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Original article

Early diagnostic value of optical coherence tomography in the clinical prediction model for optic nerve injury in saddle space occupying patients

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ABSTRACT

In this study, 50 patients with anterior ischemic optic neuropathy due to saddle block were selected as the experimental group, and 50 healthy subjects were used as the control group to conduct a study. The best corrected visual acuity examination, optical coherence tomography and visual evoked potential examination were performed on the two groups. The results of the study showed that the majority of patients were middle-aged and older people over the age of 50, but the youngest patients were only 37 years old. After various examinations, it was found that patients with optic nerve injury had a significant reduction in the best corrected visual acuity compared with healthy people. After the onset of the disease, the optic nerve fiber layer will first increase and then decline. During the course of the disease, the patient's optic nerve fiber layer will gradually thin to a much lower level than healthy people. And in comparing the thickness of the optic nerve fiber layer in patients with systemic disease and no systemic disease, it is found that the degree of optic nerve damage is more serious in patients with systemic diseases. After the VEP examination, the difference between the P100 wave latency and the N75-P100 amplitude of the diseased eye and the unaffected eye was statistically significant. Moreover, the difference between the patient's diseased eye and the healthy human eye is almost the same as that of the unaffected eye.

1. Introduction

Intracranial space-occupying lesions often lead to optic nerve damage in patients, the most common in the saddle region, including pituitary adenoma, craniopharyngioma, meningioma, and so on. Space-occupying lesions cause mechanical compression of the optic nerve. Many patients have early vision loss, visual field defects, and optic atrophy (Hayreh and Zimmerman 2017; Wright et al., 2017). Ischemic optic neuropathy often occurs when the ciliary arteries that provide nutrition to the optic nerve develop circulatory disorders. According to the affected parts, it is divided into AION (anterior ischemic optic neuropathy) and PION (posterior ischemic optic neuropathy) (Ling et al., 2017; Lee et al., 2017). In clinical practice, AION can be divided into non- arteritis anterior ischemic optic neuropathy and arteritis anterior ischemic optic neuropathy. The former is secondary to non-inflammatory small vessel disease, accounting for 95% of AION. The latter is often secondary to giant cell temporal arteritis, which is rare in the clinic (Balducci et al., 2017). AION is a common cause of acute optic neuropathy in people over 50 years of age, which can lead to severe visual impairment. Currently, there is a lack of recognized and effective treatment methods, and it is one of the ophthalmologic refractory diseases (Rougier et al., 2017; Kuhli-Hattenbach et al., 2017; Pakravan et al., 2017; Sun and Liao 2017). The main clinical features of AION are sudden visual loss, characteristic visual field defect and fundus optic disc edema occurred in one eye or both eyes. In recent years, with the increase of systemic vascular diseases, the incidence of this disease has gradually increased (Stanca et al., 2017). The disease has the characteristics of acute onset and serious illness

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condition. Once the disease occurs in the clinic, it often causes optic nerve atrophy, causing irreversible visual impairment, which brings great pain and trouble to the patient's life and work.

Visual field examination is one of the most important and essential examinations to evaluate the changes of AION patients in the clinic (Erhan Tenekecioglu et al., 2017). It can comprehensively assess the scope, extent and type of visual impairment of patients. OCT is a sophisticated, accurate and objective optical imaging technique that not only achieves high-resolution fundus tomography, but also obtains the exact numeric value of thickness of the retinal nerve fiber layer (RNFL) (Sharma et al., 2017; de Boer et al., 2017; Sambhav et al., 2017). The thickness of the RNFL examined by OCT also changed with the progression of AION. OCT has the advantages of rapid, non-contact, non-invasive, high resolution, and good reproducibility. By measuring the thickness of nerve fibers and the volume of the macula, the damage of the retina and optic nerve structure can be detected early, and is highly sensitive (Ali et al., 2017; Akil et al., 2017). It can quantitatively and objectively evaluate the damage of optic nerve diseases such as oppressive optic neuropathy; and OCT can help differential diagnosis of diseases such as oppressive optic neuropathy and glaucomatous optic neuropathy. Due to the early atypical visual field changes, difficulties in differential diagnosis and even misdiagnosis may occur, and OCT has certain advantages in identifying the two diseases (Xing et al., 2017; Matthews and Frishman, 2017); because OCT is capable of quantitative determination, it is helpful to predict the visual function of patients after decompression.

