Correlation of the Retinal Parapapillary Perfusion and the Retinal Vessel Oxygen Saturation in Glaucoma Patients

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PURPOSE. Reduced perfusion of the retinal parapapillary tissue is well documented in glaucoma patients. Whether or not this is a cause or result of the disease is however unknown. Studying the correlation of this perfusion and the retinal vascular oxygen saturation (O2S) could give clues to the retinal O2 consumption/demand and provide an answer to this question.

METHODS. Seventeen eyes of 17 healthy controls and 32 eyes of 32 patients with primary open angle glaucoma were prospectively recruited. Global and sectoral nerve fiber layer (NFL) thickness was measured with optical coherence tomography (OCT); parapapillary OCT-angiography was performed and quantified into vascular density (VD) and perfusion density (PD). Retinal vascular O2S was measured.

RESULTS. Global and sectoral NFL thickness, VD, PD (except for temporal sector of PD), and arteriovenous difference of O2S (AV-D) were lower in glaucomatous eyes compared with controls ($P < 0.05$ for all). A significant inverse correlation of venous O2S with global VD ($r = -0.37$, $P = 0.04$) and PD ($r = -0.37$, $P = 0.04$) and a direct correlation of the AV-D with global VD ($r = 0.50$, $P = 0.004$) and PD ($r = 0.49$, $P = 0.004$) were observed. In sector analysis, the strongest correlation of AV-D with VD and PD was seen in inferior (VD: $r = 0.52$, $P = 0.001$; PD: $r = 0.55$, $P = 0.002$) and superior (VD: $r = 0.45$, $P = 0.009$; PD: $r = 0.46$, $P = 0.008$) segments.

CONCLUSIONS. In glaucomatous eyes, there exists a direct correlation of the AV-D to the VD and PD with the strongest correlation being in superior and inferior segments where typically tissue loss occurs. This could possibly be explained by the loss of tissue being followed by the reduced density.

Keywords: glaucoma, retinal perfusion, retinal oxygen saturation, OCT-angiography

Glaucoma is a multifactorial disease for which multiple pathomechanisms have been discussed. Two main theories consider that the mechanical damage of retinal ganglion cells is caused by elevated intraocular pressure (IOP) and/or deficiency in vascular supply. Although each theory possesses positives and negatives, the details of each are still widely not understood. When considering the vascular theory, disturbed autoregulation of the retinal vascular system is well documented. In this line, multiple parameters can be measured in the retina and the optic nerve head of patients with both high and normal tension glaucoma. This supports vascular pathologies such as reduced perfusion of the different retinal layers, optic nerve head, and the choroid. However, decreased retinal perfusion, especially in the parapapillary area, could be a cause or a result of the glaucomatous changes. Among others, changes of the retinal vessel oxygen saturation (O2S) have been noted in glaucoma patients and are classically considered a result of tissue loss. The parapapillary perfusion of the retinal tissue and its direct correlation with the retinal O2S have not been studied so far. A correlation between these two parameters in glaucoma patients can give indirect clues to the retinal oxygen consumption and demand, leading to one of the two theories, namely, whether the reduced retinal perfusion is a cause or a result of the glaucomatous changes. The aim of this study was to investigate a possible correlation between the two parameters and to glean understanding of its role in the course of the disease.

MATERIALS AND METHODS

This was a prospective, cross-sectional, noninterventional, and nonrandomized study. The study was approved by the local ethical committee of the Jena University Hospital and was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from subjects included.

Patient Selection

Included in this study were 17 eyes of 17 healthy controls and 32 eyes of 32 consecutive glaucoma patients. The inclusion criterion for the control eyes was the absence of any ocular pathology. In the glaucoma group, eyes with the diagnosis of mild to moderate primary open angle glaucoma (POAG) were included. The exclusion criterion for both groups was history of any ocular surgery (excluding uncomplicated cataract surgery with intraocular lens implantation). Patients with controlled arterial hypertension were not excluded from the study; however, those with more severe cardiovascular diseases (e.g., myocardial infarction, cardiac insufficiency, or noncontrolled hypertension) were excluded as well as patients with...
diabetes mellitus. Patients with any kind of retinal or choroidal vascular disease, uveitis, macular degeneration, or retinal dystrophy were also excluded, as well as eyes with a spherical equivalent of more than $-6$ diopters.

