Original Article

Role of Retinal Nerve Fiber Layer Thickness and Optic Disk Measurement by OCT on Early Diagnosis of Glaucoma

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Abstract

Purpose: Glaucoma is an eye disease that can lead to irreversible optic nerve damage and cause blindness. Optical coherence tomography (OCT) allows an early diagnosis of glaucoma by the measurements of the retinal nerve fiber and optic disc parameters.A retrospective study was designed to analyze the effects of the measurement of the retinal nerve fiber layer (RNFL) thickness and the optic disc tomography by spectral-domain OCT on the early diagnosis of suspected glaucoma and primary open angle glaucoma (POAG).

Methods: This was a clinical case-control study. The RNFL thickness around the optic disc and optic disk tomographic parameters of the control (n=51, 98 eyes), suspected glaucoma (n=81, 146 eyes), and POAG groups (n=55, 106 eyes) were measured by OCT. The parameters included superior, inferior, nasal and temporal mean RNFL thickness, disc area (DA), cup area (CA), rim area (RA), disc volume (DV), cup volume (CV), rim volume (RV), cup/disc area ratio (CA/DA), rim/disc area ratio (RA/DA), cup/disc volume ratio (CV/DV) and rim/disc volume ratio (RV/DV).

Results: Superior, nasal, and mean RNFL parameters, DA, CA,RA, DV, CV, CA/DA, RA/DA, CV/DV and RV/DV significantly differed among three groups by single-factorial ANOVA. Inferior and temporal RNFL thickness significantly differed between the control and POAG groups. No significant difference was observed in RV among three groups. In the POAG group, the maximum area under the ROC curve (AROC) of mean RNFL thickness was 0.845. The maximum AROC of optic disk parameters was RA/DA (0.998), followed by CA/DA (0.997). The AROC of CA, RA, CV, and DV were all > 0.900.

Conclusion: OCT may serve as a useful diagnostic modality in distinguishing suspected glaucoma from POAG. (***Eye Science 2015; 30:7-12***)

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Introduction

Glaucoma is an ocular disease that may result in irreversible optic nerve damage and even blindness, manifested as retinal ganglion cell (RGC) apoptosis. Loss of RGCs and axons are structurally characterized as topical and/or diffusive thinning of retinal nerve fiber layer (RNFL) and progressive thinning of optic disc rim, and functionally manifest as visual acuity declines and visual field defects[1-3]. Optic disc injury is generally considered to precede visual acuity decline and visual field defects[4,5]. Therefore, RNFL thickness and optic disc parameters play a pivotal role in the early diagnosis of glaucoma.

Optical coherence tomography (OCT) is a noninvasive and reproducible auxiliary diagnostic method of glaucoma and it can quantitatively evaluate the RNFL thickness and optic disc parameters. The optic disc rim is defined as the area above the upward line perpendicular to RPE layer, while below the perpendicular line is the optic cup as seen with OCT[6]. In this study, RNFL thickness and optic disc parameters were assessed by OCT and statistically compared among normal, glaucoma-suspected, and early POAG patients.

Materials and methods

Clinical data

Patients undergoing OCT examination of the optic disc at the Department of Ophthalmology, the Second Affiliated Hospital of Guangzhou Medical University between May and September, 2014 were se-

lected for this clinical trial. All participants had refractive power <±5.0D, best corrected visual acuity ≥0.5, transparent refractive media and suffered from no retinal diseases or alternative optic neuropathy induced by glaucoma. Inclusion criteria:

Normal group: (1) naked or corrected visual acuity ≥1.0; (2) intraocular pressure ≤21 mmHg; (3) having no family history of glaucoma or other optic nerve diseases.

POAG-suspected group: those who met at least one of the three criteria were enrolled in this group: (1)those with a peak value of 24-h intraocular pressure>21 mmHg, with open chamber angle, without glaucomous fundus changes or visual field defects; (2)those with RNFL defects or optic disc morphological changes, a peak value of 24-h intraocular pressure<21 mmHg, without glaucomous visual field defects and the chamber angle is open; and(3) those with open chamber angle, with high-risk factors of glaucoma, with a family history of glaucoma and those presenting with visual field defects with unknown causes.

POAG group: those who met one of the two criteria were enrolled in this group[7]: (1) those with a peak value of 24-h intraocular pressure>21 mmHg, with glaucomous fundus injury and/or glaucomous visual field defects, with open chamber angle, and other factors causing high intraocular pressure were excluded; and (2) those with a peak value of 24-h intraocular pressure ≤21 mmHg, with glaucomous fundus injury and/or glaucomous visual field defects, with open chamber angle, and other diseases leading to fundus and visual field defects were excluded.