In this study, a retrospective clinical study was conducted to retrospectively analyze the data of AION patients with RNFL thickness measured by optical coherence tomography to understand the thickness variation of retinal nerve fiber layer (RNFL) during the pathogenesis of this disease. A review analysis of the optic nerve injury in the saddle area is conducted.

2. Methodology

2.1. Research subject

All the cases in this study were from 50 patients with anterior ischemic optic neuropathy in the ophthalmology department of XXX Hospital. All cases met the inclusion criteria. The experiment was divided into two groups, one group was the control group, and the data of 50 healthy people were statistically analyzed. The second group was the experimental group, and the data of 50 patients were statistically analyzed.

2.2. Diagnostic criteria and inclusion criteria

Diagnostic criteria: Sudden deterioration or loss of vision, usually without eyeball pain or dull pain. Some patients may have a transient blurred vision or amaurosis before onset. There is a relative afferent pupillary defect in the pupil of the eye. Fundus examination: localized edema of the optic disc, linear bleeding around the optic disc, advanced optic atrophy. A quadrant visual field defect associated with a physiological blind spot appears in the visual field, and part of it can affect the central visual field but is not bounded by the midline. Visual evoked potential examination showed that optic nerve function conduction was blocked; fluorescein fundus angiography shows slow or defective optic disc fluorescence filling. Inclusion criteria: clinically diagnosed as anterior ischemic optic neuropathy; volunteered to participate in this trial, and signed informed consent; both male and female, aged between 35 and 85; medical records are complete.

2.3. OCT examination

The RNFL thickness was measured using an optical coherence tomography scanner (Zeiss Company, China). The scanning mode was an Optic Disc Cube 200 $\times$ 200 scanning program with a scanning speed of 27,000 A scan/s and a tissue resolution of 5 μm. All healthy group subjects and AION patients underwent a scan of the OCT optic disc. OCT examinations are performed by the same physician. The OCT examination was performed in the dark room. Before the examination, the compound tropicamide eye drops were used for mydriatic (the pupil diameter was >4 mm). The examiner selected the RNFL thickness scanning program. When the eyesight of the eye to be inspected is good, it looks at the visual object (inside gaze); when the eyesight of the eye to be examined is poor, the external gaze is used. The OCT scan of the RNFL thickness is a continuous circular scan with a default diameter of 3.46 mm centered on the optic disc. The analysis scan results were automatically calculated by the built-in analysis software carried by Cirus3DOCT. The scan results provided the retinal reflex map and RNFL thickness topographic map, binocular average, upper, lower, bitamporal and nasal side RNFL thickness and other ratios and parameters. According to the OCT data of AION patients, the RNFL results were divided into 7 periods, that is 1–9 days, 10–19 days, 20–29 days, 30–39 days, 40–89 days, 90–365 days and>1 year after onset to compare the changes of RNFL thickness in AION eye one by one. The RNFL thickness between healthy and diseased eyes of AION patients with monocular onset was compared and analyzed.

2.4. Best corrected visual acuity examination

Visual acuity was assessed using an international standard visual acuity chart (SnellenE). The binocular vision of patients and healthy people are evaluated, because many tumors do not grow in the middle position, often occur on one side or slightly lateral side, the effect on bilateral optic nerve may be different, but asymmetrical vision changes in both eyes are common. In addition, the relationship between the tumor and the bilateral optic nerve, bilateral fundus conditions, bilateral anatomical variation and other factors are also different.

2.5. Visual evoked potential examination

The visual evoked potential (VEP) examination is performed in the electric shielding room. The patient takes a sitting posture and sequentially connects the recording electrode, the reference electrode and the grounding electrode to cover the opposite side of the eye and gaze at the center fixation point. Patients with Snellen vision >0.1 is can be performed with Pattern-VEP (PVEP) examination, otherwise Flash-VEP (FVEP) examination is adopted. PVEP was measured using three different spatial frequencies (1, 2, 4 cyc/deg) by the flipping checker, and the flip frequency was 2 Hz; FVEP was measured using three full-field light stimuli of different brightness.

2.6. Statistical method

The data were statistically analyzed by SPSS17.0 software. The qualitative indicators were described by frequency table and percentage. The quantitative data with normal distribution were expressed by the mean ± standard deviation (x ± SD), and quantitative indicators consistent with the skewed distribution are expressed as the median (P50). If the data is in conformity with the normality, two independent sample tests are performed. If the conditions are not met, the rank sum test is used. Paired test was used for comparison within the group; P < 0.05 was considered to be statistically significant.