All patients underwent a comprehensive ocular examination including examination at the slit lamp and fundus biomicroscopy with mydriasis. The IOP was measured by using Goldmann applanation tonometry. All patients underwent a visual field examination and measurement of the parapapillary nerve fiber layer (NFL) thickness by optical coherence tomography (OCT). On the same day, the retinal O2S was measured by using the retinal oximeter and papillary OCT-angiography was performed. If both eyes met the inclusion criteria, only the one with more advanced glaucoma was included.

**Diagnosis of POAG**

Diagnosis of POAG was based on the presence of typical morphologic optic disc glaucomatous changes (e.g., increased cup to disc ratio, notching, optic disc hemorrhage, defects of the NFL) with an open anterior chamber angle, in addition to an untreated IOP of more than 21 mm Hg, as well as the presence of typical glaucomatous visual field defects in accordance with a mean defect (MD) of the visual field of more than 2.0 dB. Mild POAG was defined as an MD of $\leq 6.0$ dB, and moderate as $\leq 12.0$ dB. Severe glaucoma patients were excluded because of the limitations of OCT and OCT-angiography in this group of eyes due to the floor effect.\textsuperscript{11,12}\n
Patients with severe disease who reached the floor level do not show additional loss of the NFL thickness or additional loss of perfusion density (PD) despite progressing disease. This could affect studying the correlations with the other parameters.

**Description of the Performed Tests**

**Visual Field.** The visual field test was performed by using the 30-2 G-Standard Program of the Octopus 900 device (Haag-Streit International, Bern, Switzerland). Only patients with an MD of more than 2.0 dB were included. The MD value was documented. The mean of the last two visual field tests performed in 3 to 6 months and only reliable tests were included in the analysis. A visual field with a false-positive or a false-negative rate of more than 33% was considered as not reliable and excluded from the study.

**OCT and OCT-Angiography.** The thickness of the NFL was measured in the peripapillary area by using the spectral-domain Cirrus HD-OCT 5000 (Carl-Zeiss Meditec, Oberkochen, Germany). This device has a central wavelength of 840 nm, a scan speed of 27,000 to 68,000 A-scans per second, an axial resolution of 5\( \mu \)m (in tissue), and a lateral resolution of 15\( \mu \)m. It provides the FastTrack retinal-tracking technology to reduce motion artifacts. The measurements of the superior, inferior, nasal, and temporal quadrants were documented, as well as the mean value of the four segments (referred to as the global value ofNFL thickness). Included were only images with a signal strength of $\geq 50\%$.

Measurement of the retinal parapapillary perfusion was performed by using the same abovementioned spectral-domain OCT device. The angiography mode was used, and the image was focused on the optic disc. A 6 $\times$ 6-mm image was taken. Included were only images with signal strength of $\geq 50\%$. A manual check of all images was also performed by the same experienced examiner (SMH), and images with shadows or artifacts were excluded.

The quantification of the image was performed by using the offered Angio-Plex tool, which was centered on the optic disc (Fig. 1). This tool enables the quantification of the OCT-angiography image (en face angiogram) for the superficial retina (internal limiting membrane and outer boundary of outer plexiform layer), based on two parameters: the PD defined as the global area of perfused vasculature per unit area in the region of measurement, and the vascular density (VD) defined as the global length of perfused vasculature per unit area in the region of measurement. Readings of the peripheral

![Figure 1. Optical coherence tomography-angiography for a control and a glaucoma eye; selected in the study was the peripheral ring. In this image the VD values are represented.](image)
ring (3- to 6-mm ring) were noted in all four quadrants (superior, inferior, nasal, and temporal) as represented in Figure 1. The mean of the four segments was also documented (superior, inferior, nasal, and temporal) as represented in Figure 1. The mean of the four segments was also documented as the global value.

