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Evaluation of ocular blood flow in glaucoma – possibilities and barriers

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ABSTRACT

Patients with glaucoma demonstrate disturbed ocular blood flow that is induced by oxidative stress, endothelial dysfunction and impaired autonomic nervous system activity. It has not yet been clarified whether the reduced blood flow in glaucoma is secondary (to tissue loss or a decrease in perfusion pressure with disturbed autoregulation) or is itself the primary cause of optic neuropathy. Due to the complex system of blood supply to the optic disc and retina there is no single diagnostic method that allows the measurement of all vascular beds in the eye important for glaucoma. The article, based on a review of the literature, discusses current and previous techniques for assessing retinal, choroidal and retrobulbar circulation in glaucoma, with particular attention to color Doppler ultrasonography and optical coherence tomography angiography. Advantages and limitations of each technology are presented and the results of the most important research with their use are listed. In the light of the latest research, optical coherence tomography angiography is an imaging modality that has great scientific and clinical potential to enhance the knowledge of glaucoma pathogenesis and to improve the ability to detect glaucomatous damage.

KEY WORDS: glaucoma, ocular perfusion, retinal microvasculature, ultrasonography, Doppler, optical coherent tomography angiography.

INTRODUCTION

Based on the current state of knowledge, glaucomatous optic neuropathy is a neurodegenerative disease involving pathological changes in the biomechanics of the optic disc, genetic factors, vascular disorders, and immunological factors. The mechanical and vascular hypotheses explaining the pathomechanism of glaucoma which prevailed in the 20th century were replaced at the turn of the millennium by a new, biomechanical concept of glaucomatous damage which takes into account the dynamic interaction between intraocular pressure (IOP), biomechanical properties of ocular tissues, dynamics of aqueous humor, and ocular blood flow [1]. Ocular hemodynamics in glaucoma can be altered both by local factors, related primarily to vascular endothelial dysfunction, impaired flow autoregulation mechanism or abnormal translaminar pressure [2, 3], and general factors, including an increased activity of the sympathetic component of the autonomic nervous system or altered rheological properties of blood [4, 5]. The factors listed above are believed to have critical pathogenetic implications in patients with normal-tension glaucoma, in whom moderate and short-term but repeated changes in perfusion pressure "sensitize" the optic nerve to damage even under conditions of statistically insignificantly elevated IOP.

Blood supply to the eye comes from the ophthalmic artery (OA), which is the first branch of the internal carotid artery. The choroidal circulation, which accounts for 85% of the total blood flow in the eye, is supplied by the anterior and posterior ciliary arteries, while the retinal circulation is supplied by the central retinal artery (CRA). The retinal vasculature feeds the inner layers of the retina up to the inner nuclear layer, and the choroidal circulation supplies the outer retinal layers. The main sources of vascularization of the optic disc are the nasal and temporal short posterior ciliary arteries (NSPCA, TSPCA), which in most people are connected by anastomoses, forming the arterial circle of Zinn-Haller. They supply the deeper layers of the prelaminar region of the optic disc, and its laminar and anterior retrolaminar parts. The vascular network of the central retinal artery supplies the superficial layers of the prelaminar part of the optic disc and the central area of the posterior retrolaminar region [6].

The small branches of the central retinal artery are both anatomically and functionally terminal vessels; the characteristic features of retinal capillaries include the absence of innervation and the presence of tight junctions between endothelial cells. As a consequence, the regulation of retinal circulation involves mainly endothelial cells, which release a number of vasoactive factors including nitric oxide or endothelin 1 (the most potent

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vasoconstrictor). In addition, the regulation mechanism relies on nerve cells and astrocytes (the so-called neurovascular coupling). Because of pores in the capillary walls, there are numerous junctions between small vessel branches in the choroidal circulation. They are also surrounded by a dense network of autonomic nerve fibers. The choroidal circulation is regulated predominantly by nervous and metabolic activity. The flow of blood within the optic disc is regulated both by endothelial cells and (because of the lack of tight blood-brain barrier) by circulating hormones including serotonin, angiotensin II or endothelin 1. The autoregulation of blood flow within the small branches of the CRA supplying the prelaminar region of the optic nerve head (II) has been found to be normal, with IOP values not exceeding 45 mmHg [7]. The extent of autoregulation of blood flow within the deeper layers of the optic disc and the choroid is, as yet, unknown.