3. Results and discussion

3.1. Analysis of general data of patients

In the experimental group, AION patients had a total of 50 patients, of which there were 28 males and 22 females with an average age of 59.2 ± 8.6 years, a minimum age of 37 years and a maximum age of 75 years. Among them, there were 2 cases between 30 and 39 years old, 11 cases of 40–49 years old, 16 cases of 50–59 years old, 13 cases of 60–69 years old, and 8 cases of 70–79 years old. Of the 50 cases, 10 cases had bilateral eye disease, 40 cases had single eye disease, 17 cases had OCT examination 1 time, 20 cases had 2 examinations, 5 cases had 3 examinations, and 8 cases had 4 examinations. The total number of OCT examinations in 50 patients was 104. The results of OCT examination of AION patients were divided into 7 groups according to the onset time and course of disease, namely 1–9 days, 10–19 days, 20–29 days, 30–39 days 40–89 days, 90–365 days, >1 year. Details are shown in Fig. 1A. The frequency of OCT in 40 cases of single eye disease was 78, and they were divided into 7 groups according to the onset time and course of disease, as shown in Fig. 1B.

Most of the 50 AION patients were associated with systemic diseases such as hypertension, hyperlipidemia, high blood viscosity, diabetes, carotid atherosclerosis or plaque, aortic sclerosis or plaque, and heart disease. There were 12 patients without systemic diseases, accounting for 24.0%; 38 patients with systemic diseases, accounting for 76.0%, of which 16 patients with one disease accounted for 42.1%, 11 patients with two diseases, accounting for 29.0%, 4 patients with 3 diseases, accounting for 10.5%, 4 patients with 4 diseases, accounting for 10.5%, 3 patients with more than 4 diseases, accounting for 7.9%, as shown in Fig. 1C, D.

At the same time, 50 healthy people in the control group have similar age with AION patients, and there were no diseases in their eyes and the whole body. There were 27 males and 23 females; aged 37–75 years, with mean age of 55.4 ± 7.8 years old; diopter was −4.00D to +4.00D. There were no significant differences in the general data of gender, age, and diopter between the above two groups (P > 0.05).

3.2. Changes in RNFL thickness in patients with AION

The average RNFL thickness results for the healthy group are detailed in Fig. 2A. Compared with the average RNFL thickness of the healthy group (96.4 μm), the average RNFL of the diseased eye increased significantly (average thickness 174.6 μm) at the 1st to 9th days, and the average thickness rose to the peak point (247.2 μm) at the 10 th to 19 th days, and then the thickness gradually decreased. The average RNFL around the optic disc changed thinly (88.1 μm) at the 40th to 89th day, and between the 90th to 365th days, the thickness of the RNFL was significantly thinned (63.5 μm). The average thickness of RNFL has stabilized (59.4 μm) when the disease duration is >365 days, as shown in Fig. 2B.

During the entire course of all quadrants of the plate, the lower quadrant had the highest RNFL thickness (331.7 μm) on days 10–19, with the heaviest edema, between the 30th and 39th day of the disease, the average quadrant thickness of the nasal side and bitemporal of the optic disc was significantly lower compared with the normal average of the corresponding quadrants of the normal healthy group (65.1 μm, 68.8 μm in order), indicating that the bitemporal and nasal sides of the optic disc were thinning at the earliest; on the 30th-39th day, the average thickness of the upper RNFL (118.5 μm) between the optic discs also began to fall below the thickness of the quadrant of the healthy group. In all quadrants, the lower portion of the optic disc became thinner at the latest.

The results of the analysis showed that the average RNFL thickness of the diseased eye of AION patients, accompanied by the progression of the disease, experienced a pathological process of early elevation and gradual decline and thinning. At the 10th-19th days of onset, the average thickness of RNFL was the thickest, with the most serious edema, suggesting that this period should be based on the elimination of optic disc edema and other treatment;