**Oxygen Saturation.** The pupil was dilated with tropicamide 5.0 mg/mL (Mydrom eye drops; Bausch + Lomb, Berlin, Germany) and phenylephrine hydrochloride 5% (Neoephin-Pos 5%; URSAPHARM, Saarbrücken, Germany). Five photos of the retina were taken with the retinal vascular oximeter (IMEDOS Systems UG, Jena, Germany), focusing on the optic nerve head and the parapapillary vessels with intervals of approximately 30 seconds between them. The technical details of the device are described elsewhere. The arteries and veins (IMEDOS Systems UG, Jena, Germany) and phenylephrine hydrochloride 5% (Neoephin-Pos 5%; URSAPHARM, Saarbrücken, Germany). Five photos of the retina were taken with the retinal vascular oximeter (IMEDOS Systems UG, Jena, Germany), focusing on the optic nerve head and the parapapillary vessels with intervals of approximately 30 seconds between them. The technical details of the device are described elsewhere.13 The arteries and veins were marked by the same experienced examiner (SMH); and O2S in the arteries, veins, and the arteriovenous difference (AV-D) were automatically measured and averaged over a circum- papillary ring with an inner and outer diameter of 2 and 3 disk radii, respectively. The software VesselMap 3.60, a component of the oximeter, was also used. Optical densities of the vessels were measured as the logarithmic ratio of the fundus reflection at the vessel and besides the vessel. To exclude specular reflex from the vessel, pixels with a reflection above 20% over the mean value were excluded. The ratio of the optical densities at 610 nm to that at the isosbestic wavelength of 548 nm is proportional to the vessel hemoglobin oxygen saturation\(^{14}\) after compensation for vessel diameter and fundus pigmentation. A linear relationship between the optical density ratio and the relative oxygen saturation measure was established by calibration. Vessel tracking and calculation of the oxygen saturation were done automatically by the software of the device.13 The reproducibility of the measurement was shown to be 2.5% in arteries and 3.2% in veins (mean standard deviation of repeated measurements).15

**Statistical Analysis**

The statistical analysis was performed with IBM SPSS Statistics Version 22.0 (IBM Corp., Armonk, NY, USA) and Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA, USA). All parameters were tested for normal distribution (Shapiro-Wilk test). In normally distributed data, the independent sample t-test and Pearson’s correlation test were used. Otherwise, the Mann-Whitney U and the Spearman correlation tests were used. Correlations were studied only among the glaucoma patients. All results are presented as mean ± standard deviation. A P value of ≤0.05 was considered significant.

**RESULTS**

**Comparing the Two Groups**

There was no difference in the age or sex between both groups. The number of patients with hypertension, the systolic and diastolic blood pressure, and the number and class of antihypertensive medications were not different between both groups. The IOP was also comparable in both groups. The characteristics of patients and comparison of the two groups are summarized in Table 1. The data for the global NFL thickness, VD, and PD, as well as those for the four quadrants, are listed in Table 2. The NFL thickness, VD, and PD were reduced in all quadrants of glaucomatous eyes compared to control eyes (\(P = 0.001\) and \(P < 0.001\), respectively). The AV-D was significantly lower in the glaucoma group compared to control eyes (\(P = 0.001\) and \(P < 0.001\), respectively). The AV-D was significantly lower in the glaucoma group compared to control eyes (\(P = 0.001\) and \(P < 0.001\), respectively).

**Studying Correlations of Different Parameters in the Glaucoma Group**

**Age and Visual Field.** There was no correlation between age and any of the studied parameters (visual field, O2S parameters, the NFL thickness, VD, and PD in all quadrants; \(P > 0.05\) for all).

The MD correlated negatively with the global NFL thickness (\(r = -0.4, P = 0.028\)). A correlation was not found between the MD and the global VD and PD (\(P > 0.05\) for both).

