Original Article
Observation of changes in retinal nerve fiber layer thickness in early diabetic retinopathy by optical coherence tomography

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Abstract: Objective: To explore the effectiveness and safety of measuring macular retinal nerve fiber layer (RFNL) thickness in early stages of diabetes retinopathy (DR) using optical coherence tomography (OCT). Methods: A total of 149 DR patients admitted from December 2018 to December 2019 were divided into non-diabetic retinopathy (NDR) group (56 cases, 110 eyes) and mild NPDR (non-proliferative DR) group (51 cases, 99 eyes) and moderate NPDR group (48 cases, 89 eyes). 46 healthy subjects (92 eyes) were included in the control group. All participants were subjected to OCT to measure RFNL thickness, including the quadrants of the optic disc (thickness, superior quadrant, inferior quadrant, and temporal quadrant), mean macular thickness (MMT), and foveal thickness. Results: Moderate NPDR group showed smaller thickness of superior quadrant, inferior quadrant and temporal quadrant than the control group (P < 0.05); temporal quadrant and inferior quadrant thickness in NDR group were not statistically different from control group (P > 0.05). However, its superior quadrant thickness is significantly smaller (P < 0.05); in contrast to NDP group, mild NPDR group showed similar thickness of superior quadrant and temporal quadrant, and smaller thickness of inferior quadrant (P < 0.05); the thickness of superior quadrant, inferior quadrant and temporal quadrant in the control group were greater than those of the mild NPDR, NDP and moderate NPDR groups (P < 0.05). The foveal thickness and MMT of the mild to moderate DR groups were significantly greater than those of the NDP and the control groups (P < 0.05); the macular RNFL thickness of each quadrant in NDR group was significantly thinner than that of the control group (P < 0.001), and it was significantly thicker in moderate NPDR group than that of NDR and mild NPDR groups (P < 0.001). Conclusion: The RNFL has thickened significantly before retinal vascular changes in DM patients. The thickness of RNFL can be used as the diagnostic indicator for evaluating the severity of DR disease.

Keywords: Diabetes, retinal nerve fiber layer, optical coherence tomography, safety analysis

Introduction

Diabetic retinopathy (DR) is a disease caused by diabetes that could lead to blindness. 60% patients with 20 years of diabetes will develop DR [1]. When DR advances into proliferative DR (PDR), it will cause blindness and seriously affect the normal life of patients [2]. The incidence of DR increases with the course of diabetes, which has reached 43.1% in China [3]. Some patients with hidden complications often did not take much attention, which eventually incur severe DR. Therefore, diabetes should be treated as soon as possible to prevent DR [4]. At present, a series of instruments can be used to quantitatively detect the papillary structure and the thickness of RNF. Among them, optical coherence tomography (OCT) is a non-contact, non-invasive, high-resolution imaging technology of biological tissue structure. In recent years, with the application of Fourier technology and broadband light source technology, a new generation of frequency domain OCT has brought higher-speed and higher-resolution OCT images than time domain OCT. RTVue OCT, manufactured by Optovue in the United States, is one of the frequency range OCT instruments currently used in ophthalmology clinical applications, which has an acquisition speed of 26,000 A scans per
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second and a resolution of up to 5 m. Studies have pointed out that when DR occurs, the thickness of RNFL will change, and the specific change pattern has not been explored in detail [5].

In this study, OCT scanning and RNFL thickness detection were used to observe the changes and discuss possible mechanism of early RNFL changes.

Materials and methods

Baseline data

149 DR patients admitted from December 2018 to December 2019 were enrolled. On the basis of DR international staging [5] standard, 56 patients (110 eyes) were divided into NDR group, including 29 men and 27 women, aged 28-76 years, average 48.46 ± 9.76 years old, course of disease 10-28 years; 51 patients (99 eyes) in mild NPDR group, including 26 males and 25 females, aged 25-74 years, average 46.46 ± 8.76 years old, course of disease 11-27 years; 48 patients (89 eyes) in the moderate NPDR group, including 23 men and 25 women, aged 23-73 years, average 47.42 ± 8.96 years, course of disease 11-21 years; 45 healthy persons (90 eyes) were enrolled as the control group, including 22 males and 24 females, aged 21-77 years, with an average age of 50.16 ± 7.26 years.

Inclusion criteria: All patients were diagnosed as DR by ophthalmology specialists [6]. The clinical symptoms included vascular degeneration, lint spots, bleeding, retinal hypoxia and edema. There was no significant difference in baseline data such as gender and age among three groups (P > 0.05), which were comparable. None of the enrollees had congenital visual impairment, and all enrollees or their families had signed informed consent. This study has been approved by the Ethics Committee of First People’s Hospital of Kashgar.