In patients with glaucoma, blood flow abnormalities are seen in virtually all parts of the eye, including the iris, retina, and choroid, but the blood perfusion deficit is particularly pronounced in the region of the vessels supplying the optic nerve. Ocular blood flow is more impaired in patients with progressive glaucoma than stable glaucoma. For many years, it has been debated whether the observed vascular changes cause the atrophy of retinal ganglion cells and their axons or perhaps they are an effect of decreased nutritional needs of the reduced mass of nervous tissue and glial cells. The issue, which is impossible to resolve conclusively within the scope of a cross-sectional study, must be considered along a number of dimensions by analyzing deviations observed in the ocular and systemic vascular systems in patients with glaucoma, taking into account perfusion pressure abnormalities, endothelial-derived factors, and the regulation of the cardiovascular system by the nervous system [8]. To date, no evidence has been discovered to substantiate the claim that changes in blood pressure affect the course of glaucoma, while the clinical effects of ocular blood flow fluctuations or the effect of blood supply to the entire visual pathway on the course of glaucomatous neuropathy are unknown [9].

TECHNIQUES FOR MEASURING RETINAL AND CHOROIDAL CIRCULATION

The system of blood supply to the optic disc and the retina is complex, so there is no single diagnostic method for measuring all vascular beds within the eye that are important in glaucoma. Ocular hemodynamics in glaucoma patients has been evaluated in a number of scientific studies, both basic and clinical, using a number of diagnostic techniques.

In 1967, Hayreh and Walker [10], using fluorescein angiography, were the first to demonstrate abnormal fluorescence in the capillary bed of the superficial layer of the optic disc in patients with glaucoma. Over subsequent decades, a number of technologies were employed for the evaluation of retinal circulation, including laser Doppler flowmeter (LDF) or Heidelberg retinal flowmeter (HRF), laser Doppler velocimeter (LDV), scanning laser ophthalmoscopy (SLO), retinal vessel analyzer (RVA), and retinal oxymeter (RO).

Studies using the techniques listed above have identified a number of features in patients with glaucoma including: 1) a significant impairment of capillary blood flow within the neuroretinal rim and in the peripapillary region of the retina determined by HRF [11], 2) prolonged retinal arteriovenous passage time in SLO, 3) abnormal reactivity of the retinal vessels due to elevated IOP [12] or decreased oxygen saturation of hemoglobin in retinal arterioles in patients with normal-tension glaucoma [13].

Choroidal circulation can be assessed by using SLO and measuring the displacements of various parts of the eye due to ocular pulsation related to the inflow of blood into the ophthalmic artery with each heart systole, or by measuring IOP oscillations synchronous with the heart rate. Techniques suitable for such measurements include pulsatile ocular blood flowmeter (POBF), dynamic contour tonometry (DCT), Triggerfish® contact lens sensor, and ultrasound non-contact measurement of corneal indentation pulse (CIP) [14, 15].

POBF- and DCT-based studies conducted in patients with glaucoma have provided scientific evidence indicating a reduction in pulsatile choroidal blood flow [16] and a reduced amplitude of ocular pulse in patients with primary open-angle glaucoma and normal-tension glaucoma.

The description of the above methods, together with their advantages and limitations, is presented in Tables I and II.

DOPPLER ULTRASOUND

A technique suitable for the assessment of hemodynamics in the retrobulbar arteries (ophthalmic artery, central retinal artery, and short posterior ciliary arteries) is color Doppler imaging (CDI). CDI is based on the phenomenon of changes in the frequency of the wave reflected off a moving medium, i.e. blood flowing in the vessel (the so-called Doppler shift). The technology is not suitable for direct volumetric blood measurements, as it does not evaluate blood vessel diameter, but it is an effective means of determining blood velocity parameters (such as peak systolic velocity and end-diastolic velocity) and flow resistance (Pourcelot resistive index) within the examined arteries, and thus indirectly evaluating blood flow in these vessels. It must be noted, though, that the interpretation of Doppler parameters in retrobulbar blood vessels is a complex task.