No significant correlation was found between the MD and the arterial O2S (\(P > 0.05\)). However, a direct correlation was
The strength of correlation of the AV-D with the global NFL thickness was compared with the correlation of the AV-D with the global VD and PD. This showed no difference (VD: $z = 0.54; P = 0.59$; PD: $z = 0.59; P = 0.55$).15

**DISCUSSION**

A vascular hypothesis has long been discussed when considering the pathogenesis of glaucoma.1,2,10,17 One of the multiple components of this hypothesis is the reduced perfusion of the retinal tissue, which is well documented in the glaucomatous eyes.2,18,19 Still, it is unknown whether this is a result of tissue loss in glaucoma or a cause of it. In this study, we investigated the correlation of the parapapillary retinal PD and the retinal O2S because the combination of these often gives indirect clues to the retinal oxygen consumption and demand in both glaucomatous and healthy eyes and could also help answer the abovementioned question.

A comparison study between healthy and glaucomatous eyes was performed to test the different parameters of our glaucoma group. The global and sectorial NFL thicknesses were significantly lower in the glaucomatous eyes than in controls. This is in accordance with the published data20,21 and is a main finding in glaucomatous eyes. The VD and the PD were also reduced in glaucomatous eyes compared to controls. This was seen in the global values and in all sectors studied, except for the temporal segment of the VD. A reduced PD in the parapapillary area as seen in our study has been also reported previously in different studies.21–25

When considering the O2S, an increased arterial and venous O2S, along with reduced AV-D, were found in the glaucomatous eyes compared to healthy controls. Many authors7,9,10 have reported increased venous O2S and reduced AV-D in glaucoma patients, especially in advanced cases. We were able to observe a difference also for moderate glaucoma. However, we had a mean MD of 6.53 $\pm$ 3.3 dB in the glaucoma group and excluded patients with preperimetric glaucoma, meaning most patients had more than mild disease. The reduced AV-D in the glaucomatous eyes is likely a sign of affected oxygen metabolism and reduced oxygen consumption associated with tissue loss.22,25

**Table 2.** Summarizing NFL Thickness (in $\mu$m) and OCT-Angiography Data in Four Quadrants in Controls and Glaucoma Eyes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls</th>
<th>Glaucoma</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NFL thickness–G</td>
<td>96.00 $\pm$ 8.25</td>
<td>65.37 $\pm$ 10.69</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>VD–G</td>
<td>16.26 $\pm$ 2.05</td>
<td>12.87 $\pm$ 3.02</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>PD–G</td>
<td>0.41 $\pm$ 0.05</td>
<td>0.32 $\pm$ 0.08</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>NFL thickness–I</td>
<td>122.88 $\pm$ 73.87</td>
<td>73.87 $\pm$ 14.83</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>VD–I</td>
<td>17.56 $\pm$ 2.25</td>
<td>12.76 $\pm$ 5.25</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>PD–I</td>
<td>0.44 $\pm$ 0.06</td>
<td>0.32 $\pm$ 0.08</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>NFL thickness–S</td>
<td>116.76 $\pm$ 10.44</td>
<td>79.41 $\pm$ 19.67</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>VD–S</td>
<td>17.55 $\pm$ 1.64</td>
<td>13.07 $\pm$ 3.79</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>PD–S</td>
<td>0.45 $\pm$ 0.04</td>
<td>0.33 $\pm$ 0.10</td>
<td>0.002</td>
</tr>
<tr>
<td>NFL thickness–T</td>
<td>66.65 $\pm$ 8.09</td>
<td>48.59 $\pm$ 10.75</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>VD–T</td>
<td>15.25 $\pm$ 2.58</td>
<td>13.51 $\pm$ 4.51</td>
<td>0.35</td>
</tr>
<tr>
<td>PD–T</td>
<td>0.38 $\pm$ 0.07</td>
<td>0.31 $\pm$ 0.12</td>
<td>0.03</td>
</tr>
<tr>
<td>NFL thickness–N</td>
<td>74.59 $\pm$ 17.20</td>
<td>59.61 $\pm$ 9.90</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>VD–N</td>
<td>14.89 $\pm$ 4.02</td>
<td>12.15 $\pm$ 3.64</td>
<td>0.02</td>
</tr>
<tr>
<td>PD–N</td>
<td>0.38 $\pm$ 0.09</td>
<td>0.32 $\pm$ 0.09</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Significant $P$ values marked in bold. I, inferior; N, nasal; S, superior; T, temporal.