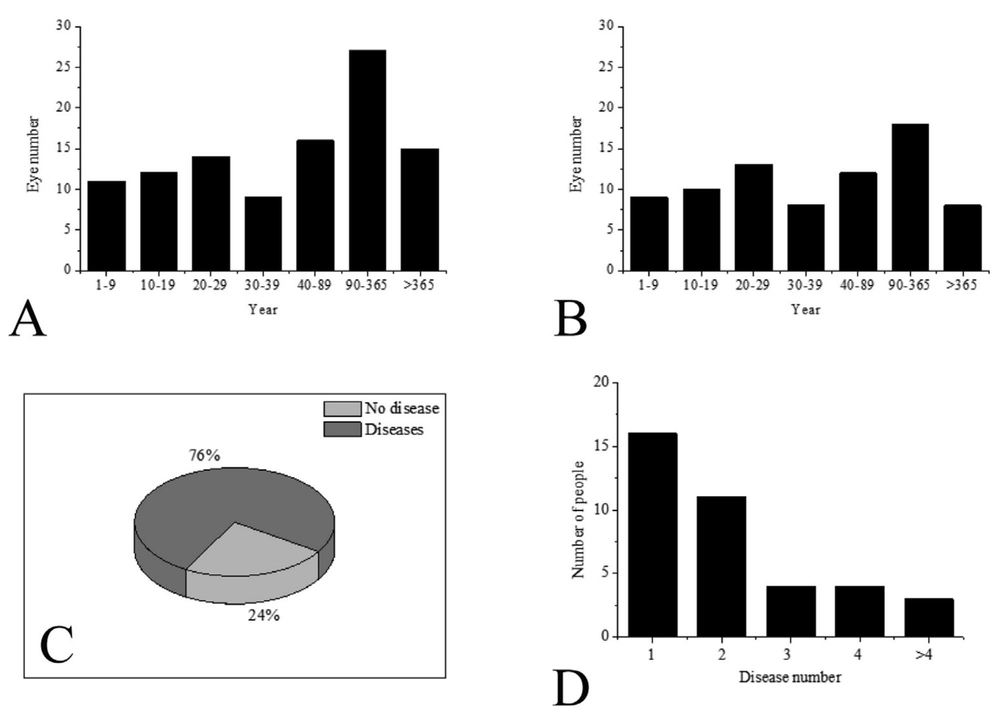

Fig. 1. General patient data.