Outcome measurement

Optovue Fourier domain optical coherence tomography scanner (RTVUE-100, axial resolution 5 μm, scanning rate 26,000 times/s) was applied. Before examination, compound topical camide was used to enlarge the pupils. During the examination, the subject took the sitting position, placed their lower jaw on the bracket, and adopted internal fixation. The center point of the optic disc was taken as the center of the circle, and the optic disc was scanned in a circle with a diameter of 3.45 mm. The same eye was scanned for 3 times. The computer image analysis system was used to measure the RNFL thickness. The measurement parameters included average RNFL thickness around optic disc, temporal, superior, nasal and inferior RNFL thickness. The average value of the three measurements was taken as the RNFL thickness of the subject eye. Then, macular fovea was taken as the center, and linear scanning was performed along the horizontal and vertical meridians, and in the temporal-superior, temporal-inferior, nasal-superior and nasal-inferior directions, respectively. The thickness of macular fovea and average retinal thickness (the area around the fovea with a diameter of 1000 μm) were recorded. Macular topographic map software was used for analysis and measurement. All subjects were measured by the same technician.

Statistical analysis

SPSS19.0 was used for data analysis. Measurement data were expressed by mean ± standard deviation (x ± sd), and t test was used for examination. The count data were tested by chi-square X² test, P < 0.05 was considered statistically significant.

Results

Comparison of general data

There was no statistically significant difference in gender, age, course of disease and number of included eyes among the four groups (P > 0.05). Except for the control group without course of disease data, there was no significant difference in other clinical data compared with each group (P > 0.05, Table 1).

Comparison of optic disc quadrants and RNFL thickness

Moderate NPDR group showed smaller thickness of quadrants and RNFL thickness than the control group (P < 0.05); NDP, NPDR (mild, moderate) groups showed smaller thickness of superior quadrant, inferior quadrant, and temporal quadrant than the control group (P < 0.05, Table 2; Figure 1).
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Table 1. Comparison of general data

<table>
<thead>
<tr>
<th>General data</th>
<th>NDR group</th>
<th>Mild NPDR</th>
<th>Moderate NPDR</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>48.46 ± 9.76</td>
<td>46.46 ± 8.76</td>
<td>47.42 ± 8.96</td>
<td>50.16 ± 7.26</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>29/27</td>
<td>26/25</td>
<td>23/25</td>
<td>22/24</td>
</tr>
<tr>
<td>Course of disease (year)</td>
<td>10-28</td>
<td>11-27</td>
<td>11-21</td>
<td>-</td>
</tr>
<tr>
<td>Eye (number)</td>
<td>110</td>
<td>99</td>
<td>89</td>
<td>90</td>
</tr>
</tbody>
</table>

Table 2. The quadrants and RNFL thickness (x ± sd)

<table>
<thead>
<tr>
<th>Group</th>
<th>Eyes</th>
<th>Thickness</th>
<th>superior quadrant</th>
<th>inferior quadrant</th>
<th>temporal quadrant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>90</td>
<td>107.83 ± 8.36</td>
<td>132.92 ± 14.22</td>
<td>135.32 ± 17.32</td>
<td>78.29 ± 9.28</td>
</tr>
<tr>
<td>NDR group</td>
<td>110</td>
<td>105.22 ± 9.82</td>
<td>125.27 ± 16.28*</td>
<td>133.38 ± 12.32</td>
<td>77.27 ± 10.24</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>99</td>
<td>103.09 ± 8.02</td>
<td>123.98 ± 13.72*</td>
<td>127.82 ± 14.21*</td>
<td>77.01 ± 8.24</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>89</td>
<td>101.28 ± 7.25*</td>
<td>118.28 ± 11.21*</td>
<td>120.38 ± 9.28*</td>
<td>72.1 ± 9.18*</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>7.03</td>
<td>7.16</td>
<td>7.29</td>
<td>7.06</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Note: *Compared with the control group, P < 0.05.

Figure 1. Thickness of quadrants and RNFL in the 4 groups. The RNFL, inferior quadrant and temporal quadrant thickness of the control group were different from those of the NDR group, mild NPDR and moderate NPDR groups (P < 0.05).

Discussion

Diabetic retinopathy is the ocular complication of diabetes and its risk will increase over the course of diabetes [7]. Therefore, early prevention and diagnosis of DR can effectively avoid the occurrence and reduce the severity [8, 9]. Studies have shown that the early symptom of DR is the change in RNFL thickness resulted from damage to the optic nerve and abnormal retinal blood vessels [10, 11]. If the RNFL thickness is monitored and appropriate therapy is given in time, rate of blindness in DR patients will be greatly improved. Retinal thickness is an important index to evaluate macular disease. Previous studies have confirmed that there are differences in the thickness of the retina in different regions of the macula, and the macular fovea is the thinnest in normal people and the thickest in the 3 mm inner ring area, suggesting that DR may start with diffuse tissue edema and vascular leakage, while mild NPDR begins to show retinal sponge-like thickening, indicating that with the aggravation of retinopathy, the thickness of the retina increases.
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Table 3. The thickness of RNFL in each quadrant of macular retina in 4 groups (x ± sd)