No correlation was found between the MD and the venous O2S ($r = 0.450$ and $P = 0.01$) and an inverse correlation with the AV-D ($r = -0.38$, $P = 0.04$).

**Nerve Fiber Layer Thickness.** A correlation was found between the global NFL thickness and the global VD ($r = 0.50$, $P = 0.003$) and PD ($r = 0.47$, $P = 0.006$). No correlation of the global NFL thickness was found with arterial O2S ($P > 0.05$). Inverse correlation of the global NFL thickness with the venous O2S ($r = -0.38$, $P = 0.03$) and a direct correlation with the AV-D ($r = 0.58$, $P = 0.001$) were found.

**Vascular/Perfusion Density and Oxygen Saturation.** No correlation was found between the global PD or the arterial O2 saturation. Additionally, no correlation was found between the segmental measurements of these parameters to the arterial O2S. A significant correlation was found between the global measurements of VD/PD on one hand and the venous O2S and the AV-D on the other (Fig. 2). Detailed correlation data for the NFL thickness, VD, and PD in all four quadrants with the arterial O2S, venous O2S, and the AV-D are listed in Table 3. The strongest correlation of AV-D with VD and PD was found in the inferior (VD: $r = 0.52$, $P = 0.002$; PD: $r = 0.55$, $P = 0.001$), global (VD: $r = 0.50$, $P = 0.004$; PD: $r = 0.49$, $P = 0.004$), and superior (VD: $r = 0.454$, $P = 0.009$; PD: $r = 0.46$, $P = 0.008$) quadrants.

**Table 3.** Correlation of the NFL Thickness, PD, and VD in the Four Quadrants With the O2S

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Arterial O2S</th>
<th>Venous O2S</th>
<th>AV-Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$P$</td>
<td>$r$</td>
</tr>
<tr>
<td>NFL thickness–G</td>
<td>0.27</td>
<td>0.13</td>
<td>$-0.38$</td>
</tr>
<tr>
<td>VD–G</td>
<td>0.15</td>
<td>0.41</td>
<td>$-0.37$</td>
</tr>
<tr>
<td>PD–G</td>
<td>0.14</td>
<td>0.45</td>
<td>$-0.37$</td>
</tr>
<tr>
<td>NFL thickness–I</td>
<td>$-0.10$</td>
<td>0.56</td>
<td>$-0.46$</td>
</tr>
<tr>
<td>VD–I</td>
<td>$-0.29$</td>
<td>0.87</td>
<td>$-0.45$</td>
</tr>
<tr>
<td>PD–I</td>
<td>$-0.03$</td>
<td>0.85</td>
<td>$-0.47$</td>
</tr>
<tr>
<td>NFL thickness–S</td>
<td>$-0.21$</td>
<td>0.24</td>
<td>$-0.40$</td>
</tr>
<tr>
<td>VD–S</td>
<td>0.10</td>
<td>0.57</td>
<td>$-0.35$</td>
</tr>
<tr>
<td>PD–S</td>
<td>$-0.09$</td>
<td>0.62</td>
<td>$-0.36$</td>
</tr>
<tr>
<td>NFL thickness–T</td>
<td>$-0.19$</td>
<td>0.50</td>
<td>$-0.27$</td>
</tr>
<tr>
<td>VD–T</td>
<td>0.13</td>
<td>0.46</td>
<td>$-0.26$</td>
</tr>
<tr>
<td>PD–T</td>
<td>0.23</td>
<td>0.21</td>
<td>$-0.14$</td>
</tr>
<tr>
<td>NFL thickness–N</td>
<td>0.43</td>
<td>0.01</td>
<td>$-0.01$</td>
</tr>
<tr>
<td>VD–N</td>
<td>$-0.20$</td>
<td>0.28</td>
<td>$-0.14$</td>
</tr>
<tr>
<td>PD–N</td>
<td>$-0.05$</td>
<td>0.79</td>
<td>$-0.27$</td>
</tr>
</tbody>
</table>

