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Study of age-related retinal hemodynamic changes by laser speckle flowgraphy

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ABSTRACT

BACKGROUND: Diagnostics of hemodynamic changes is important both for clarifying the features of the course of pathological process of many ophthalmic diseases and for optimizing treatment tactics. Laser speckle flowgraphy (LSFG) is a new non-invasive method for quantitative assessment of retinal blood flow.

AIM: To study age-related changes of pulse waves both in large blood vessels and microvasculature in the optic nerve head and macula by laser speckle flowgraphy.

MATERIALS AND METHODS: Age-related changes in blood flow were studied in 60 healthy volunteers using LSFG-RetFlow. We analyzed MBR — main parameter of pulse wave assessed by the laser speckle flowgraphy and also another 8 pulse wave parameters for large vessels and microvasculature in the areas of optic nerve head and macula.

RESULTS: The study revealed statistically significant ($p \leqslant 0.05$) age-related changes in pulse waves for most parameters under study. In the large vessels of the optic disc blood flow dropped after 60 years, while in the microvasculature it decreased progradiently in the groups older than 40 and 60 years. In the macular region, blood flow in large vessels and microvasculature decreased mainly in the group aged over 61. Age-related changes in pulse wave parameters were unidirectional for both large vessels and microvasculature; trends were similar in both areas under investigation.

CONCLUSIONS: The study demonstrated statistically significant (age-related changes in most laser speckle flowgraphy pulse wave parameters. The MBR, MV (MBR of Vascular area), MT (MBR of Tissue area) indicators are most informative in the ophthalmic hemodinamic screening. The study of another pulse wave parameters seems sufficient for the general MBR.

Keywords: laser speckle flowgraphy; ocular blood flow; age-related changes; microvasculature; main retinal vessels; MBR; pulse wave parameters.

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Исследование возрастных изменений ретинальной гемодинамики методом лазерной спекл-флоуграфии

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АННОТАЦИЯ

Актуальность. Диагностика гемодинамических изменений важна как для уточнения особенностей течения патологического процесса многих глазных заболеваний, так и для оптимизации тактики лечения. Лазерная спекл-флоуграфия (LSFG) — новый неинвазивный метод количественной оценки ретинального кровотока.

Цель — исследовать возрастные изменения пульсовой волны в крупных сосудах и микроциркуляторном русле в области диска зрительного нерва и макулы с помощью лазерной спекл-флоуграфии.

Материалы и методы. Возрастные изменения кровотока исследовали на 60 здоровых добровольцах на приборе LSFG-RetFlow. Оценивали значение основного параметра пульсовой волны — MBR, а также 8 параметров пульсовой волны для крупных сосудов и микроциркуляторного русла в области диска зрительного нерва и макулы.

Результаты. Выявлены достоверно значимые ($p \leqslant 0,05$) изменения пульсовой волны с возрастом по большинству исследуемых показателей. В области диска зрительного нерва кровоток в крупных сосудах начинал снижаться после 60 лет, кровоток в микроциркуляторном русле проградиентно снижался в группах 41–60 лет и старше 61 года. В макулярной области кровоток в крупных сосудах и микроциркуляторном русле снижался преимущественно в группе старше 61 года. Возрастные изменения параметров пульсовой волны были однонаправленны как для крупных ретинальных сосудов, так и для микроциркуляторного русла, тенденции были сходными в обоих исследуемых зонах.

Заключение. Настоящее исследование продемонстрировало статистически значимое изменение большинства параметров пульсовой волны с возрастом. Показатели MBR: для крупных сосудов (MBR of Vascular area, MV) и сосудов микроциркуляторного русла (MBR of Tissue area, MT), наиболее информативны для скринингового исследования микроциркуляции, изучение отдельных параметров пульсовой волны представляется целесообразным для общей MBR.

Ключевые слова: лазерная спекл-флоуграфия; глазной кровоток; возрастные изменения; микроциркуляторное русло; магистральные ретинальные сосуды; MBR; параметры пульсовой волны.

Как цитировать

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BACKGROUND

Hemodynamic disorders are the cause of the pathogenesis of many ophthalmological diseases, and often determine the prognosis of visual functions. Therefore, the diagnosis of these changes is important to clarify the features of the pathological process course and optimize treatment tactics.