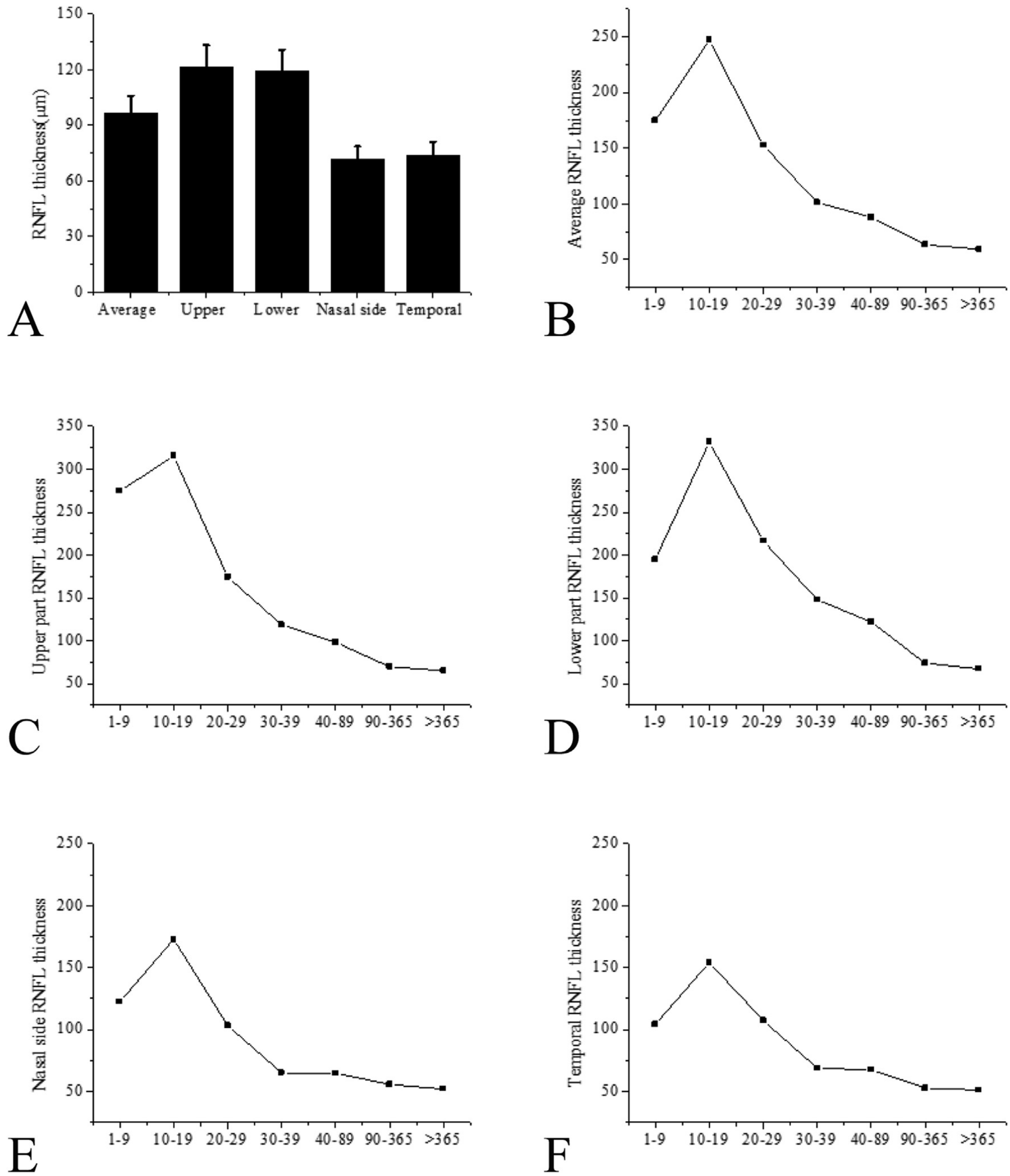

Fig. 2. Average RNFL thickness results of both groups (*$P < 0.05$).

40–89 days RNFL thickness is significantly thinner, this period should be based on nutritional nerves and other treatment; at 365 days after the course of disease, RNFL thinning trend is slow, this is The pathological manifestations of optic atrophy, so the period should be based on improving circulation and nutritional nerves. The RNFL thickness of the average, upper, lower, nasal and bitemporal sides of both eyes of the affected group is shown in Fig. 2B–F.

3.3. Comparison of RNFL thickness between diseased eyes and contralateral healthy eyes in monocular AION patients

Forty patients with AION monocular disease, the RNFL thickness change analysis between the affected eye and the healthy eye, and the comparison between the AION patient mentioned above and the healthy group were basically consistent. On the 1st to 9th day of the disease, the average RNFL thickness (187.3 μm) of the affected eye was significantly higher than that of the healthy eye ($P < 0.05$). On the 11th-19th day, the difference in average RNFL thickness of the affected eye and healthy eye was the most significant (243.7 μm). As the disease progressed, the average RNFL thickness decreased in the affected eye, and the average RNFL thickness between the affected eye and the healthy eye was closer between the 30th and 39th days. After the comparison between the two, the difference was not statistically significant ($P > 0.05$). During the course of 40–89 days, the average thickness of the affected eye decreased and began to be lower than the normal RNFL thickness of the contralateral eye ($P < 0.05$); after the course of disease was more than 365 days, the average thickness of the affected eye was slowed down and stabilized (P < 0.05), as shown in Fig. 3.

3.4. The effect of systemic disease on the average RNFL thickness of different stages of the disease

The average RNFL thickness of AION patients with systemic disease was higher than that of patients without systemic disease from the onset to the 29-day course of disease. After 30 days of disease, the average thickness of RNFL in patients with systemic disease was significantly lower than that in patients without systemic disease and was still lower than that of patients without systemic disease at 365 days of the course, and the thickness of the two was close. Therefore, the results show that compared with AION patients without systemic diseases, the degree of papilledema in patients with systemic diseases such as hypertension and diabetes will be more severe in the same situation, and the degree of thinning of the optic nerve fiber layer will be more significant, as shown in Fig. 4.

Systemic diseases play an important role in the development of ischemic optic neuropathy. It is more common in middle-aged and elderly people. It can cause insufficient blood supply to the optic disc caused by various factors or systemic diseases, which leads to the occurrence of this disease. In this study, by comparing the average RNFL thickness of different disease stages in patients with diseases such as hypertension, coronary heart disease, diabetes, and those without systemic disease, it is found that in the optic disc edema, the affected eye of patients with systemic diseases are more edematous than those with no systemic diseases. In the optic nerve thinning period, the degree of thinning and the trend are more obvious in the affected eye of patients with the systemic disease than that without the systemic disease. It can be seen that high-risk systemic disease factors can not only induce ischemic optic neuropathy, but also promote the deterioration of the disease and aggravate the disease during the occurrence of the disease. This suggests that in the treatment, the blood pressure, blood lipids, blood sugar, etc. should be controlled firstly to reduce the AION optic nerve damage and improve the visual function prognosis.