Peak systolic velocity (PSV) refers to the maximum blood flow velocity achieved during systole, and indirectly reflects the degree of perfusion within a blood vessel. End-diastolic velocity (EDV) is the lowest blood flow velocity achieved during the cardiac diastolic phase, serving as a marker of distal organ perfusion and elevated vascular impedance. In patients with glaucoma, the decrease in EDV results from elevated vascular resistance, either due to a rise in IOP or as a consequence of increasing vascular wall tone after vessel contraction or in the course of atherosclerosis [18]. A decrease in PSV and EDV indicates a volumetric reduction in total blood flow. Resistance index (RI), a function of both velocity parameters, expressed as RI = (PSV – EDV)/PSV, reflects the resistance of the vessel located distally from the measure-

Table I. Characteristics of diagnostic methods for assessing retinal circulation in glaucoma

Technology	Characteristics	Advantages	Limitations
Laser doppler flowmeter (LDF)	It calculates the volumetric total capillary flow in the retina and the flow velocity in the tested area	High resolution Enables measurement of small changes in flow	Measurement of blood flow in arbitrary units Susceptibility to fixation errors and opacity of optical media
Retinal vessel analyzer (RVA)	Enables measurement of the diameter of the artery or vein of the retina in real time	Examines vascular reactivity	Does not measure flow Susceptibility to fixation errors and opacity of optical media
Laser doppler velocimeter (LDV)	Calculates the maximum blood flow velocity in larger retinal vessels	The total retinal blood flow can be calculated based on the blood cell velocity and vessel diameter	Does not measure flow within the optic disc
Scanning laser ophthalmoscopy-fluorescein angiography (SLO-FA)	Enables direct visualization of retinal circulation with fluorescein (SLO-FA)	Measures mean dye velocity, arteriovenous passage time (AVP), mean transit time (MTT)	Invasive examination, expensive, no commercial algorithms of analysis available
Retinal oximeter (RO)	It enables non-invasive measurement of oxygen saturation of hemoglobin in retinal vessels	Provides data on retinal metabolism	Method not validated Depends on the transparency of optical media

Table II. Characteristics of diagnostic methods for assessing choroid circulation in glaucoma

Technology	Characteristics	Advantages	Limitations
Scanning laser ophthalmoscopy-indocyanine green angiography (SLO-ICGA)	Enables direct visualization of choroidal circulation with indocyanine	Measures dye transit time in the peripapillary region and macular region	Invasive examination, expensive, no commercial algorithms of analysis available
Pulsatile ocular blood flowmeter (POBF)	It measures pulsatile intraocular pressure (IOP) changes caused by blood flow in the eye (ocular pulse)	It measures the change in total circulation volume based on the pulse wave amplitude	Does not measure flow The result depends on the axial length of the eye, age, blood pressure and heart rate Measurements are insensitive to hypoxia and hypercapnia
Dynamic contour Pascal tonometry (DCT)	Enables measurement of IOP changes synchronous with the heart rate (ocular pulse amplitude – OPA)	A relationship between OPA and glaucoma severity and type of glaucoma has been demonstrated	Does not measure flow The relationship between OPA and ocular blood flow is unknown Touch measurement
Contact lens sensor Triggerfish (CLS)	It enables 24-hour measurement of volumetric changes in the corneal scleral sulcus	The device samples data for 30 seconds at a frequency of 10 Hz every 5 min; the record covers 288 points; each is a median of 300 measurements	The interpretation of the record is complex; influence of IOP, scleral and corneal biomechanics, biological systems and patient activity on the result
Corneal indentation pulse (CIP)	It measures the longitudinal displacement of the cornea using non-contact ultrasonic technique	The correlation between corneal pulse and ocular pulsation and ECG was demonstrated; a dicrotic pulse was found in the elderly	The method is being tested

ment site. The simultaneous decrease in EDV and increase in RI values in the retrobulbar arteries is indicative of possible ischemia of the optic disc. The interpretation of color Doppler ultrasound findings in patients with glaucoma is additionally hampered by the fact that deviations in hemodynamic parameters may occur only in some retrobulbar arteries, as these vessels vary in their sensitivity to IOP fluctuations and reactivity to vasoactive agents. The ophthalmic artery is selectively sensitive to hypoxia. Hemodynamic modifications caused, for example, by changes in ocular perfusion pressure due to elevated IOP, may be at the sub-threshold level, insufficient to induce a measurable change in the OA but sufficient to trigger a change in blood flow velocity within small-caliber vessels – the CRA and SPCA [19].