The presence of constant blood flow in the vessels of the retina, choroid and optic nerve in conditions of rapid transient shifts in systemic blood pressure is maintained due to autoregulation, which depends on the state of the endothelium, pericytes, vasoactive molecules [1]. Risk factors for the development of microvascular pathology in ophthalmological practice are cardiovascular disorders (arterial hypertension and hypotension), diabetes mellitus, atherosclerosis, cerebrovascular diseases. In addition, structural and functional changes in the vascular wall occur with age, even in the absence of additional risk factors (lifestyle, concomitant diseases). There is thickening and compaction of the vascular wall [2–4], increase in the velocity of pulse wave propagation [5]. It is believed that an increase in arterial stiffness leads to spreading of pulsating blood flow to the microcirculatory bed causing gradual violation of the autoregulation mechanism, which is manifested by a decrease in choroidal and retinal perfusion and plays an important role in the development of age-related ophthalmological diseases such as glaucoma and age-related macular degeneration [6].

Laser speckle flowgraphy (LSFG) is a new noninvasive method for quantifying blood flow in the area of the optic nerve disc and macula, which allows tracking changes in perfusion in real time. The essence of the method is to study the quantitative parameters of the pulse wave of blood flow obtained by analyzing speckle images created by reflecting a laser beam from moving blood elements. The radiation reflected from the fabric creates a certain speckle pattern on the plane where the area sensor is focused. Reflection from moving blood elements leads to a “blurring” of the recorded speckle pattern and a decrease in speckle contrast. The technology, the scope of application of LSFG and the main parameters determined using this method were described in detail in our previous studies [7, 8].

It has been shown that age-related changes in blood flow can be effectively verified using LSFG. Significant age-related changes in ocular hemoperfusion were revealed, namely the main indicator LSFG – MBR (Mean Blur Rate, average image blurring index), which is a measure of the relative blood flow rate. In addition to the integral indicator MBR, the parameters MBR for large vessels (MBR of Vascular area, MV) and vessels of the microcirculatory bed (MBR of Tissue area, MT) and MBR for the entire study area (MBR of all area, MA) can be calculated separately (Fig. 1, 2).

The pulse wave parameters measured by the LSFG method are synchronized with cardiac cycles which can be useful for studying the relationship between systemic and ocular blood flow and assessing the physiological aging of the microcirculatory bed in healthy individuals of different age groups [9]. It is believed that the time (Blowout Time, BOT) and volume (Blowout Score, BOS) of blood flow per heartbeat are associated with stiffness of large arteries, diastolic function of the left ventricle and systemic vascular resistance [10, 11]. The Acceleration Time index (ATI) correlates with the ratio of the final diastolic contraction and the mass of the left ventricle [12, 13].

LSFG allows you to analyze 13 pulse wave parameters, which can be determined for both the total MBR and MV and MT – that is, both in large vessels and in the microcirculatory bed separately. No studies have been found in the available literature on age-related changes in individual pulse wave parameters for MV and MT, which determines the relevance of this work. In this paper the 8 most significant pulse wave indicators determined for MV and MT were analyzed.

The aim is to use LSFG to investigate age-related changes in the pulse wave in large vessels (MV) and microcirculatory bed (MT) in the area of the optic disk and macula.

MATERIALS AND METHODS

The study included 60 healthy volunteers (120 eyes). The subjects were divided into groups of 20 people depending on their age – 20–40 years old, 41–60 years old and 61 years and older. Exclusion criteria: the presence of ametropia ⩾6 diopters, any eye surgery for 3 months prior to participation in the study, significant opacities of optical media, any other clinically significant ophthalmological disease according to the researchers as well as systemic diseases (uncompensated hypertension, dyslipidemia, diabetes mellitus, cardiovascular or cerebrovascular disorders). All subjects underwent comprehensive screening diagnostics, which included anamnesis collection, physical and standard ophthalmological examination. All the examined persons had high visual acuity, normal parameters of arterial and intraocular pressure.

Blood pressure and LPH were measured after a 10-minute rest of the patients in a quiet, ventilated room. All participants abstained from smoking, alcohol and caffeine for ⩾24 hours prior to the examination.

The study was performed on the LSFG-RetFlow device (Nidek, Japan) according to the standard method, without the use of mydriasis. The scan of the optic disk and macula was carried out during a 4-second period, involving the recording of 118 frames, which were transformed by superimposition into a so-called composite blood flow map.