3.5. Analysis of the best corrected visual acuity test in the two groups

Of the 50 patients (100 eyes) with AION, 60 eyes were affected, and 56 eyes were of BCVA 20.02. The mean BCVA of 56 affected eyes of AION patients with BCVA 20.02 was 0.52 ± 0.24. There were 40 cases of monocular disease in AION patients, so the BCVA of 40 eyes of AION patients was counted. The average BCVA of the unaffected eyes of these 40 patients with AION was 0.96 ± 0.12. The BCVA of the experimental group and the unaffected eyes were tested for normal distribution, and the P values were all <0.05, which did not conform to the normal distribution. The BCVA status between the patient's diseased eye and the unaffected eye was compared, P value <0.05, showing the difference between the BCVA of the affected eye and the unaffected eye was statistically significant, as shown in Fig. 5A. The visual acuity of the eyes of the control group and the experimental group were compared. After the normality test of BCVA, the P values were all <0.05, which did not conform to the normal distribution. The difference between the two groups of BCVA was statistically significant, as shown in Fig. 5B for details.

3.6. Analysis of OCT examination in two groups

40 patients with monocular onset in the experimental group were analyzed. The RNFL thickness of 40 affected eyes and 40 non-affected eyes were statistically analyzed. The results showed that the P values were all <0.05, indicating that the difference in RNFL thickness between the affected eyes and the unaffected eyes was statistical significance, as shown in Fig. 6A for details. Normality test of RNFL thickness in control group and experimental group showed the P value of the control group was >0.05. Therefore, the RNFL thickness of the control group was in a normal distribution, and the values of the control group were comparable. The RNFL thicknesses of the two groups were compared, P value <0.05, showing a statistically significant difference between the RNFL thickness of two groups, as shown in Fig. 6B for details.

3.7. Analysis of VEP examination in two groups

Of the 40 patients with monocular AION, 15 had not performed this test for various reasons, and only 25 patients underwent VEP, including 25 affected eyes and 25 unaffected eyes. The P100 wave latent time and N75-P100 amplitudes of the VEP examination of AION patients; affected and unaffected eyes were performed with normal distribution test, and the results showed that the P values were all <0.05. The results showed that the P values were all <0.05, so the VEP examination P100 wave latency and N75-P100 amplitude were consistent with normal distribution. The VEP examination P100 wave latency and N75-P100 amplitude were compared between the affected and non-affected eyes, and two independent samples were used, P < 0.05. The difference between the amplitudes of N75-P100 was statistically significant, as shown in Fig. 7A and B.

The P100 wave latent time of the control group and the experimental group was tested for normality. When comparing the P100 wave latent time, two independent samples *t* test were used, P

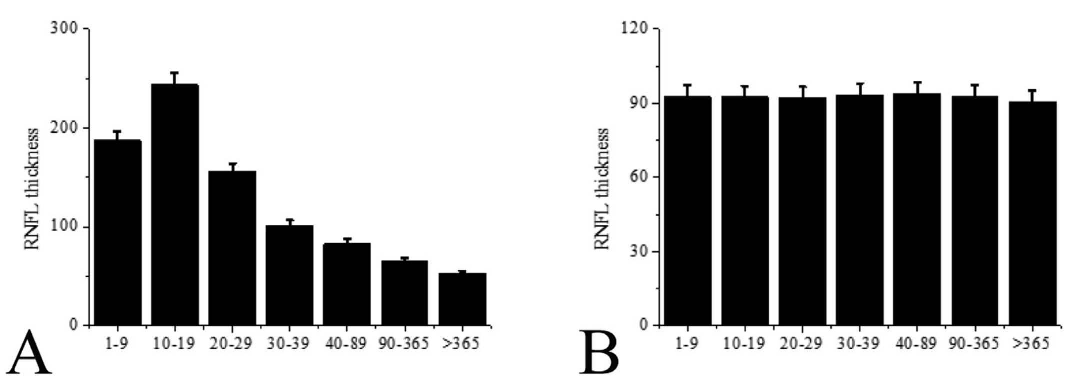

Fig. 3. Comparison of RNFL thickness between diseased eyes and contralateral healthy eyes in a monocular AION patient.