Examination methods

Conventional examination: visual acuity, intraocular pressure, fundus, automatic computer optometry, and anterior segment slit-lamp tests.

OCT examination: the pupil diameter of each eye was dilated to approximately 5 mm using 1% tropicamide eye drops. The patients' affected eyes gazed at the screen with their lower mandible on the bracket. The OCT examination was performed at optic disc scanning mode. The experienced operator carefully observed the scanning site on the monitor screen with optic disc as the scanning center using Topcon 3D-OCT1000 equipment. The boundary between optic disc and optic cup was 120 μm above the RPE layer.

The RNFL thickness of four quadrants including the superior, inferior, nasal, and temporal sites was measured to calculate the mean RNFL thickness. Optic disc parameters consisted of DA, CA, RA CA/DA ratio, RA/DA ratio, DV, CV, RV, CV/DV ratio, and RV/DV ratio.

Statistical analysis

SPSS 18.0 statistical software was used for data analysis. RNFL thickness of each quadrant, mean RNFL thickness, and optic disc parameters were statistically compared among three groups using single-factorial ANOVA. The optimal diagnostic index was determined by the area under ROC. $P<0.05$ was considered as statistical significance.

Results

In the normal group, 51 individuals (98 eyes) were enrolled, including 27 males (53 eyes) and 24 females (45 eyes), aged 43.21±13.53 years, on average. In the glaucoma-suspected group, 81 patients (146 eyes) were included: 43 males (79 eyes) and 38 females (67 eyes), aged 45.38±12.46 years, on average. In the POAG group, 55 patients (106 eyes) were enrolled, including 29 males (56 eyes) and 26 females (50 eyes), aged 46.15±11.76 years on average.

Comparison of different parameters among the three groups revealed that the RNFL thickness of each quadrant and mean RNFL thickness were significantly thinner in the POAG group than in the normal groups (all $P<0.05$). The DA, CA, DV, CV, CA/DA, and CV/DV ratio in the POAG group were significantly increased, whereas the RA, RA/DA and RV/DV ratios were significantly decreased compared to the normal group(all $P<0.05$). The RNFL thickness of the superior and nasal quadrant and mean RNFL thickness were significantly attenuated compared to the normal group and, the DA, CA, DV, CV, CA/DA, and CV/DV ratio were dramatically increased and the RA, RA/DA, and RV/DV ratios were significantly reduced in the glaucoma-suspected group (all $P<0.05$). Compared with the glaucoma-suspected group, the RNFL thickness of the superior, inferior and temporal quadrant and

mean RNFL thickness were significantly thinner, the DA, CA, DV and CV were significantly increased, and the RA, RA/DA and RV/DV ratio were dramatically reduced in the POAG group (all $P<0.05$), as illustrated in Table 1.

The RNFL thickness of each quadrant and mean RNFL thickness decreased progressively in all groups (Figure 1). The DA, CA, DV, and CV in three groups were elevated, whereas the RA was declined progressively. No significant pattern was observed in the RV among three groups (Figure 2). In all groups, the CA/DA and CV/DV ratio increased progressively, whereas the RA/DA and RV/DV ratio was reduced progressively (Figure 3).

Table 1 Comparison of each parameter among the normal, glaucoma-suspected and POAG groups

	Normal group	Glaucoma-suspected group	POAG group
Superior quadrant (μm)	133.93±13.52	122.91±21.75*	104.76±28.16*△
Inferior quadrant (μm)	132.86±11.88	126.26±20.73	100.62±31.01*△
Nasal quadrant (μm)	96.31±10.86	87.06±18.51*	85.89±15.18*
Temporal quadrant(μm)	78.24±9.36	79.17±15.10	67.38±16.36*△
Mean RNFL (μm)	110.33±6.84	103.85±15.40*	89.66±18.03*△
DA (mm^2)	2.10±0.39	2.75±0.44*	3.06±0.62*△
CA(mm^2)	0.57±0.43	1.53±0.52*	2.12±0.62*△
RA(mm^2)	1.53±0.31	1.21±0.26*	0.93±0.31*△
DV(mm^2)	0.21±0.11	0.48±0.18*	0.59±0.19*△
CV(mm^2)	0.10±0.10	0.39±0.19*	0.50±0.22*△
RV(mm^2)	0.10±0.07	0.09±0.06	0.085±0.10
CA/DA	0.26±0.16	0.55±0.11*	0.70±0.11*△
CV/DV	0.40±0.29	0.80±0.15*	0.81±0.22*
RA/DA	0.74±0.16	0.45±0.11*	0.30±0.10*△
RV/DV	0.60±0.28	0.20±0.15*	0.19±0.22*

* denotes $P<0.05$ compared with the normal group; △represents $P<0.05$ compared with the glaucoma-suspected group.