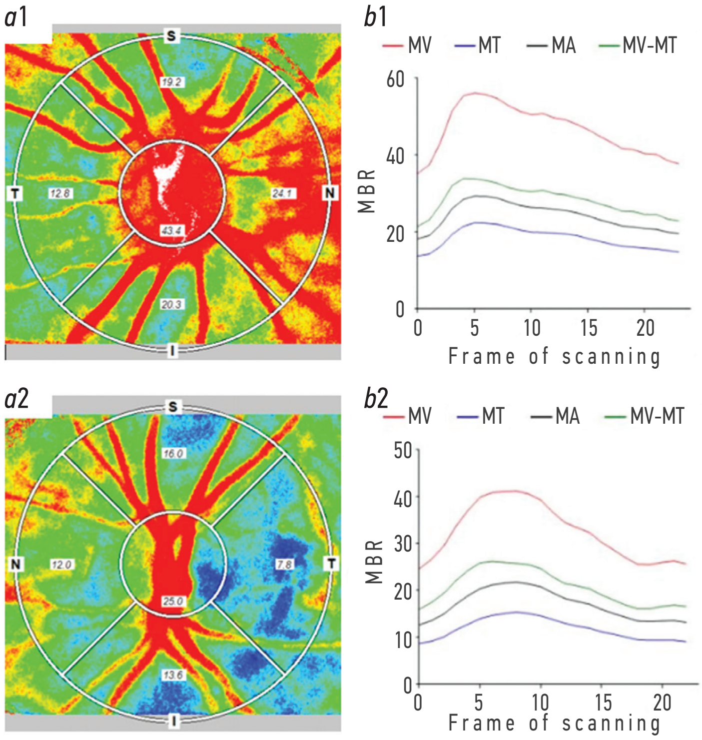

Fig. 1. ONH blood flow parameters obtained by laser speckle flowgraphy: *a* — cartogram of blood flow; *b* — graphic representation of mean blur rate (MBR) in the age groups of 20–40 years (*a*1 and *b*1) and over 60 years (*a*2 and *b*2), respectively, the x-axis reflects scanning frames. MV — MBR of Vascular area, MT — MBR of Tissue area, MA — MBR of all area

Рис. 1. Параметры кровотока диска зрительного нерва, полученные методом лазерной спекл-флоуграфии: *a* — картограмма кровотока; *b* — графическое изображение среднего показателя размытия изображения (MBR) в возрастных группах 20–40 лет (*a*1 и *b*1) и старше 60 лет (*a*2 и *b*2) соответственно. MV — MBR для крупных сосудов, MT — MBR для сосудов микроциркуляторного русла, MA — MBR для всей исследуемой области

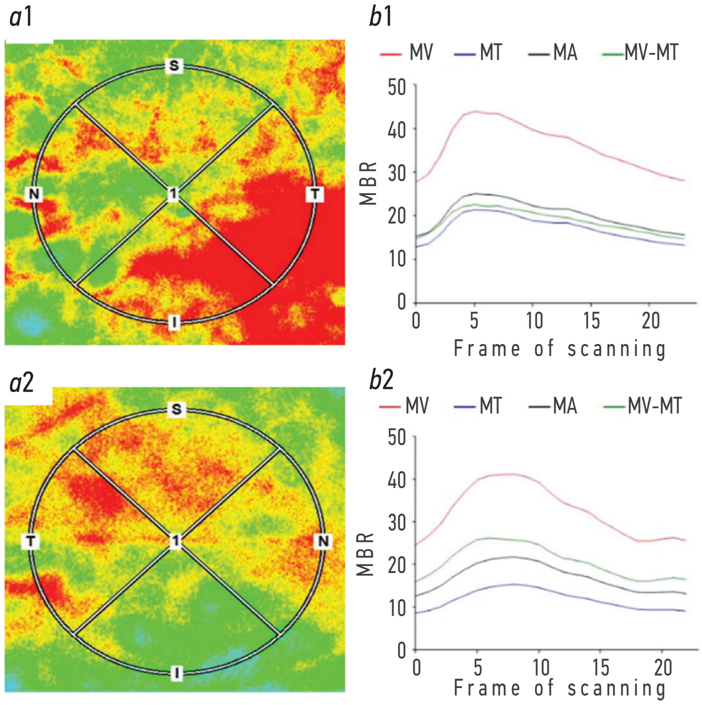

Fig. 2. Macula blood flow parameters obtained by laser speckle flowgraphy: *a* — cartogram of blood flow; *b* — graphic representation of MBR in the age groups of 20–40 years old (*a*1 and *b*1) and over 60 years old (*a*2 and *b*2), respectively, the x-axis reflects scanning frames. MV — MBR of Vascular area, MT — MBR of Tissue area, MA — MBR of all area