A metaanalysis performed by Xu *et al*. [20], comprising 23 randomized and observational studies conducted in 925 patients with normal-tension glaucoma and 744 healthy individuals, showed a statistically significant reduction in

PSV and EDV values in each retrobulbar artery, and an RI increase in the CRA and the temporal branch of the SPCA in the group of eyes with normal-tension glaucoma [20]. Some authors have found that decreased PSV in glaucoma patients is observed more frequently in small blood vessels (such as the CRA and SPCA) [21, 22], while reductions in EDV are greater than in PSV. A correlation has been identified between reduced EDV in each of the retrobulbar arteries, and a decrease in the peripapillary thickness of the retinal nerve fiber layer and reduced area of the neuroretinal rim. A relationship between hemodynamic parameters of the retrobulbar arteries and visual field parameters was also corroborated [23]. Gherghel *et al.* [24] noted a significant reduction in EDV within the OA and CRA in patients with advanced and progressive glaucoma, but no differences were observed in patients with stable glaucoma. Other researchers have also confirmed a relationship between reduced velocity parameters within the CRA (EDV) and SPCA (PSCV and EDV) and glaucoma progression. Synder *et al.* [25] demonstrated an improvement in hemodynamic parameters in the SPCA measured by color Doppler imaging after trabeculectomy.

Color Doppler ultrasound has a number of advantages. In addition to being non-invasive and safe, the technique is independent of the transparency of optical media, and allows measurement of blood flow velocities in arteries expressed in absolute values. However, it is also associated with numerous limitations, such as the lack of possibility to measure the volume of blood flow, and difficulties with locating and evaluating the hemodynamics of the short posterior ciliary arteries. In addition, color Doppler ultrasound requires taking into account the angle between the direction of the ultrasound wave and the vascular long axis (the so-called insonation angle), and the measurement results depend on the experience of the examiner. Another disadvantage is the high cost of color flow Doppler systems.

Studies conducted to date to evaluate ocular blood flow in glaucoma using the above-described techniques have varied significantly in terms of the study procedure, patient number and characteristics, methodology of hemodynamic measurements, or the analysis of results, and failed provide sufficient data to justify the measurement of ocular blood flow in daily clinical practice. Also, the studies have not determined conclusively which of the hemodynamic techniques in glaucoma is the most effective, which vessel is most closely associated with the course of neuropathy, or which vascular bed correlates best with structural changes in glaucoma [9].

OPTICAL COHERENT TOMOGRAPHY ANGIOGRAPHY

The most modern technique proving non-invasive, fast and detailed quantitative measurements of ocular microcirculation is optical coherent tomography angiography (OCTA). The technique utilizes red blood cells as a natural contrast agent to obtain three-dimensional (3D) images of microvascular networks. The key principle of OCTA is the observation that within the scanned tissue area static spots produce a signal of constant intensity (and are displayed as black pixels), whereas moving spots (blood) yield signals with variable reflectance (shown as light pixels). Quantitative analysis of changes in reflection signals can be done using three types of algorithms, based on: 1) phasic signal, 2) signal intensity, and 3) the so-called "complex signal".

The first attempts to visualize blood flow by means of OCT date back to 1997, and were based on the time-domain approach (TD-OCT). The limitations of this method included very low scanning speed (100-800 μm/s), low resolution (2-10 μm), and low sensitivity. The next milestone involved the application of phasic signal algorithms and the development of Doppler OCT – initially time-domain OCT, followed by spectral-domain OCT (in use since 2007) – which has increased scanning speed, allowed flow measurement in any orientation of the scanning beam, and improved method sensitivity. In the same year, Wang [26] proposed a new research algorithm called optical microangiography (OMAG), also known as "phase-based Doppler OCT" or "ultra-high sensitive OMAG", incorporating a special mathematical formula that separates the information generated by a moving object from the scattered background of static motionless tissue. OMAG-based examinations produced a better contrast and reduced background noise, and for the first time enabled the detection of capillary microcirculation. The year 2007 marks the onset of the era of OCTA. The techniques based on signal intensity developed in subsequent years compared the intensity or amplitude of reflected OCT signals between consecutive scans of the same cross-section. Of the three signal intensity-based OCTA techniques – speckle variance, correlation mapping, and split spectrum amplitude decorrelation angiography (SSADA), the latter algorithm has become the main technology employed in a number of currently used OCTA systems. The basic principles of the SSADA algorithm include differences in decorrelation values between static tissue (close to zero) and moving tissue (higher values correlate with higher flow rates) and the division of the full spectrum of the OCT signal into narrower bands followed by averaging the decorrelation detected in each band. Motion correction systems are employed in order to minimize artifacts. Other algorithms incorporated into current OCTA platforms include OCTARA (OCTA ratio analysis) and OMAG, which are based on a "complex signal" combining elements of phasic signal techniques with signal intensity techniques [27-31].