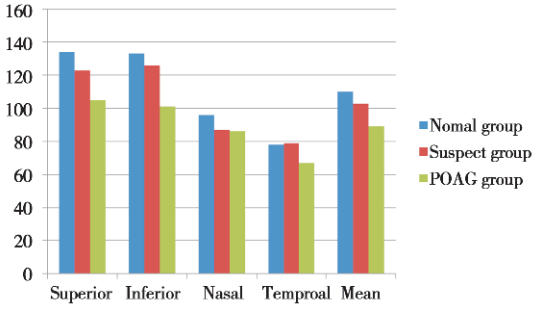

Figure 1 Comparison of RNFL thickness of each quadrant and mean RNFL thickness among the three groups

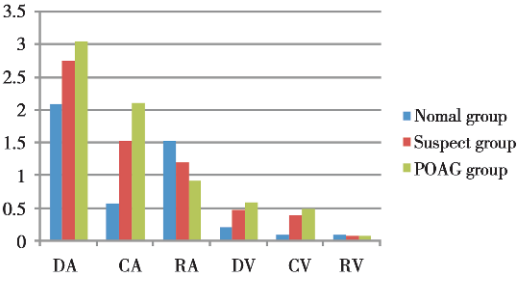

Figure 2 Comparison of DA, CA, DV, CV, RA, and RV among the three groups

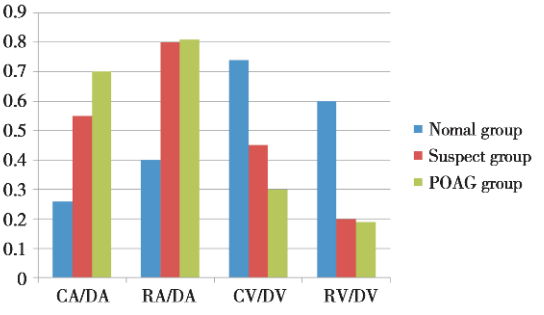

Figure 3 Comparison of CA/DA, CV/DV, RA/DA, and RV/DV ratio among the three groups

The optimal diagnostic index of POAG during OCT examination was determined as below: the area under the ROC curve(AROC) was calculated. A larger AROC was associated with a higher diagnostic value. AROC =0.5 denoted no diagnostic value. In the POAG group, the AROC of each parameter was of diagnostic value ($P<0.05$). Among the RNFL thicknesses, the AROC of the mean RNFL thickness was the largest, at up to 0.845. The AROC of the RA/DA ratio was the highest (0.998) among optic disc

parameters, followed by CA/DA ratio (0.997), and the AROCs of CA, DV, DA, RA were all >0.900, as illustrated in Table 2 and Figure 4.

Table 2 AROC value of each parameter in the POAG group

	AROC	*P*
Superior quadrant (μm)	0.805	0.000
Inferior quadrant (μm)	0.809	0.000
Nasal quadrant (μm)	0.706	0.004
Temporal quadrant (μm)	0.708	0.004
Mean RNFL (μm)	0.845	0.000
DA (mm^2)	0.863	0.000
CA(mm^2)	0.988	0.000
RA(mm^2)	0.900	0.000
DV(mm^3)	0.969	0.000
CV(mm^3)	0.955	0.000
RV(mm^3)	0.691	0.008
CA/DA	0.997	0.000
CV/DV	0.998	0.000
RA/DA	0.899	0.000
RV/DV	0.899	0.000

