Retinitis pigmentosa (RP) is the most widespread congenital degenerative disease of retina with the impairment of twilight vision and abnormal electroretinograms in early stages. The progression of RP is characterized by the damage caused to the macula and that can lead to visual loss [1, 2].

Pathogenesis of RP is complex and still remains unclear. With laser Doppler flowmetry [3-6], calibrometry of the retinal vessels [7], measurement of amplitude of pulsatile ocular blood flow [8], laser Doppler velocimetry [9] and Color Doppler Imaging (CDI) [6, 10, 11] many authors showed the impairment of ocular blood flow (OBF) in patients with RP.

K. Schmidt et al. [8] assessed the ocular pulse amplitude, which was decreased in late stages of RP. Based on the analysis of current studies of ocular blood flow examinations K. Konieczka et al. [12] supported the hypothesis of primary vascular dysregulation syndrome with the impairment of ocular blood flow in early stages of RP.

The correlation between the changes of visual functions and the impairment of retinal blood flow was presented by Y. Zhang et al. [13]. Using the new method of the magnetic resonance angiography (MRA) they determined significant correlation between the reduced choroidal and retinal blood flow and the decrease of the amplitude of a-wave of full-field electrotetinography (ERG) in 6 patients with RP. However there was no assessment of ocular blood flow in early stages of RP.

Other CDI studies have shown reduced peak systolic velocity (PSV) of the central retinal artery (CRA) and the short posterior ciliary artery (sPCA) in patients with RP [6, 10]. Considering strong correlation between the neuronal system and the vascular system of retina, parallel investigations of ocular blood flow and electrophysiological studies of retinal cells function appear to be interesting in patients with RP.

The aim of present study has been to investigate the correlation between changes in ocular hemodynamics revealed by CDI and pulsed-wave (PW) Doppler, on the one hand, and the bioelectrical activity of the retina, on the other, in patients with the early stage, the intermediate stage and the late stage of RP.

Material and methods

Twenty patients (40 eyes) aged from 16 to 40 years (28.4±8.2 years on average) with RP were enrolled. The control group consisted of 20 healthy volunteers of the same age range. Depending on the stage of disease and the degree of visual field changes, all patients were divided into three groups. The first group included 6 patients (12 eyes) with early stage of RP and mean visual acuity of 0.98±0.05. The second group consisted of 7 patients (14 eyes) with the intermediate stage of RP and mean visual acuity of 0.49±0.34. The third group included 7 patients (14 eyes) with the late stage of RP and mean visual acuity of 0.36±0.17.

Except for a standardized ophthalmological investigation, including measurement of visual acuity and visual field, slit lamp examination, dilated fundoscopy, all pa-
tients underwent full-field electroretinography (ERG), flicker ERG, and macular ERG to red stimulus using “Electroretinograph” (MBN-6, Russia). The full-field ERG and flicker ERG were registered according to ISCEV Standards for clinical ERG [14]. The active electrode suction cup and the standard silver chloride reference cup electrode were used.

The methods of investigation of the ocular blood flow included CDI and PW Doppler with Voluson 730 Pro Ultrasound system (Healthcare,GE). We measured the blood-flow spectrum of the ophthalmic artery (OA), short posterior ciliary arteries (sPCA), the central retinal artery (CRA) and the central retinal vein (CRV) and their main quantitative indices: the peak systolic velocity (PSV), end-diastolic velocity (EDV) and resistance index (RI).

Statistical analysis was performed using SPSS statistical software and statistical measure of the strength of a linear relationship between paired data (Pearson’s correlation coefficient). The \( p \) values of <0.05 were considered significant.

**Results and discussion**

Clinical findings included solitary bone spicule-shaped pigment deposits in the middle of the periphery of retina, monotone optic nerve head and concentric constriction of visual field to 40 degrees in patients with early stage of RP. Severe bone-spicule retinal pigmentation in the middle of the periphery of ocular fundus, waxy-pale optic nerve head and concentric constriction of visual field from 40 to 20 degrees were detected in patients with the intermediate stage of RP. The severe bone-spicule retinal pigmentation in the middle of the periphery, atrophy of optic nerve and chorioretinal atrophy and concentric constriction of visual field to <20 degrees were registered in patients with the late stage of RP.