OCTA is a static method which is capable of visualizing blood vessels in different retinal layers at a given time. The OCTA software performs automatic segmentation of all layers of retinal blood vessels located in: 1) superficial vascular plexus formed by small branches of the central retinal artery, 2) deep capillary plexus formed by the vessels of the inner nuclear and outer plexiform layer, 3) at the level of the outer retinal layers, where the vessels are absent, and 4) in the choriocapillaries.

The macular blood flow in glaucomatous eyes is best evaluated at the 6 mm × 6 mm scan range. The analysis can cover the whole *en face* image, and the parafoveal and perifoveal regions. The optimum method to evaluate blood flow in the

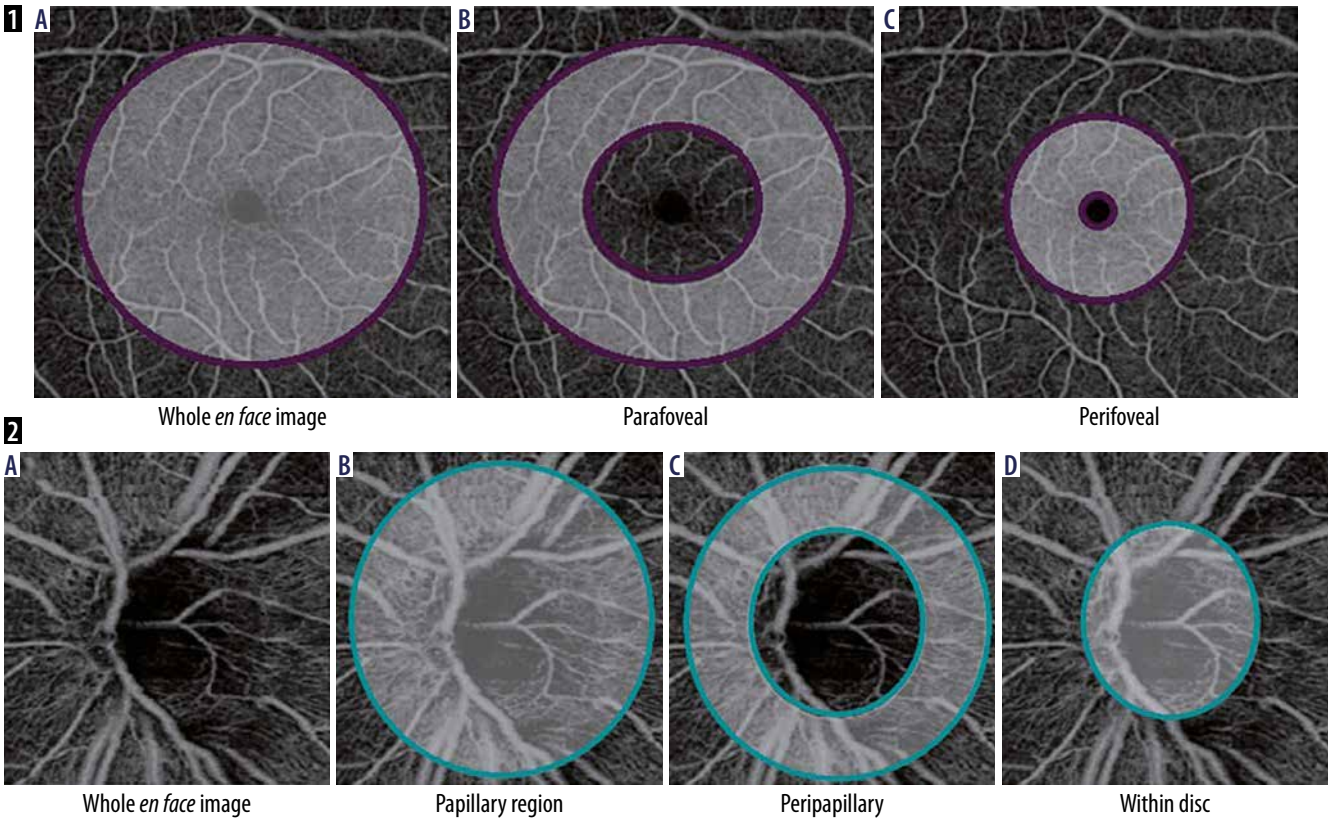

Figure 1. *En face* optical coherent tomography angiography (OCTA) images and flow analysis maps in the macula (1) and the optic disc region (2) [32]