Рис. 2. Параметры кровотока макулярной области, полученные методом лазерной спекл-флоуграфии: *a* — картограмма кровотока; *b* — графическое изображение среднего показателя размытия изображения в возрастных группах 20–40 лет (*a*1 и *b*1) и старше 60 лет (*a*2 и *b*2) соответственно. MV — MBR для крупных сосудов, MT — MBR для сосудов микроциркуляторного русла, MA — MBR для всей исследуемой области

Then the studied area was outlined on the resulting image inside which measurements were carried out. A template in the form of an ETDRS “lattice” with a diameter of 4.5 mm was applied to the area of the optic disk and peripapillary retina – a single size specified by the manufacturer. The macular area was outlined in the form of a circle with a diameter of 5 mm. Blood flow parameters were calculated using LSFG Analyzer software. The value of the main parameter of LSFG — MBR, as well as MV and MT, was estimated, on the basis of which graphs were automatically built to analyze pulse wave indicators. In this work, 8 most significant indicators were analyzed: BOT (Blowout Time) — the percentage of pulse wave time during which MBR values were higher than the average values in the current series of measurements, BOS (Blowout Score) — blood flow volume per heartbeat, ATI, blood Flow Acceleration Index (FAI), the indicator of the asymmetric deformation/skew distribution (Skew), the rate of increase and decrease of the MBR — Rr (Rising rate) and Fr (Falling rate) curve, and the resistance Index (RI). The research was carried out in the macula and in the field of optic disk. The central nervous system is the site of localization of large retinal vessels, therefore, the study of this zone gives an idea not only about the blood supply to the optic nerve head but also about retinal blood flow in general. The study of the macular area by the LSFG method provides a comprehensive understanding of retinal and choroidal blood flow.

Statistical processing of the research results was performed using the Microsoft Excel 2016 application. When analyzing the data of 60 patients, the values of the median (Me) and quartile parameters were calculated [Q_{25}; Q_{75}]. All samples obeyed the normal distribution law. To verify the validity of the differences between the mean values of the samples, a parametric two-sided Student’s *t*-test was used. The differences were considered significant at the significance level of $p \leqslant 0.05$.

RESULTS

According to the results of the study, significantly valued ($p \leqslant 0.05$) changes in the pulse wave were revealed in people of older age groups according to most of the studied parameters (Table 1 and 2).

The relationship between the absolute value of the MBR index and the caliber of the studied vessels is traced. The maximum MBR values were determined for MV DSN (large retinal vessels), followed by MV macula, MT macula (in the macula, due to the contribution of choroidal vessels to the volume of the studied blood flow, the values increase). The minimum values were determined for MT optic disk.

Similar patterns were found for FAI, which is considered as an indicator of the maximum change in the increasing MBR value and displays the possibility of a rapid increase in blood flow over a short period of time (one frame, 1/30 s). The FAI MV values were higher than

Table 1. Flowgraphic parameters of blood flow in large vessels (MV) and microvasculature (MT) of the optic disc area in different age groups, *Me* [Q_{25}; Q_{75}]

Таблица 1. Флоуграфические параметры кровотока крупных сосудов (MV) и микроциркуляторного русла (MT) в области диска зрительного нерва в разных возрастных группах, *Me* [Q_{25}; Q_{75}]