The full-field ERG (combined rod-cone response) has shown a statistically significant reduced amplitude of a-and b-waves directly related to the stage of RP that indicated progressive decrease of function of photoreceptors and neurons in the middle layers of the retina (Fig.1). The absence of ERG was registered in 5 (10 eyes) of 8 patients with the late stage of RP (Tabl.1). Increased implicit time of a- and b-waves were associated with the severity of disease. The reduced amplitude of 30 Hz flicker ERG indicated an early damage of the cones photoreceptors in this disease (Fig.2). Impaired cones’ functions were increased during the pathological process according to the stage of the disease and cones’ functions were significantly decreased in patients of the third group. The flicker ERG of 30 Hz was nonrecordable in 5 of 7 patients with the late of RP (Tabl.2). The investigation of the macular ERG to red stimulus demonstrated a significant decrease (developing dependant on the stage of disease) of a- and b-waves amplitudes in patients with early stage of RP (Fig.3). The macular ERG amplitude was significantly reduced in patients with the late stage of RP. These

![Fig. 1. The full-field ERG](image)

- a — right eye, b — left eye with the early stage of RP; c — right eye, d — left eye with the intermediate stage of RP; e — right eye, f — left eye with the late stage of RP.
findings indicated severe impairment of macula function (Table 2). The a-and b-waves implicit times were longer in correlation with the degree of the disease severity.

Analysis of ultrasound investigations data of ocular blood flow showed no significant changes of the hemodynamic parameters in the OA of patients with RP compared to control group. There were no significant changes of blood flow in the CRA of patients with the early RP (Vsyst = 12.5 cm/s, Vdiast = 4.24 cm/s, RI = 0.66) (Fig. 4a). In cases of the intermediate stage and the late stage of RP, the peak systolic velocity of CRA blood flow was significantly decreased (Vsyst = 6.5 cm/s, Vdiast = 2.6 cm/s, RI = 0.6) (Fig. 4b). However, mean Vdiast and RI in CRA in patients with RP did not differ significantly from those in healthy subjects (Table 3). We registered similar changes of blood flow in sPCA. There were no significant changes of blood flow in the sPCA in early stage of RP (Vsyst = 12.17 cm/s, Vdiast = 4.35 cm/s, RI = 0.64). There were significant decreases of Vsyst and normal resistance indices in the sPCA in patients with intermediate stage of RP (Vsyst = 8.93 cm/s, Vdiast = 2.32 cm/s, RI = 0.74) and in patients with the late stage of RP (Vsyst = 6.03 cm/s, Vdiast = 2.66 cm/s, RI = 0.56) (Table 3).

Significantly decreased Vsyst in the CRA, CRV and sPCA indicated the substantial deficiency of blood flow in the retinal and choroidal vessels in patient with the intermediate stage and the late stage of RP.

The correlation of hemodynamic indices and parameters of retinal function revealed the statistically significant direct association between the peak systolic end diastolic blood flow velocities (Vsyst and Vdiast) in sPCA and the a-wave amplitude of full-field ERG (r = 0.81 and r = 0.82, respectively), but they correlated negatively with the implicit time of full-field ERG a-wave (r = -0.47 and Table 1. Mean parameters of the full-field ERG in patients with RP (mean±SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>Parameters of the full-field ERG</th>
<th>Control group</th>
<th>I group (n=12)</th>
<th>II group (n=14)</th>
<th>III group (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amplitude</td>
<td>Implicit time</td>
<td>Amplitude</td>
<td>Implicit time</td>
<td>Amplitude</td>
</tr>
<tr>
<td>a-wave</td>
<td>94.6±17.0</td>
<td>30.4±2.5</td>
<td>406.0±81.0</td>
<td>61.5±1.4</td>
<td>5.0±1.9</td>
</tr>
<tr>
<td>b-wave</td>
<td>70.5±119.9</td>
<td>63.4±4.8</td>
<td>3.7±1.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b/a</td>
<td>-</td>
<td>-</td>
<td>4.2±2.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Mean parameters of the macular ERG and the 30 Hz flicker ERG in patients with RP (mean±SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>macular ERG</th>
<th>30 Hz flicker</th>
<th>Control group</th>
<th>I group (n=12)</th>
<th>II group (n=14)</th>
<th>III group (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Amplitude</td>
<td>Implicit time</td>
<td>Amplitude</td>
<td>Implicit time</td>
<td>Amplitude</td>
<td>Implicit time</td>
</tr>
<tr>
<td>a-wave</td>
<td>3.6±1.1</td>
<td>24.8±2.1</td>
<td>16.7±4.0</td>
<td>54.8±4.1</td>
<td>29.3±9.1</td>
<td></td>
</tr>
<tr>
<td>b-wave</td>
<td>2.3±0.7*</td>
<td>27.7±1.8*</td>
<td>5.8±2.0*</td>
<td>54.9±2.9</td>
<td>27.8±5.6</td>
<td></td>
</tr>
<tr>
<td>b/a</td>
<td>-</td>
<td>-</td>
<td>17.1±15.4*</td>
<td></td>
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</table>