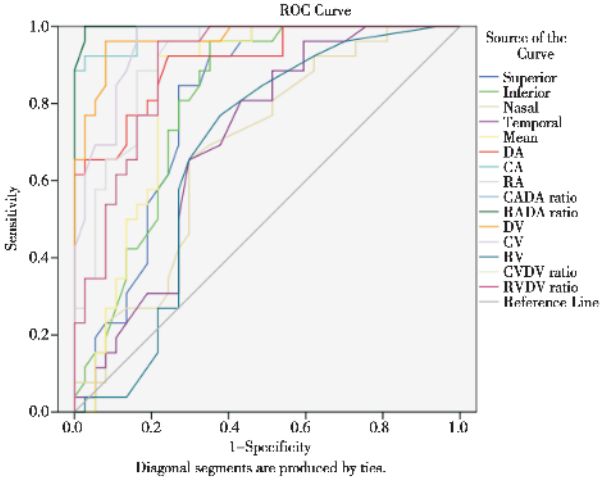

Figure 4 ROC curve of each parameter in the POAG group

Discussion

Glaucomatous optic nerve damage substantially results from retinal ganglion cells and axon pathological changes. Making an early diagnosis of POAG is difficult due to the slow progression of the disease. Therefore, delivery of early diagnosis is essential for the treatment of POAG. The morphological changes of the glaucomous optic disc are generally viewed as preceding the visual field defects, which are mainly characterized as decreased peripapillary RNFL thickness, increased CA/DA ratio, and loss of rim. An OCT examination could objectively and quantitatively measure the RNFL thickness and optic disc parameters with high accuracy and good reproducibility. This examination is of clinical significance in diagnosing early POAG[8-11].

In this study, the RNFL thickness of each quadrant presented with "twin peaks," shaped as thicker at the superior and inferior sites and thinner at nasal and temporal sides. The RNFL thickness of each quadrant and mean RNFL thickness were thinner in the glaucoma-suspected and POAG groups than in the normal counterparts, which is consistent with previous findings[12-14]. Moreover, compared with those in normal counterparts, the DA, DV, CA, CV, CA/DA, and CV/DV ratio were increased in glaucoma-suspected and POAG patients, whereas the RA, RV, RA/DA, and RV/DV ratio were decreased, which is almost consistent with the findings reported by Hu et al[15].

The mean RNFL thickness played the most crucial role in diagnosing glaucoma, which is basically in accordance with previous findings[12,16]. The parameters including CV/DV, RA/DA, and RV/DV ratio, which were not investigated in previous research, were measured and statistically compared among different populations in this study. These parameters are of clinical significance in the diagnosis of glaucoma. Among all optic disc parameters, the RA/DA and CA/DA ratios, and CA, DV, DA and RA were of relatively significant diagnostic value. The AROC of the RA/DA ratio was the largest, suggesting that it probably served as an optimal parameter for early diagnosis of glaucoma. The loss of cup rim was also one of the vital characteristics of early glaucoma. The RA/DA ratios in the three groups were 0.74±0.16, 0.45±0.11, and 0.30±0.10, indicating the possibility of suspected glaucoma when the RA/DA ratio was < 0.45. Visual field and dynamic intraocular pressure examination and regular follow-up should be conducted.

The possibility of early glaucoma should be considered for an RA/DA ratio <0.3. Considering the function and purpose of the RA/DA ratio, it was not regarded as a diagnostic index in this study, whereas it could provide evidence for the early diagnosis of glaucoma. The parameters including CV/DV, RA/

DA, and RV/DV ratio, which were not investigated in previous research, were measured and statistically compared among different populations in this study. These parameters are of clinical significance in the diagnosis of glaucoma.

Due to the slow progression of POAG, auxiliary examinations with relatively high sensitivity should be performed to make an early diagnosis and subsequent follow-up. At present, perimetry is still the gold standard for the diagnosis of glaucoma. However, the visual field progression of POAG is significantly slower than those of optic disc and optic nerve changes. Hence, OCT examination plays a pivotal role in the early diagnosis of glaucoma. Wollstein et al[17]. conducted a 4.7-year follow-up of the stability of visual field and OCT examinations in glaucoma-suspected and POAG patients, and suggested that 66% of patients had stable examination outcomes, 22% with progression detected by OCT, 9% with progression by perimetry and 3% with progression by both perimetry and OCT examination. Mitra Sehi[18] and Serbecic[19] have demonstrated that OCT examination is superior to perimetry in terms of evaluating the progression of POAG.

To sum up, the results from this study confirm that OCT examination showed high reproducibility and sensitivity, was convenient to operate, and appeared to reflect the changes in the optic disc parameters. OCT examination might therefore be applied to conduct screening and diagnosis of glaucoma by evaluating the changes in the RNFL thickness and optic disc parameters in glaucoma-suspected and early glaucoma patients, thereby contributing to early diagnosis and treatment of POAG.

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