Blood flow parameters	MV			MT		
	20–40 years	41–60 years	≥61 years	20–40 years	41–60 years	≥61 years
MV/MT	51.25 [44; 61.83]	47.15 [42.9; 53.95]*	38.5 [32.78; 45.2]*	19.55 [16.63; 24.35]	16.1 [13.08; 18.73]*	13.35 [12.13; 17.25]**
BOT	57.60 [54.55; 58.9]	54.20 [50.55; 57.6]	47.90 [46.98; 50.9]**	55.00 [51.3; 56.43]	51.35 [48.95; 53.1]*	44.90 [42.8; 47.93]**
BOS	80.30 [79.1; 81.93]	81.30 [79.13; 83.58]	76.15 [72; 78.9]**	78.15 [76.8; 79.9]	77.70 [75.38; 80.18]	72.60 [69.65; 75.15]**
Skew	10.90 [9.6; 12.23]	10.90 [10.15; 11.9]	12.10 [11.13; 13.28]**	11.95 [10.9; 12.73]	11.90 [11.33; 13]	12.95 [12.23; 14.6]**
ATI	23.45 [21.2; 27.65]	33.40 [28.85; 34.83]*	33.40 [30.3; 35.8]*	23.60 [22.38; 27.38]	31.70 [28.75; 33.2]*	33.00 [30.8; 35.5]*
Rising rate	12.60 [10.9; 13.93]	14.05 [13.3; 14.35]*	13.05 [12.7; 13.95]	12.25 [10.95; 13.2]	13.05 [12.8; 13.7]*	12.80 [12.03; 13.45]
Falling rate	12.30 [11.78; 13.3]	13.35 [12.73; 14.08]*	13.80 [13.53; 14.58]*	12.70 [12.08; 13.23]	13.50 [13; 14.18]*	14.80 [14.1; 15.2]*
FAI	6.80 [6.1; 8.23]	4.90 [4.5; 6.4]*	4.90 [3.9; 6.08]*	2.75 [2.38; 3.5]	2.00 [1.83; 2.4]	1.90 [1.53; 2.8]
RI	0.31 [0.29; 0.33]	0.30 [0.27; 0.33]	0.37 [0.33; 0.42]	0.34 [0.31; 0.36]	0.35 [0.31; 0.38]	0.41 [0.37; 0.45]

Note. BOT — Blowout Time; BOS — Blowout Score; *$p \leqslant 0.05$, the difference is statistically significant with the 20–40 years group; **$p \leqslant 0.05$, the difference is statistically significant between the ≥61 years group and the other two groups.

Примечание. BOT — время выброса; BOS — объём выброса; Skew — асимметричное распределение деформация/перекос; ATI — индекс времени ускорения; Rising rate — скорость возрастания кривой MBR; Falling rate — скорость убывания кривой MBR; FAI — индекс ускорения кровотока; RI — индекс резистентности. *$p \leqslant 0{,}05$, разница статистически достоверна с группой 20–40 лет; **$p \leqslant 0{,}05$, разница статистически достоверна между группой ≥61 года и двумя другими группами.

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Table 2. Flowographic parameters of blood flow in large vessels (MV) and microvasculature (MT) of the macula in different age groups, *Me* [Q_{25}; Q_{75}]

Таблица 2. Флуографические параметры кровотока крупных сосудов (MV) и микроциркуляторного русла (MT) в макуле в разных возрастных группах, *Me* [Q_{25}; Q_{75}]

Blood flow parameters	MV			MT		
	20–40 years	41–60 years	≥61 years	20–40 years	41–60 years	≥61 years
MV/MT	36.55 [30.53; 51.38]	33.95 [29.93; 38.78]*	24.65 [18.68; 31.95]**	23.75 [17.73; 32.25]	21.15 [15.38; 25.48]*	14.6 [11.6; 18.95]**
BOT	52.85 [49.15; 55]	50.45 [45.23; 52.5]	43.60 [40.83; 45.38]**	52.40 [49.7; 55.4]	47.15 [44.1; 52.1]*	43.35 [41.33; 45.8]**
BOS	78.55 [76.33; 81.28]	78.85 [76.55; 81.7]	71.40 [68.2; 74.28]**	80.00 [77.28; 83.6]	78.40 [75.65; 82.08]	72.15 [68.83; 74.5]**
Skew	13.05 [11.08; 13.93]	13.05 [11.73; 13.78]	14.70 [13.05; 16.13]**	12.90 [10.78; 14]	13.15 [12.43; 14.6]	14.35 [13; 15.08]**
ATI	23.80 [19.9; 26.05]	30.15 [29; 32.7]*	31.45 [28.65; 34.38]*	24.70 [20.4; 26.33]	30.55 [28.65; 32.28]*	32.00 [29.6; 34.93]*
Rising rate	11.75 [10.6; 13.33]	13.40 [12.4; 13.75]*	12.45 [11.23; 12.98]#	12.35 [10.88; 13.58]	12.90 [12.15; 13.6]	12.70 [11.08; 13.38]
Falling rate	13.00 [12.1; 13.93]	13.80 [12.93; 14.55]*	14.90 [14.13; 15.6]**	13.00 [12.38; 13.63]	13.85 [13.3; 14.58]*	14.70 [14.4; 15.2]**
FAI	5.60 [4.45; 6.53]	4.25 [2.68; 4.98]*	3.35 [2.6; 4.5]*	3.35 [2.8; 4.13]	2.50 [1.7; 3.15]*	2.10 [1.7; 2.7]*
RI	0.33 [0.3; 0.36]	0.33 [0.29; 0.36]	0.42 [0.39; 0.46]**	0.32 [0.27; 0.35]	0.33 [0.28; 0.38]	0.42 [0.39; 0.44]**

