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The changes of RNFL thickness and its influence on visual field defect in patients with PXG at different stages

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Abstract. – OBJECTIVE: To investigate the changes of retinal nerve fiber layer (RNFL) thickness and its influence on visual field defect in pseudoexfoliation glaucoma (PXG) patients at different stages, including early stage, middle stage and late stage.

PATIENTS AND METHODS: Clinical data of 194 PXG patients who were treated in our hospital from January 2017 to December 2019 were retrospectively analyzed. All patients were grouped according to the disease stage of PXG, including 56 eyes in the early stage, 54 eyes in the middle stage and 84 eyes in the late stage. Meanwhile, 50 cases with normal eyes were selected as the control group. The baseline clinical data, visual field defect and RNFL thickness in different groups were compared and the correlation between RNFL thickness and visual field defect was analyzed.

RESULTS: There was no significant difference in baseline clinical data among different groups ($p>0.05$). There was significant difference in visual field defect and RNFL thickness among different groups ($p<0.05$). The visual field defect, mean, supratemporal, infratemporal and subnasal of RNFL thickness in the early group were significantly lower than those of control group ($p<0.05$). The visual field defect, mean, nasal, supranasal, supratemporal, infratemporal and infratemporal of RNFL thickness in the middle group were significantly lower than those of control group ($p<0.05$). The visual field defect and RNFL thickness in the late group were significantly lower than those of control group and early group ($p<0.05$). The visual field defect, mean, supratemporal, infratemporal and infratemporal of RNFL thickness in the middle group were significantly lower than those of early group ($p<0.05$). Pearson correlation analysis showed that there was no correlation between RNFL thickness and visual field defect in pseudoexfoliation glaucoma patients in the early stage (r=-0.09, $p=0.63$). There was the positive correlation between RNFL thickness and visual field defect in PXG patients in the middle and late stages (r=0.43, 0.60; $p=0.04$, 0.00).

CONCLUSIONS: RNFL thickness is closely related to visual field defect in patients with PXG in middle and late stage. Dynamic monitoring of RNFL thickness can be used for clinical diagnosis, staging and prognosis evaluation.

Key Words:

Pseudoexfoliation glaucoma, Retinal nerve fiber layer, Visual field defect, Correlation.

Introduction

PXG is a special type of glaucoma caused by exfoliation syndrome, and patients with PXG accounts for 20%-25% of the total number of patients with open-angle (OAG)[1]. Compared with primary OAG, patients with PXG are characterized by high mean intraocular pressure, large fluctuation range, retrobulbar hypoperfusion and aggravated visual field damage, etc. and the disease progresses quickly[2]. PXG is an independent risk factor for RNFL damage[3]. Patients with early glaucoma have optic disc damage before the occurrence of visual field defect, and more than 60% of patients have abnormal RNFL 5 years before the occurrence of visual field defect, so ganglion cells should be detected early during the progression of exfoliation syndrome into PXG[4]. In recent years, new eye imaging technologies represented by spectral domain Optical Coherence tomography (SD-OCT) have gradually been applied in clinical practice and lay a good foundation for the morphological evaluation of glaucoma RNFL, by offering high-resolution RNFL images[5]. In this paper, the clinical data of 194 patients and 194 eyes with PXG admitted to our hospital from January 2017 to December 2019 were analyzed retrospectively, to investigate the changes of RNFL thickness and its influence on visual field defect

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in patients with PXG at different stages, explore new methods and accumulate more data for the early diagnosis and follow-up evaluation of PXG.

Patients and Methods

Clinical Data

The study was approved by our hospital Ethics Committee. The clinical data of 194 patients and 194 eyes with PXG admitted to our hospital from January 2017 to December 2019 were analyzed retrospectively. All patients were grouped according to the disease stage of PXG included 56 eyes for early stage, 54 eyes for middle stage and 84 eyes for late stage, and 50 cases with normal eyes were selected as the control group. PXG was staged based on Hodapp-Anderson-Parrish (HAP) classification, with MD≥-6dB standing for early stage, -12dB≤MD<-6dB for middle stage and MD<-12dB for late stage[6]. The inclusion criteria for PXG patients: (1) PXG was confirmed by slit lamp, gonioscopy and tonometry; (2) age ≥18; (3) intraocular pressure ≥2l mmHg; (4) accompanied by glaucomatous optic nerve damage and change of visual field; (5) with complete clinical data. The inclusion criteria for control group: (1) the dioptric media was transparent; (2) the morphology of optic nerve head was normal; (3) C/D≤0.3 and binocular disparity≤0.2; (3) intraocular pressure <21 mmHg; (4) sphere and cylinder powers ≤-6.0D and -3.0D respectively; (5) without a family history of glaucoma, visual field defect or chamber angle abnormality. Exclusion criteria: (1) previous history of eye surgery; (2) the dioptric media affected eye examination; (3) complicated by retinal disease or other optic nerve damage; (4) unable to cooperate in examination.