Significant $P$ values marked in bold.
Considering the correlations in the glaucoma group, NFL thickness correlated with the MD value of the visual field, a known and previously reported finding, and points to an increasing loss of the NFL with disease progression. Global NFL thickness was also correlated with the global VD and PD as shown in many studies. Although this correlation showed a reduced PD with increasing tissue loss and progressive disease, the reduced perfusion as a cause of the tissue loss and reduction of NFL thickness still cannot be ruled out. The NFL correlated inversely with the venous O2S and directly with the AV-D, which has been previously reported. In an earlier study, we have found no correlation of the retinal O2S with the NFL thickness in milder glaucomatous eyes supports the theory that this correlation is only seen post disease progression and after significant tissue loss occurs.

In this study, we did not find a correlation between the VD or PD and the MD of visual field. Although comparison of different OCT-angiography studies is not always possible because of the different methods applied for the quantification of the images and the different parameters used in the interpretation, still, most published data have found a correlation of the PD parameters and the MD value. One reason for this discrepancy could be the use of the 3- to 6-mm ring and the avoidance of the peripapillary area in our study. This leads to an increase in the surface area examined and quantified, and may be a cause of loss of peripapillary changes, an area that has been previously studied. When considering oxygen saturation and the visual field, we noticed no correlation with the arterial O2S. A significant positive correlation of the venous O2S and an inverse correlation with the AV-D were also found. This is in accordance with published data, possibly explained by the reduced oxygen consumption with progressing disease and increasing loss of tissue.

When studying the correlation of the parapapillary retinal PD and the retinal vascular O2S, the main outcome of this study, global perfusion parameters (PD and VD) in the glaucomatous eyes were inversely correlated with the venous O2S and directly correlated with the AV-D. Reduced perfusion and increased venous O2S are separate, well-documented findings and correlate with disease progression. The strongest correlation of the VD and PD with the AV-D was found in the superior and inferior quadrants in addition to the global value. The superior and inferior segments are typical areas where the glaucomatous damage of the NFL appears.

In healthy tissue, a balanced state is maintained where the vascular perfusion remains able to provide the oxygen needs of the tissue, leading to venous O2S lower than that of the arteries and relatively constant in the normal range of the known venous O2S levels. A blood flow autoregulation mechanism, which allows the retinal perfusion system to compensate in cases of increased or decreased oxygen needs, is well documented. In this study, we found in retinal tissue of glaucomatous eyes an increased venous O2S, reduced PD, and reduced NFL thickness as compared with healthy individuals. If the reduced PD was a factor responsible for the loss of tissue by means of reduced oxygen supply, then the reduced venous O2S would have been lower than for healthy controls, as the tissue being underperfused would extract more oxygen from the vascular bed, resulting in reduced venous O2S levels. Such changes are observed in eyes with central and branch retinal vein occlusion, where the decreased retinal blood flow results in tissue underperfusion and increased oxygen extraction, producing reduced venous O2S levels. This was not observed in our study. At the same time, an inverse correlation was found between the venous O2S and the PD, therefore showing that decreased PD correlates with increasing venous O2S levels, possibly explained by the loss of tissue being followed by reduced perfusion; and decreased perfusion, being the primary pathology as explained above, would likely be positively correlated with the venous O2S. In eyes with diabetic retinopathy, changes in retinal O2S with in-
increased venous O2S and reduced AV-D are also reported, which is similar to our findings in glaucomatous eyes. However, in diabetic eyes this could be explained by shunting of blood through preferential channels, bypassing nonperfused capillaries in the capillary network, and/or reduced oxygen permeability due to thickening of capillary vessel walls, all well-known pathologies in diabetes mellitus but absent in glaucomatous eyes.