Table 3. Mean hemodynamic parameters in the orbital arteries in patients with RP

<table>
<thead>
<tr>
<th>Group</th>
<th>OA</th>
<th>CRA</th>
<th>sPCA</th>
<th>CRV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V syst, cm/s</td>
<td>Vdiast, cm/s</td>
<td>RI</td>
<td>V syst, cm/s</td>
</tr>
<tr>
<td>Control group</td>
<td>32.7±3.7</td>
<td>9.2±2.1</td>
<td>0.72±0.1</td>
<td>10.6±0.8</td>
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<tr>
<td>I group (n=12)</td>
<td>40.2±4.0</td>
<td>8.0±4.4</td>
<td>0.8±0.09</td>
<td>10.0±3.1</td>
</tr>
<tr>
<td>II group (n=14)</td>
<td>42.4±3.9</td>
<td>10.3±2.9</td>
<td>0.7±0.07</td>
<td>6.4±1.7*</td>
</tr>
<tr>
<td>III group (n=14)</td>
<td>32.3±7.7</td>
<td>8.6±4.8</td>
<td>0.7±0.11</td>
<td>5.6±0.9*</td>
</tr>
</tbody>
</table>

Abbreviations: CRA — central retinal artery; OA — ophthalmic artery; sPCA — short posterior ciliary arteries (medial and lateral); Vsyst — peak systolic velocity; Vdiast — end-diastolic velocity; RI — resistance index

Note: n – number of eyes; * – p<0.05 – significance relative to the parameters recorded in the control group.
The Vsyst and Vdiast in CRA were directly related to b-wave amplitude of full-field ERG ($r=0.55$ and $r=0.44$, respectively), but correlated negatively with the latency of full-field ERG b-wave.

Our results revealed the reduced Vsyst in CRA and in sPCA in patients with RP similar to the results obtained by M.Cellini et al. [6] and N.Akyol et al.[10].

Unlike the study by Y.Zhang et al. [13] that reported correlation between the state of chorioretinal complex and electrogenesis of photoreceptors, our study suggests data about statistically significant correlation between the reduced parameters of choroidal blood flow velocities (sPCA) and the function of photoreceptors (the amplitude and the latency of full-field ERG a-wave) and also between the reduced parameters of retinal blood flow velocities (CRA) and abnormal bipolar cell function (the amplitude and latency of full-field ERG b-wave). These correlations show parallel changes of ocular blood flow and electrogenesis of external and middle layers of retina, which expands our understanding of the pathogenesis of RP.

**Conclusion**

The revealed decrease in CRA and SPCA blood flow indices proves retinal and choroidal circulation deficit in patients with advanced RP. As shown, moderate blood flow changes are already present in early RP and progress as retinal photoreceptors and bipolar cells become degenerated, which may be useful for RP diagnosis and monitoring.
Fig. 4. Doppler spectrum of blood flow in the CRA and CRV.

a — in patient with the early stage of RP (Vsyst = 12.5 cm/s, Vdyast = 4.24 cm/s, RI = 0.66); b — in patient with the intermediate stage of RP (Vsyst = 6.5 cm/s, Vdyast = 2.6 cm/s, RI = 0.6); c — in patient with the late stage of RP (Vsyst = 4.37 cm/s, Vdyast = 2.02 cm/s, RI = 0.54).

Fig. 5. Doppler spectrum of blood flow in the sPCA.

a — in patient with the early stage of RP (Vsyst = 12.17 cm/s, Vdyast = 4.35 cm/s, RI = 0.64); b — in patient with the intermediate stage of RP (Vsyst = 8.93 cm/s, Vdyast = 2.32 cm/s, RI = 0.74); c — in patient with the late stage of RP (Vsyst = 6.03 cm/s, Vdyast = 2.66 cm/s, RI = 0.56).

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Statistical analysis of data — I.Z., O.D.

Drafting of manuscript — T.K., I.Z., O.D., I.E., E.R.
Critical revision — T.K., I.Z., O.D., I.E., E.R.

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