Observed Indicators

The examinations included the history of eye diseases, family history, best corrected visual acuity, slit lamp, intraocular pressure, gonioscopy, fundus and visual field examinations. The intraocular pressure was tested using Tomey FT-1000 tonometer from Japan; the optic disk RNFL was tested using Heidelberg Spectralis OCT scanner from Germany, with the optic disk as the scanning center. The circular scanning was performed with a diameter of 3.5 mm. The nasal, bitemporal, supranasal, subnasal, supratemporal and infratemporal RNFL thickness were measured and the mean RNFL thickness was calculated; (3) the visual field was examined with Carl Zeiss Humphrey 700 Field Analyzer and SITA software from Germany and the values of visual field MD were recorded.

Statistical Analysis

The data were processed using SPSS 17.0 (Chigago, IL, USA); the measurement data were compared using ANOVA and independent sample *t*-test and expressed as ($\bar{x} \pm s$) ; the enumeration data were compared using χ^2-test and expressed as %. Pearson test was used for correlation analysis and the test level was α=0.05.

Results

Comparison of Baseline Clinical Data among Different Groups

There was no significant difference in baseline clinical data among different groups (p>0.05), as shown in Table I.

Comparison of Visual Field Defect and RNFL Thickness among Different Groups

There was significant difference in visual field defect and RNFL thickness among different groups (p<0.05). The visual field defect, mean, supratemporal, infratemporal and subnasal RNFL thickness of early group were significantly lower than those of control group (p<0.05). The visual field defect, mean, nasal, supranasal, supratempo-

Table I. Comparison of baseline clinical data among different groups.

Group	Number of Cases	M/F	Age (yrs)	Diopter (D)
Control Group	50	22/28	69.51 ± 9.09	-0.98 ± 0.23
Early Group	56	22/34	72.84 ± 8.42	-1.13 ± 0.31
Middle Group	54	22/32	73.20 ± 9.04	-1.20 ± 0.35
Late Group	84	40/44	70.11 ± 7.97	-1.27 ± 0.28
F/χ^2		2.06	0.93	1.18
p		0.54	0.40	0.23

ral, infratemporal and infratemporal RNFL thickness of middle group were significantly lower than those of control group ($p<0.05$). The visual field defect and RNFL thickness of late group were significantly lower than those of control group and early group ($p<0.05$). The visual field defect, mean, supratemporal, infratemporal and infratemporal RNFL thickness of middle group were significantly less than those of early group ($p<0.05$), as shown in Table II.

Correlation Analysis between RNFL Thickness and Visual Field Defect

Pearson correlation analysis showed that there was no correlation between RNFL thickness and visual field defect in patients with early PXG (r=-0.09, p=0.63). There was the positive correlation between RNFL thickness and visual field defect in patients with middle and late PXG (r=0.43, 0.60; p=0.04, 0.00).

Discussion

Previous studies have shown that the incidence of exudation syndrome among people above 60 was up to 30%, which led to an increasing incidence of PXG year by year[7].A long-term follow-up study confirmed that 35%-45% of patients with monocular exudation syndrome can turn into binocular, and more than 30% of patients can progress to PXG[8]. At present, the mechanism underlying PEX's progression into PXG has not been fully elucidated in the medical community, and most people believe that exfoliation blocks the trabecular meshwork and lead to visual field damage. The exfoliation is deposited in related arteries and veins, optic nerve sheaths and lamina cribrosa region, resulting in optic nerve damage that is closely related to the occurrence and development of disease[9]. Decreased blood flow of the optic nerve head and peripheral retinal microvessels in patients with exfoliation syndrome was an important cause of optic nerve damage[10-11]. Meanwhile, the elastosis of lamina cribrosa in exfoliation syndrome can further aggravate optic nerve damage. The amount of exfoliation in the lamina cribrosa region of optic disc was proved to be closely related to the severity of PXG.