Note. BOT — Blowout Time; BOS — Blowout Score; *$p \leq 0.05$, the difference is statistically significant with the 20–40 years group; **$p \leq 0.05$, the difference is statistically significant between the ≥61 years group and the other two groups; #$p \leq 0.05$, the difference is statistically significant with the 41–60 years group

Примечание. BOT — время выброса; BOS — объём выброса; Skew — асимметричное распределение деформация/перекос; ATI — индекс времени ускорения; Rising rate — скорость возрастания кривой MBR; Falling rate — скорость убывания кривой MBR; FAI — индекс ускорения кровотока; RI — индекс резистентности. *$p \leq 0,05$, разница статистически достоверна с группой 20–40 лет; **$p \leq 0,05$, разница статистически достоверна между группой ≥61 года и двумя другими группами; #$p \leq 0,05$, разница статистически достоверна с группой 41–60 лет.

the FAI MT. The maximum FAI values were found for MV optic disk, and the minimum values for MT optic disk.

For the rest of the pulse wave parameters, the absolute values in the study of hemodynamics in large vessels and microcirculatory bed did not differ significantly.

The relative changes in pulse wave parameters in the age groups 41–60 years and ≥61 years relative to the group 20–40 years are shown in Fig. 3. It was revealed that the trends in the pulse wave parameters were generally unidirectional for both large retinal vessels and the microcirculatory bed, the trends were similar in both studied zones.

Values of MV indicators/MT began to decline after the age of 40 but the most significant changes in the indicator were noted after the age of 60. BOT, BOS decreased, and Skew, RI increased mainly in the group over 61 years old, there was little difference between the first two groups. The ATI index increased, and FAI decreased after 41 years. The falling rate increased progressively in the groups after 40 and after 60 years. For the Rising rate indicator, the maximum values were observed in the 41–60-year-old group. The greatest age dynamics was observed for MV/MT, FAI, ATI and RI indices. The increase in RI was more pronounced for MV and MT in the macula region, for ATI — in the optic disk region. The maximum decrease in FAI was observed in the macula area in people over 61 years of age.

DISCUSSION

Laser speckle fluorography (LSFG) is a new non-invasive method for assessing ocular blood flow, which demonstrates effectiveness in the comprehensive diagnosis and monitoring of various systemic and ophthalmological diseases.

The vascular network of the eye is part of the cardiovascular system of the body, exposed to the same internal and external influences. Due to the possibilities of visualization, qualitative and quantitative assessment, ocular blood flow can be considered as a kind of “window” for the study of vascular changes in the body, and LSFG expands the possibilities of studying ocular blood flow and blood circulation in general.

A number of studies have shown the relationship between individual parameters of LSPH and the state of the cardiovascular system. H. Kunikata et al. [14] reported that the BOT-Tissue indicator (BOT-MT) can be used to detect latent cerebral infarction in primary aldosteronism. It was also found that lower values of BOS in the region of the heart correlate with a decrease in diastolic function of the left ventricle [10] and an increase in the formation of atherosclerotic plaques within the carotid arteries [11]. A study by T. Shiba et al. [15] showed that the average values of total MBR obtained in patients with coronary artery disease were significantly lower than in patients without this pathology. And in their previous study, the ATI-MV index in the area of optic disk was negatively correlated with the mass of the left ventricle [13].