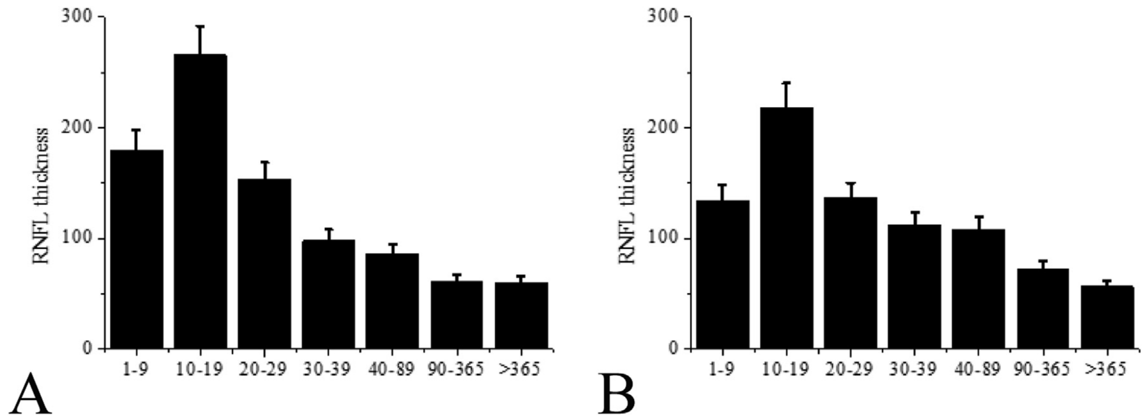

Fig. 4. Effect of systemic disease on mean RNFL thickness during different disease stages of the disease.

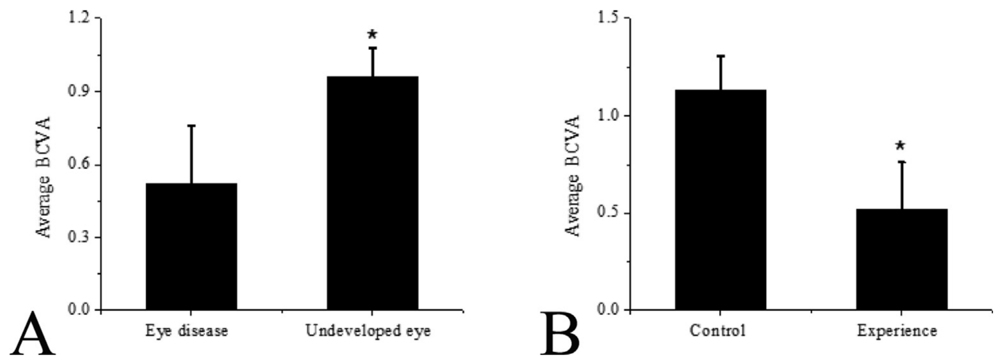

Fig. 5. Comparison of mean BCVA values (*P < 0.05).

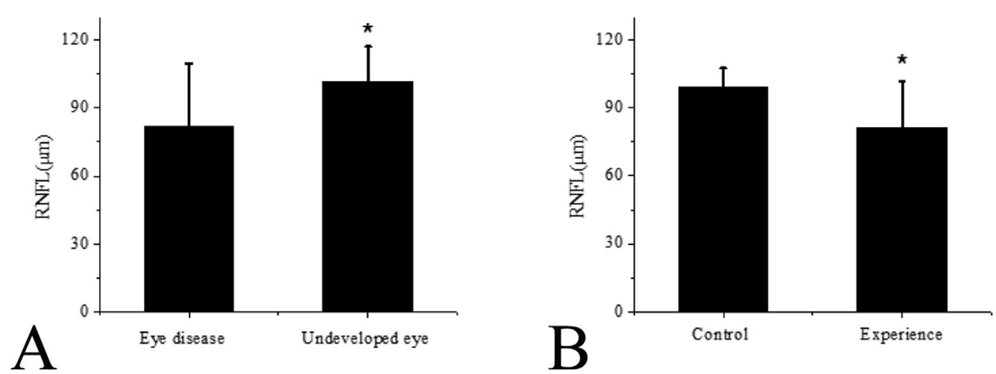

Fig. 6. Comparison of average RNFL thickness values (*P < 0.05).

value < 0.05, showing the difference between the two groups of P100 wave latent time was statistically significant, as shown in Fig. 7C. The amplitude of N75-P100 of two groups of VEP examination was tested for normality. The amplitude of N75-P100 was compared and two independent samples *t* test were used. The P value was < 0.05, indicating that the difference between the two groups of N75-P100 amplitude was statistically significant, as shown in Fig. 7D.