optic disc region in glaucomatous eyes is 4.5 mm × 4.5 mm scanning. The analysis may cover: 1) whole *en face* image, 2) the papillary region defined as a circle with a diameter of 3 mm, with the center in the middle of the optic disc, 3) the peripapillary region defined as a ring with an inner diameter of 500 μm and an outer diameter of 700 μm, and 4) the optic disc only (Figure 1) [32].

In the optic disc region, OCTA captures the images of four layers: 1) vessels at the level of the vitreous body (visible in cases involving neovascularization on the optic nerve disc), 2) vessels on the surface of the retina and the optic nerve disc, i.e. the central retinal artery and vein together with their branches, 3) radial peripapillary capillaries (RPC), located in the retinal nerve fiber layer, and 4) vessels at the level of the retinal pigment epithelium (absent under physiological conditions).

The OCTA software performs the mapping and measurements of the following hemodynamic parameters: 1) vessel density (VD), defined as the percentage area occupied by blood vessels in the evaluated region, 2) disc flow index (DFI) or flow index (FI), i.e. the mean value of the flow signal (decorrelation) in the examined OCTA region and expressed in values from 0 to 1, 3) blood flow index (BFI), and 4) peripapillary deep-layer microvascular dropout (MvD) area, i.e. an avascular spot that should be vascularized.

OCTA performed in glaucoma patients reveals areas or foci with a thinned atrophic RPC network, often coexisting with the focal thinning of the peripapillary retinal nerve fiber layer and correlated with the severity of glaucomatous neuropathy (Figure 2).

The greatest differences in OCTA parameters in the peripapillary region between glaucoma patients and healthy individuals were found in the inferior-temporal and superior-temporal sectors [33-38]. The area in the macular region that is the most susceptible to glaucomatous damage is the inferior-temporal region, and this is where the most prominent differences are observed between glaucoma-affected and healthy eyes [39-42]. Kurysheva *et al.* [43] found that in the differentiation between early glaucomatous eyes and healthy eyes the diagnostic accuracy of vessel density in the superficial plexus in the whole *en face* image was significantly higher than that determined for the peripapillary region and the optic disc. The authors attributed the observed differences to the dense concentration of retinal ganglion cells in the macula and their damage in the very early stages of neuropathy. In contrast, in the differentiation of eyes with moderate and advanced glaucoma, and eyes with early glaucoma, the greatest benefit as an OCTA marker has been demonstrated for the density of RPC in the inferior-temporal sector (whole *en face* image) [43]. Reduced microcirculation in the optic disc in patients with glaucoma was also observed by Topolska *et al.* [44].

The benefits of OCTA in patients with glaucoma were analyzed in the 2018 study by van Melkebeke *et al.* [45], comprising 54 full-text articles derived from the MEDLINE, Embase and Web of Science databases, and 26 abstracts presented at the Association of Research in Vision and Ophthalmology (ARVO) conferences until July 2017. OCTA was performed in patients with various glaucoma types (primary