Corneal endothelial cell density in patients with exfoliative OAG was lower than that in patients with primary OAG, suggesting that the protection of corneal endothelial cells should be strengthened during clinical treatment[12]. At the same time, compared with normal people and patients with exfoliation syndrome, the macular thickness of patients with PXG was generally thinner, so the detection of changes of macular thickness can assist the clinical diagnosis and treatment of PXG. In this study, the RNF thickness of the control group and patients with PXG at different stages was analyzed with an SD-OCT scanner, and the results showed that there was statistically significant difference in RNFL thickness among different groups ($p<0.05$). Among them, the mean RNFL thickness of normal people was the thickest, followed by that of early, middle and late PXG, suggesting that the progression of PXG can make RNFL thickness grow thinner. Consistent with previous reports, the regional distribution rule of RNFL thickness in normal people was that infratemporal RNFL was the thickest, and supratemporal, subnasal, supranasal, nasal and bitemporal RNFLs grew thinner[13]; the RNFL thickness of early and middle PXG decreased successively from infratemporal, supratemporal, supranasal, subnasal, bitemporal to nasal, while the RNFL thickness of late PXG decreased successively from supratemporal, infratemporal, subnasal, supranasal, bitemporal to nasal. The regional distribution rules of the RNFL thickness of patients with early and middle PXG were consistent. While compared with normal people, for patients with early and middle PXG, the thickness of supranasal RNFL was greater than subnasal RNFL, and the thickness of bitemporal RNFL was greater than nasal RNFL, suggesting that the thinning speed of subnasal RNFL was higher than that of supranasal RNFL and the thinning speed of nasal RNFL was higher than bitamporal RNFL. While for patients with late PXG, the thinning speed of infratemporal RNFL was higher than supratemporal RNFL and the thinning speed of supranasal RNFL was higher than subnasal RNFL. The RNFL thickness of all optic disc areas of patients with PXG was thinner than that of patients with exfoliation syndrome and normal people[14], while compared with normal people, the RNFL of patients with exfoliation syndrome was only thinner in the infratemporal area. The distribution of RNFL thickness in PXG was the same as that of patients with early and middle PXG in this study. The authors believe that to monitor the changes of RNFL thickness in the optic disc of patients with PXG using SD-OCT is helpful for the early diagnosis of the progression of glaucoma.

Table II. Comparison of visual field defect and RNFL thickness among different groups.

Group	Number of Cases	Visual Field Defect	RNFL Thickness						
			Mean	Nasal	Supranasal	Supratemporal	Bitemporal	Infratemporal	Subnasal
Control Group	50	-1.19 ± 0.47	105.37 ± 13.56	77.43 ± 15.66	119.43 ± 29.95	142.98 ± 37.72	75.56 ± 19.61	151.58 ± 21.93	121.53 ± 32.42
Early Group	56	-3.93 ± 1.22	93.52 ± 14.69	72.35 ± 17.02	110.38 ± 22.66	115.13 ± 30.89	72.23 ± 21.28	133.70 ± 30.67	107.41 ± 26.52
Middle Group	54	-9.53 ± 2.42	84.12 ± 10.50	65.69 ± 11.47	95.76 ± 18.50	101.37 ± 28.56	71.96 ± 14.41	100.81 ± 17.88	86.37 ± 17.80
Late Group	84	-24.22 ± 6.72	56.90 ± 7.09	46.93 ± 8.62	58.93 ± 14.27	64.52 ± 17.69	55.52 ± 8.88	64.94 ± 15.71	54.83 ± 13.50
F		337.04	80.15	25.62	34.87	49.83	8.06	93.85	57.49
p		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

The relationship between RNFL defect and visual field damage has been observed. Compared with normal people, the RNFL of patients with primary OAG grew thinner as visual field defect aggravated[15]. According to the results of this study, there was a statistically significant difference in visual field defect among different groups ($p<0.05$), and the visual fields of patients with early, middle and late PXG were worse than that of normal people, and visual field defect gradually aggravated with the progression of PXG. Pearson correlation analysis showed that there was no correlation between RNFL thickness and visual field defect in patients with early PXG (r=-0.09, p=0.63). There was the positive correlation between RNFL thickness and visual field defect in patients with middle and late PXG (r=0.43, 0.60; p=0.04, 0.00), suggesting that there was a positive correlation between RNFL thickness and visual field MD in patients with middle and late PXG. Retinal light sensitivity decreased with the onset of loss of retinal ganglion cells in glaucoma[16]. If the loss of ganglion cells reached 20%, the light sensitivity would decrease by 5dB, and the occurrence of characteristic visual field damage required a loss of ganglion cells of more than 50%. Visual field examination alone lacked sufficient sensitivity to detect the earliest changes in glaucoma, while the changes of RNFL thickness had already occurred.

Conclusions

To sum up, RNFL thickness is closely related to visual field defect in patients with PXG in middle and late stage. Dynamic monitoring of RNFL thickness can be used for clinical diagnosis, staging and prognosis evaluation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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