The stronger correlation in the typically affected segments where the tissue atrophy is more prominent could be another clue into why these changes are possibly a result rather than a cause of the atrophy. However, because our study was cross-sectional in design, we measured all variables at the same time point, making impossible a more definite conclusion regarding the exact time sequence in which the changes of the parameters happened. Our study is, to our knowledge, the first to report the direct correlation of these perfusion parameters with the retinal O2S and to document this correlation in all four quadrants separately. Still, these results should be verified in performing longitudinal long-term studies that document the progression of the different parameters to give more conclusive evidence of the time sequences.

Regarding the vascular theory of glaucoma pathophysiology, our study was not designed to detect the effect of the disturbed retinal vascular autoregulation, which is well known and extensively studied in glaucoma patients. This leads to transient hypoxia and reperfusion injury causing damage of the ganglion cells under certain circumstances (e.g., retinal activation with flashlight, transient decreased perfusion pressure) without affecting the retinal blood flow at rest in the early phases of glaucoma. A vascular theory of glaucoma could not be excluded as an important mechanism, as this theory is based on the reduced ability of the retinal circulation to compensate for changes of perfusion pressure, which we did not measure.

Some limitations of our study have to be mentioned. First, PD value, given by OCT-angiography, measures the fraction of perfused vessels per area of tissue. This does not represent blood flow, as flow velocity is not measured quantitatively, so this measurement should not be interpreted as the blood flow. Furthermore, because of the cross-sectional design, glaucoma patients were not asked to stop their glaucoma therapy, which could have influenced the O2S and/or the perfusion parameters. The effect of glaucoma therapy on the retinal O2S could not be measured. This leads to controversy as some studies have shown an increased retinal O2S after management with dorzolamide, whereas others report no change. The effect of medications on the perfusion measured with OCT-angiography has been studied in a small sample population and after a reduction of the IOP to more than 50% (starting from high levels of 35–42 mm Hg). Although the study population is not comparable with ours, we still cannot exclude an effect of medical therapy on the perfusion parameters. We excluded patients who had undergone glaucoma surgery, as this affects the retinal perfusion and could affect the retinal O2S, although this topic is also controversial. Only mild to moderate glaucoma patients were included in order to avoid the floor effect of OCT. Therefore, our results may not be applicable in more progressive disease, in glaucoma suspects, or in preperimetric glaucoma patients.

Owing to the cross-sectional design, we were not able to separate patients with progressing disease from those with stable disease. These two groups could have had different correlations of the O2S and the PD/NFL thickness from those seen in our study. We studied the parapapillary vascular bed by using the 3- to 6-mm ring of the OCT-angiography system. Using the 3- to 6-mm ring has some advantages such as excluding the peripapillary defects (e.g., the choroidal atrophies or optic disc drusen), which could affect the interpretation of the images. The use of this peripheral ring enables the measurement of a wider area of the parapapillary vascular bed. At the same time, the 3-mm distance from the center of the optic disc can cause oversight of glaucomatous changes directly along the optic disc. The quantification was performed by using the Angio-Plex software, which is provided with the Cirrus HD-OCT 5000 system. Although this quantification system is built to study macular images, there is no contraindication for its use to quantify other OCT-angiography images if the same study parameters (VD and PD) are suitable. This has already been done by other authors. 44

CONCLUSIONS

In this study, a correlation was found between the perfusion parameters of retinal superficial parapapillary tissue measured with OCT-angiography and the retinal venous and AV-D O2S. The correlation was stronger in the segments where the glaucomatous atrophy is more pronounced. This correlation might possibly point to the idea that tissue atrophy could be responsible for reduced retinal perfusion in mild to moderate glaucoma patients. As this was a cross-sectional study, long-term longitudinal studies still are needed to make more conclusive statements.

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References


