratio depend on the disease prevalence in examined groups.

In this study, we evaluated and compared the diagnostic accuracy for detecting glaucoma in high myopic eyes from normative database of mGCC thickness based on normal nonmyopic and long AL high myopic eyes. The mean mGCC thicknesses of the glaucoma group were significantly less than that of the normal group. In addition, when the long AL high myopic normative database was used, the specificity and positive likelihood ratio was raised and the false positive rate was significantly lower. The difference of sensitivity among these two groups was not statistically significant. This

Table 3
Discriminating ability of the regular normative database on macular ganglion cell complex thickness for glaucoma detection.

	Glaucoma ($n = 34$)	Normal ($n = 15$)
Regular normative database		
Superior/inferior		
Abnormal thinning	28	6
Within normal range	6	9
Sensitivity (95% CI)	0.824 (0.655–0.932)	
Specificity (95% CI)	0.600 (0.323–0.837)	
Positive predictive value (95% CI)	0.824 (0.655–0.932)	
Negative predictive value (95% CI)	0.600 (0.323–0.837)	
Positive likelihood ratio	2.059	
Negative likelihood ratio	0.294	
Diagnostic accuracy	0.755	
GChart		
Abnormal thinning	32	8
Within normal range	2	7
Sensitivity (95% CI)	0.941 (0.803–0.993)	
Specificity (95% CI)	0.467 (0.213–0.734)	
Positive predictive value (95% CI)	0.800 (0.644–0.909)	
Negative predictive value (95% CI)	0.778 (0.400–0.972)	
Positive likelihood ratio	1.765	
Negative likelihood ratio	0.126	
Diagnostic accuracy	0.796	

CI = confidence interval.

Table 4
Discriminating ability of the long axial length normative database on macular ganglion cell complex thickness for glaucoma detection.

	Glaucoma ($n = 34$)	Normal ($n = 15$)
Long axial length normative database		
Superior/inferior		
Abnormal thinning	24	1
Within normal range	10	14
Sensitivity (95% CI)	0.706 (0.525–0.849)	
Specificity (95% CI)	0.933 (0.681–0.998)	
Positive predictive value (95% CI)	0.960 (0.796–0.999)	
Negative predictive value (95% CI)	0.583 (0.366–0.779)	
Positive likelihood ratio	10.588	
Negative likelihood ratio	0.315	
Diagnostic accuracy	0.776	
GChart		
Abnormal thinning	29	3
Within normal range	5	12
Sensitivity (95% CI)	0.853 (0.689–0.950)	
Specificity (95% CI)	0.800 (0.519–0.957)	
Positive predictive value (95% CI)	0.906 (0.750–0.980)	
Negative predictive value (95% CI)	0.706 (0.440–0.897)	
Positive likelihood ratio	4.265	
Negative likelihood ratio	1.084	
Diagnostic accuracy	0.837	

CI = confidence interval.

may be explained by the fact that most of SD-OCT instruments have their own normative database and were obtained from a group of healthy patients. The normative database may be adjusted for age or race, but usually not for refractive error or axial length. The ability to discriminate highly myopic health from glaucomatous optic nerves is dependent on the quality of reference databases of imaging platforms. Adjusting normative mGCC thickness data for long AL or high myopia patients would provide better OCT specificity for glaucoma detection. Thus, we may require imaging devices that contain normal high myopic databases with high diagnostic ability or accuracy for detecting glaucoma accurately.

We also found that when using long AL high myopic database, the S/I map and GChart map maintain relatively high sensitivities and specificities for separating normal high myopia and glaucoma. In addition, the reason for the diagnostic accuracy of S/I map analysis had high positive predictive ratio (10.588) and high specificity (0.933) compared with less specificity (0.800) and relatively higher negative predictive ratio (1.084), a good indicator for ruling out the disease, of GChart analysis when using the long AL high myopic database for detecting glaucoma. This may be due to our study design including various stages of glaucoma patients rather than early glaucoma groups. Thus, when using the regular reference database to evaluate mGCC thickness of high myopic eyes, we should consider carefully the opportunity of possible false positives, which may lead to misdiagnosis of normal eyes as having glaucoma.

Nakanishi and associates[24] showed that the S/I maps had lower sensitivity and higher specificity than the GChart maps when analyzed by the long AL high myopic database, and we had similar results in this study. They also suggested that when a thinning focal area of mGCC occurred, the analysis result may be also within the normal range if this area is averaged with a wider normal mGCC thickness (S/I map).

There are several limitations to our study, which include a limitation by observational retrospective design and a relatively small sample size. Moreover, we need to consider and interpret the values of diagnostic accuracy parameters carefully, because the research with a case–control design, including patients with established disease and a group of normal unsuspected individuals as hospital-based controls, can commonly overestimate the performance of an examination. Therefore, prospective, longitudinal designed studies with larger sample sizes are required in the future. A final limitation is that because the included population was entirely Taiwanese, differences may exist among ethnic groups that restrict the external validity of the current study.

In conclusion, our study shows that mGCC thickness of high myopic eyes determined by the long AL high myopic normative database in the RS-3000 SD-OCT has significantly better specificity to discriminate eyes of normal high myopia and glaucoma. The high myopic normative database can provide valuable information and should be built into SD-OCT instruments.

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