Abstract

**Purpose:** To analyze the retinal nerve fiber layer thickness (RNFL) in CKD patients by means of optical coherence tomography, ascertaining mean overall RNFL and mean RNFL in the nasal, temporal, superior, and inferior quadrants and comparing these measurements to those obtained from a control group.

**Methods:** This was a prospective, analytical, cross-sectional case-control study. The study sample comprised 22 eyes from 11 patients and 33 eyes from 17 patients in the case and control groups respectively. RNFLT was measured with a model 3000 OCT unit (Stratus OCT-3™, Carl Zeiss Meditec Inc., Dublin, CA). The fast RNFL protocol was used, which consists of three consecutive 3.4 mm-diameter circular scans centered on the optic nerve. Measured parameters included overall mean RNFL and mean RNFL at the temporal (316-45°), superior (46-135°), nasal (136-225°), and inferior (226-315°) quadrants.

The Mann-Whitney U was employed to assess possible between-group differences in mean overall RNFL and RNFL at the superior, temporal, nasal, and inferior quadrants. The null hypothesis was rejected when p-values were smaller than the set significance level of <0.05.

**Results:** Mean RNFL overall and at the superior, nasal, and inferior quadrants was greater in the control group, and that no significant between-group differences were detected in RNFL at the temporal quadrant.
Introduction
Chronic kidney disease (CKD) is defined as a reduction in glomerular filtration rate (GFR) and implies irreversible, progressive loss of renal function, rendering patients dependent on renal replacement therapy (dialysis or kidney transplant) to prevent development of potentially fatal uremia [1].

Several ophthalmological changes have been described in patients with CKD, such as decreased tear output, calcium deposits in the cornea, cataract, glaucoma, retinal changes, and optic neuropathy [2-6].

Dialysis toxicity, ischemia (due to anemia, hypotension, and generalized atherosclerosis) and uremia-associated systemic disorders are believed to play a role in the pathogenesis of optic neuropathy [5, 7-9].

Optical coherence tomography (OCT) is a high-resolution, noninvasive, non-contact diagnostic technique that allows acquisition of two-dimensional image representations of pathological conditions in the epiretinal, intraretinal layers, choroid, and optic nerve (ON). OCT permits assessment of several relevant aspects, including changes in reflectivity secondary to inflammatory infiltrates, atrophy, and fibrosis of the neurosensory retina, of the retinal pigment epithelium-choriocapillaris complex, and of the vitreoretinal interface, and also provides a tool for analysis of the retinal nerve fiber layer (RNFL) [10-13]. The hypothesis that chronic kidney disease and its treatment with dialysis could induce changes in the retinal microvasculature, leading to ischemia and RNFL damage, provides the rationale for this study.

The objective of this study was to analyze the retinal nerve fiber layer thickness (RNFLT) in CKD patients by means of optical coherence tomography, ascertaining mean overall RNFLT and mean RNFLT in the nasal, temporal, superior, and inferior quadrants and comparing these measurements to those obtained from a control group.

Methods
Patients were recruited from the hemodialysis clinic of the Hospital das Clínicas de Pernambuco and examined at the hospital Ophthalmology department and at Fundação Altino Ventura.

This was a prospective, analytical, cross-sectional case-control study.

The study sample comprised 11 chronic kidney disease patients with a history of at least 1 year of hemodialysis (6 male [21%] and 5 female [18%]; mean age, 48±16.9 years) and 17 healthy controls (7 male [25%] and 10 female [36%]; mean age, 51.4±19.3 years).

Patients with hepatitis, alcoholism, malnutrition, diabetes, or opacity of the transparent media of...
the eye preventing OCT were excluded from the sample, as were those who declined to provide informed consent for participation in the study.

All participants underwent a comprehensive eye examination, which consisted of uncorrected high-contrast visual acuity testing with an ETDRSTM chart (Lighthouse Inc., New York, NY); thorough biomicroscopy; measurement of intraocular pressure with a Goldmann tonometer (Haag-Streit, Bern, Switzerland); and funduscopy (including assessment of the optic disc and peripapillary nerve fiber layer) with a Volk 90D lens (Volk Optical Inc., Cleveland, OH). After this examination, participants were referred to Fundação Altino Ventura for OCT.

RNFLT was measured with a model 3000 OCT unit (Stratus OCT-3™, Carl Zeiss Meditec Inc., Dublin, CA). Mydriasis was induced with 0.5% tropicamide drops in each eye. The fast RNFL protocol was used, which consists of three consecutive 3.4-mm-diameter circular scans centered on the optic nerve. Measured parameters included overall mean RNFLT and mean RNFLT at the temporal (316-45°), superior (46-135°), nasal (136-225°), and inferior (226-315°) quadrants.

Quantitative variables were expressed as means and standard deviations. Qualitative variables were expressed as absolute and relative frequencies.

The Mann-Whitney U was employed to assess possible between-group differences in mean overall RNFLT and RNFLT at the temporal (316-45°), superior (46-135°), nasal (136-225°), and inferior (226-315°) quadrants. The null hypothesis was rejected when p-values were smaller than the set significance level of <0.05.