Similar changes were revealed in the study of patients with diabetes mellitus (DM). In patients with DM, the thickening of intima media detected by ultrasound correlated with a decrease in the average values of all MBR indicators in the SD [16]. Y. Ueno et al. [17] investigating the relationship of morphological changes in retinal arteries with general blood flow and systemic changes in patients with type 2 diabetes, concluded that MBR, the presence of hypertension and low-density lipoprotein levels are independent predictors of an increase in vascular wall thickness, which leads to narrowing of the vessel lumen and a decrease in blood flow in diabetic retinopathy.

Despite the fact that LSFG can be used in the diagnosis of both systemic diseases and ophthalmopathologies, at the moment there is no specific regulatory framework for pulse wave indicators although a number of authors have made attempts to solve this issue. N. Luft et al. [18] studied the parameters of ocular blood flow in healthy individuals. It was shown that all three MBR indices (total MBR, MV, MT) decreased significantly with age ($p < 0.01$). There was also a statistically significant decrease in BOT, BOS, FAI, an increase in Skew, ATI, Falling rate (FR) and RI. The rising rate did not show a significant age dependence. According to the researchers, pulse wave variables such as FR ($r = 0.747$) and BOT ($r = -0.714$) were most strongly correlated with age.

The mechanism that maintains blood pressure between heartbeats (Windkessel effect) is disrupted with age causing an increase in systolic pulse and a decrease in diastolic pressure — the nature of blood flow becomes more pulsating [18]. This change is reflected in an age-related increase in FR, which characterizes a more pronounced drop in blood flow after the peak, as well as an age-related decrease in BOT, expressed in a decrease in peripheral perfusion during diastole. Similar age-related changes in BOT and FR parameters were obtained by Japanese authors [19]. N Aizawa et al. [20] also revealed a decrease in the MBR index for large vessels relative to age. It should be noted that in these studies, blood flow was studied only in the field of optic disk, and in addition it was the correlation relationship between age and blood flow indicators that was analyzed without attempts to create a regulatory framework [18–20].

The literature data on age-related changes in LPH are generally consistent with the results obtained earlier in our Center [7, 8]. The conducted studies have shown a significant decrease in the volume parameters of blood flow in the area of the spinal cord and macula with age. The highest MBR parameters were observed in the group of 20–40 years old. In the macular region, MBR indicators decreased more significantly in the group over 60 years old,

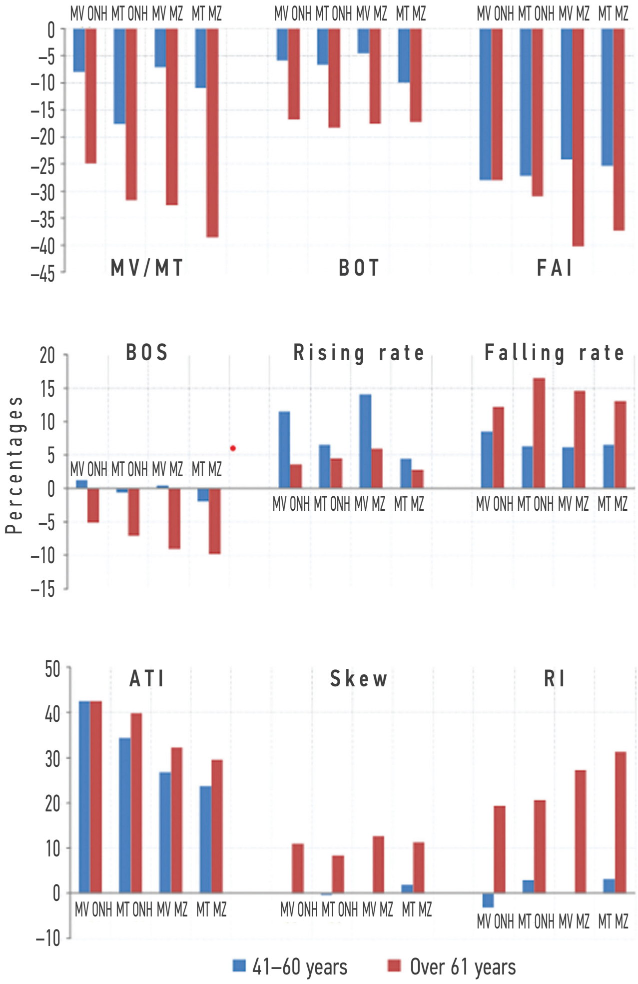

Fig. 3. Dynamics of pulse wave parameters within the groups 41–60 years and ≥61 years relative to the group of 20–40 years (corresponds to the isoline). BOT — Blowout Time; BOS — Blowout Score; Skew — asymmetric distribution; ATI — Acceleration Time Index; Rising rate — rate of increase of MBR curve; Falling rate — rate of decay of MBR curve; FAI — Flow Acceleration Index; RI — Resistivity Index; ДЗН — optic nerve head; MZ — macular area