4. Conclusion

The thickness of the retinal nerve fiber layer was measured by optical coherence tomography, and the change of papilledema in patients with anterior ischemic optic neuropathy can be monitored. After analyzing the patient's general data, the disease was found to be mostly occurred in the middle-aged and elderly population. The youngest patient was only 37 years old, indicating that the disease is becoming younger. After visual acuity, OCT, and VEP ophthalmologic examination, the BCVA value of patients with optic nerve injury was significantly reduced, which was significantly statistically different from that of healthy people. After the OCT examination, it was found that the optic edema was most severe between the 10th and 19th days of the AION course. At 30–39 days, the nasal and bitamporal sides of the optic disc became thin at earliest. When the disease progressed to 40–89 days, the average RNFL thickness of each quadrant is thinned. Patients with systemic disease are more likely to develop the disease and the condition is

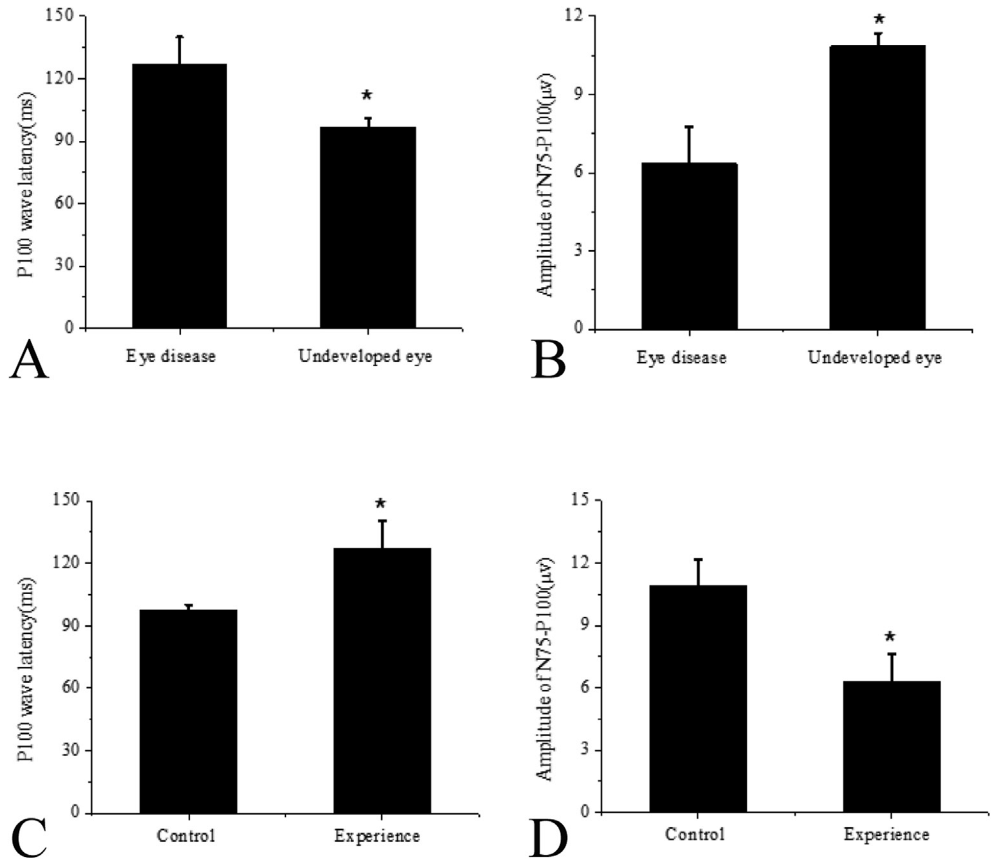

Fig. 7. Comparison of VEP between the two groups (*P < 0.05).

more severe. After the VEP examination, the difference between the P100 wave latency and the N75-P100 amplitude of the diseased eye and the unaffected eye was statistically significant, and the difference between the patient's diseased eye and the healthy human eye is almost the same as that of the unaffected eye.

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