The study project was approved by the Hospital das Clínicas da UFPE Research Ethics Committee. All participants provided informed consent prior to inclusion in the sample.

Results

Twenty-two and 33 eyes were assessed in the case and control groups respectively. RNFLT measures for the retina as a whole and at the superior, temporal, nasal, and inferior quadrants in healthy controls are shown in Table 1. Table 2 shows these measurements as obtained in the case group (CKD patients).

Table 3 shows that mean RNFLT overall and at the superior, nasal, and inferior quadrants was greater in the control group, and that no significant between-group differences were detected in RNFLT at the temporal quadrant. Figure 1 provides a clearer visualization of these measurements.

Table 1. Overall retinal nerve fiber layer thickness (RNFLT) and RNFLT at the superior, temporal, nasal, and inferior quadrants in healthy controls (in micrometers).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Min</th>
<th>Mean</th>
<th>Max</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL</td>
<td>89.18</td>
<td>111.48</td>
<td>130.56</td>
<td>10.46</td>
</tr>
<tr>
<td>Superior</td>
<td>104</td>
<td>145.42</td>
<td>187</td>
<td>18.45</td>
</tr>
<tr>
<td>Temporal</td>
<td>42</td>
<td>71.33</td>
<td>92</td>
<td>11.05</td>
</tr>
<tr>
<td>Nasal</td>
<td>66</td>
<td>93.27</td>
<td>125</td>
<td>14.95</td>
</tr>
<tr>
<td>Inferior</td>
<td>83</td>
<td>136</td>
<td>164</td>
<td>16.68</td>
</tr>
</tbody>
</table>

Table 2. Overall retinal nerve fiber layer thickness (RNFLT) and RNFLT at the superior, temporal, nasal, and inferior quadrants in participants in the case group (in micrometers).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Min</th>
<th>Mean</th>
<th>Max</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL</td>
<td>84.94</td>
<td>100.21</td>
<td>124</td>
<td>12.08</td>
</tr>
<tr>
<td>Superior</td>
<td>91</td>
<td>126.68</td>
<td>161</td>
<td>17.12</td>
</tr>
<tr>
<td>Temporal</td>
<td>56</td>
<td>71.09</td>
<td>155</td>
<td>20.24</td>
</tr>
<tr>
<td>Nasal</td>
<td>57</td>
<td>77.36</td>
<td>122</td>
<td>15.18</td>
</tr>
<tr>
<td>Inferior</td>
<td>97</td>
<td>126.41</td>
<td>160</td>
<td>17.47</td>
</tr>
</tbody>
</table>

Table 3. Comparison of means in the case and control groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNFL</td>
<td>0.000***</td>
</tr>
<tr>
<td>Superior</td>
<td>0.001***</td>
</tr>
<tr>
<td>Temporal</td>
<td>0.095</td>
</tr>
<tr>
<td>Nasal</td>
<td>0.000***</td>
</tr>
<tr>
<td>Inferior</td>
<td>0.033***</td>
</tr>
</tbody>
</table>

*: statistically significant.
Discussion
The retinal nerve fiber layer (RNFL) can be effectively evaluated using optical coherence tomography, and changes in RNFL have been found in some diseases, such as glaucoma and diabetes [6].

A decrease in RNFL thickness may be a useful sign of the early stages of optic neuropathy before visual disturbances are detected [12].

Patients were excluded from the study if they had hepatitis, alcoholism, malnutrition or diabetes because these diseases may cause ischemia not associated with uremia [7].

In this study, the difference in mean total RNFL thickness and thickness of the superior, nasal and inferior quadrants, but not of the temporal quadrant, was statistically significant for the control group when compared with the case group. The temporal quadrant is physiologically thinner [11]. The mean thickness of the temporal quadrant in the case group was lower than in the control group, but this difference was probably not significant based only on sample size.

Chronic renal failure (CRF) is responsible for vascular ischemia that affects the retinal microvasculature and may result in a blood supply deficit for the nerve fiber layer and a consequent decrease in its thickness. Some authors suggest that dialysis alone may cause transient fluid and electrolyte imbalance that eventually leads to retinal ischemia. Using fluoroangiography, Niutta et al [8] found focal choroidal perfusion defects mainly in the posterior pole in patients treated with hemodialysis. However, other authors reported that RNFL thickness decreases with age and in cases of myopia [13, 14], and that hemodialysis might have little influence over retinal circulation, even when there are disorders of the blood-retinal barrier or in the autoregulation of blood flow [10].

Our findings showed that CRF may be a source of false-positive results and induce overestimation of cases of glaucomatous optic neuropathy. The possibility that a decrease in RNFL thickness may be due to subclinical uremic optic neuropathy should be taken into consideration in these cases.

Conclusion
Mean retinal nerve fiber thickness was significantly lower in the group of patients with CRF than in the control group. Ischemia resulting from uremia may explain the overestimation of cases of glaucomatous optic neuropathy.

Financial disclosure
The authors have no financial relationships relevant to this article to disclose.

Conflict of Interest
The authors have no conflicts of interest to disclose.
References