<table>
<thead>
<tr>
<th>Group</th>
<th>eyes</th>
<th>Superior nasal</th>
<th>Superior temporal</th>
<th>Lateral temporal</th>
<th>Inferior temporal</th>
<th>Inferior nasal</th>
<th>Lateral nasal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>90</td>
<td>47.76 ± 5.15</td>
<td>36.59 ± 3.11</td>
<td>28.26 ± 2.36</td>
<td>39.27 ± 4.13</td>
<td>44.53 ± 4.27</td>
<td>40.35 ± 2.93</td>
</tr>
<tr>
<td>NDR group</td>
<td>110</td>
<td>39.16 ± 5.49*</td>
<td>31.14 ± 3.45*</td>
<td>24.01 ± 2.18*</td>
<td>34.36 ± 4.19*</td>
<td>39.78 ± 5.61*</td>
<td>36.29 ± 4.64*</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>99</td>
<td>44.32 ± 6.85*</td>
<td>34.39 ± 3.34*</td>
<td>25.70 ± 3.09*</td>
<td>37.36 ± 4.32*</td>
<td>43.62 ± 5.43*</td>
<td>40.33 ± 6.36*</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>89</td>
<td>45.46 ± 5.77*</td>
<td>35.23 ± 4.11*</td>
<td>26.74 ± 2.88*</td>
<td>38.56 ± 4.27*</td>
<td>44.87 ± 4.25*</td>
<td>41.76 ± 5.28*</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.001</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Note: *Compared with the control group, P < 0.05.

The thickness of RNFL and all quadrants in the control group were significantly higher than those of the NDR, mild NPDR and moderate NPDR groups (P < 0.05), indicating that DR will increase the RNFL thickness, namely, the superior quadrant thickness of the optic disc is indicative of DR lesions [14, 15]. This study found that the thickness of superior quadrant is more sensitive and can be directly used as the main indicator for DR. In moderate NPDR group, the optic disc quadrants and RNFL thickness were significantly smaller than those in the control group (P < 0.05), indicating that the change of RNFL thickness in patients with moderate DR was significantly greater than that in the NPDR and mild NPDR groups. Thickness of each quadrant may be related to the severity of DR [16-18].

The MMT and foveal thickness in the mild and moderate NPDR groups were significantly thicker than those in the control group (P < 0.05), indicating that DR affects MMT and foveal thickness, which can be used as an indicator for DR condition. The MMT of NPDR and NDR groups was significantly greater than that of the control group (P < 0.05), indicating that DR has a significant effect on retinal thickness and can be used in diagnosis of DR [19-22].

Since RNFL thickness can reflect the severity of DR, this study formulated treatment measures on the basis of above results. Specifically, if the retinal neovascularization is located 1.2 to 2.5 mm outside the optic disc, without protruding into vitreous cavity, the patients with NPDR should receive regular inspections and strict blood sugar control, and follow the doctor’s instructions to take the medicine on time. When bleeding occurs in the retina, patients should do strenuous exercise, and should not intake high-sugar food, tobacco and alcohol to prevent hypoxia [23-25].

In summary, the thickness of RNFL can accurately reflect the condition of DR. DR can be detected by observing changes in RNFL and...
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Table 4. MMT and foveal thickness (x ± sd, μm)

<table>
<thead>
<tr>
<th>Group</th>
<th>Eyes</th>
<th>Foveal thickness</th>
<th>Mean RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control group</td>
<td>90</td>
<td>174.83 ± 26.36</td>
<td>212.92 ± 29.22</td>
</tr>
<tr>
<td>NDR group</td>
<td>110</td>
<td>186.22 ± 24.82</td>
<td>262.27 ± 31.28*</td>
</tr>
<tr>
<td>Mild NPDR</td>
<td>99</td>
<td>213.09 ± 32.02*</td>
<td>284.98 ± 30.72*</td>
</tr>
<tr>
<td>Moderate NPDR</td>
<td>89</td>
<td>221.28 ± 30.25*</td>
<td>296.28 ± 33.21*</td>
</tr>
<tr>
<td></td>
<td>t</td>
<td>7.11</td>
<td>7.34</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>&lt; 0.05</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

Note: *Compared with the control group, P < 0.05.

Figure 3. MMT and foveal thickness of the four groups. The MMT and foveal thickness did not differ between moderate and mild NPDR groups (P > 0.05). MMT in NDR group is different from mild and moderate NPDR groups (P < 0.05). The fovea thickness and MMT of the control group were significantly smaller than those of other three groups.

Figure 4. MMT and foveal thickness (x ± sd, μm).


treated as soon as possible. Targeted treatment of DM patients can effectively reduce the incidence of DR.

Disclosure of conflict of interest

None.

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References

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