Рис. 3. Динамика показателей пульсовой волны в группах 41–60 лет и ≥61 года относительно группы 20–40 лет (соответствует изолинии). BOT — время выброса; BOS — объём выброса; Skew — асимметричное распределение деформация/перекос; ATI — индекс времени ускорения; Rising rate — скорость возрастания кривой MBR; Falling rate — скорость убывания кривой MBR; FAI — индекс ускорения кровотока; RI — индекс резистентности; ДЗН — диск зрительного нерва; MZ — макулярная область

whereas for the optic disk, the decrease was noted after 40 years. There was also a significantly significant age-related change in most parameters of the pulse wave of the integral MBR.

In this paper, the pulse wave parameters for MV and MT are studied. Such work, according to the literature, has not been carried out before. When comparing the individual parameters of the pulse wave MV, MT and total MBR, there was no significant difference in the absolute values of most indicators in different age groups.

Significant variability is shown for the FAI index, which has a strong correlation (r = 0.93) with MBR. At the same time, the degree of FAI changes for MV relative to FAI for the total MBR was almost twice as high as the degree of MV changes relative to the total MBR.

Thus, the conducted study showed the informative value of the MV and MT pulse wave indicators, which reflect the blood flow in large vessels and the microcirculatory vascular bed. The indicators can be effectively used in clinical practice for screening studies. To determine individual pulse wave parameters (except FAI) it is sufficient to analyze the parameters of the general MBR.

CONCLUSION

The present study demonstrated a statistically significant relationship between most of the pulse wave parameters obtained using LSFG and age. It can be assumed that the studied parameters can be considered as biomarkers of age-related changes in ocular perfusion. Due to the convenience of conducting the study for the doctor and the patient, the speed of the study, LSFG is a promising method for further studying blood flow in cardiovascular diseases and various ophthalmopathology in order to assess the development of macro- and microvascular changes.

The MBR, MV and MT indicators are the most informative for the screening study of microcirculation. The study of individual pulse wave parameters seems appropriate for the general MBR. The analysis of individual pulse wave parameters for MV and MT may be effective in certain ophthalmopathologies, however, this issue requires separate study.

ADDITIONAL INFO

Authors' contribution. All authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study. Personal contribution of each author: V.V. Neroev, T.D. Okhotsimskaya — experimental design, collecting and preparation of samples, chromatographic study, data analysis, writing the main part of the text, literature review, making final edits; O.V. Zaytseva — experimental design, writing the main part of the text; S.Yu. Petrov — experimental design; A.I. Ushakov — collecting and preparation of samples, data analysis, writing the main part of the text, literature review; N.E. Deryugina — experimental design, collecting and preparation of sample, writing the main part of the text, literature review; O.I. Markelova — experimental design, collecting and preparation of samples, data analysis, writing the main part of the text, literature review.

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ДОПОЛНИТЕЛЬНАЯ ИНФОРМАЦИЯ

Вклад авторов. Все авторы внесли существенный вклад в разработку концепции, проведение исследования и подготовку статьи, прочли и одобрили финальную версию перед публикацией. Личный вклад каждого автора: В.В. Нероев, Т.Д. Охоцимская — концепция и дизайн исследования, сбор и обработка материалов, хроматографическое исследование, анализ полученных данных, написание текста, обзор литературы; О.В. Зайцева — концепция и дизайн исследования, написание текста; С.Ю. Петров — концепция и дизайн исследования; А.И. Ушаков — сбор и обработка материалов, анализ полученных данных, написание текста, обзор литературы; Н.Е. Дерюгина — концепция и дизайн исследования, сбор и обработка материалов, написание текста, обзор литературы; О.И. Маркелова — концепция и дизайн исследования, сбор и обработка материалов, анализ полученных данных, написание текста, обзор литературы.

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