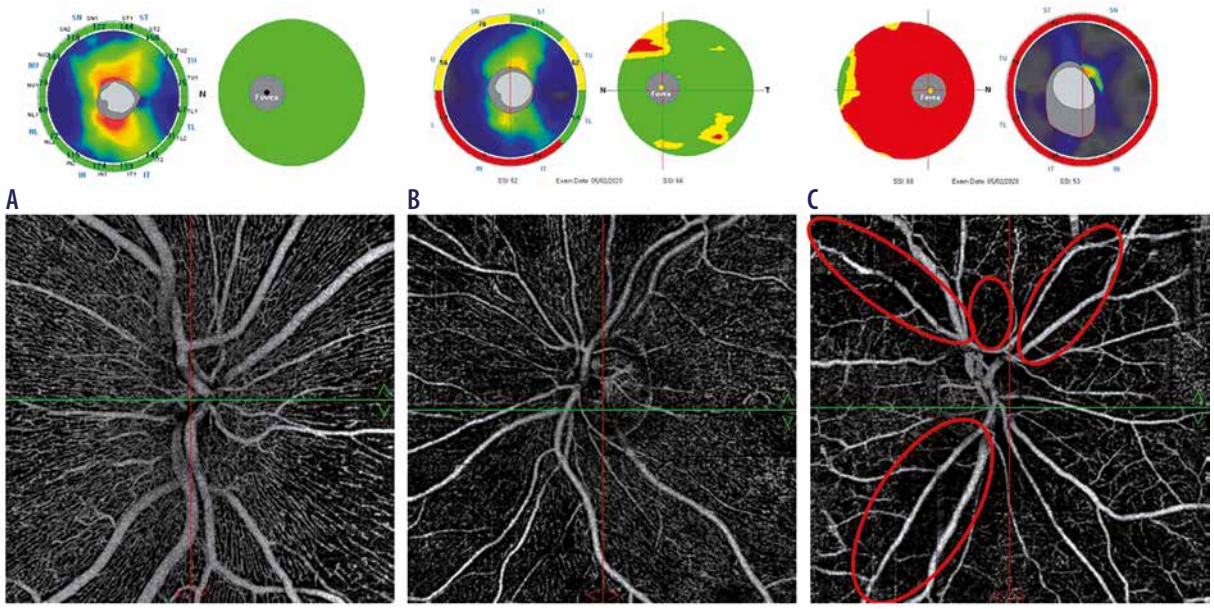

Figure 2. Angiograms of radial peripapillary capillaries (RPC) and thickness maps of the peripapillary retinal nerve fiber layer in the healthy eye (**A**), in the eye with early glaucoma (**B**) and in the eye with advanced glaucoma (**C**). Areas with atrophic capillary network or zones with no capillaries are marked with a red ellipse

open-angle glaucoma, normal-tension glaucoma, and angle closure glaucoma), preperimetric glaucoma, and ocular hypertension; in patients with suspected glaucoma; and in healthy individuals. OCTA was analyzed on the basis of four examination algorithms: OMAG, SSADA, OCTARA, and speckle variance. The aim of the analysis was to: 1) assess the repeatability of OCTA, 2) evaluate the diagnostic accuracy of hemodynamic parameters (VD, FI or BFI) as markers in patients with diagnosed or suspected glaucoma, and 3) determine the correlation between OCTA parameters and OCT structural parameters (peripapillary retinal nerve fiber layer (RNFL) thickness and ganglion cell complex (GCC) thickness), and functional visual field parameters measured by standard automatic perimetry. The analysis showed OCTA to be characterized by high repeatability and reproducibility both in healthy and glaucomatous eyes (coefficient of repeatability, CR < 7%). The OCTA parameters were significantly reduced in glaucomatous eyes, and their diagnostic accuracy was similar to OCT structural parameters as glaucoma markers. The highest diagnostic accuracy, measured as the area under receiver operating characteristic (AUROC), was shown for VD and FI in the peripapillary region and in the 6 mm × 6 mm area of the macular region. The OCTA parameters were also significantly decreased in the eyes with ocular hypertension and preperimetric glaucoma, as well as in individuals with a suspicion of glaucoma. In these patients, the most sensitive markers of damage were peripapillary VD and FI in the peripapillary region. Moreover, the analysis revealed that the OCTA hemodynamic parameters measured in the peripapillary region and in the macular and optic disc areas correlated with the OCT structural and functional visual field parameters. Importantly, the correlations found between the OCTA results and the visual field parameters were stronger than those between the OCT structural parameters and the functional parameters. Studies to date indicate that the OCTA parameters measured in the peripapillary region in the eyes with advanced glaucoma are a more sensitive biomarker of damage than the OCT structural parameters (RNFL, GCC) because of the technological limitation associated with advanced atrophy of the nervous tissue, glial cells, and blood vessels (the so-called "floor effect"), which is manifested in the OCTA technology at a later stage. The results of OCTA-based studies conducted to date in the eyes with normal-tension glaucoma have shown a significant damage to the microcirculation compared to healthy eyes, and slight hemodynamic differences between this subtype of glaucoma and primary open-angle glaucoma. In the group of eyes with angle closure glaucoma, the OCTA parameters appeared to be a less accurate diagnostic parameter than the OCT structural parameters, presumably because of the lower prevalence of perfusion abnormalities compared to primary open-angle glaucoma. The studies published to date have failed to provide evidence on the usefulness of OCTA in monitoring the progression of glaucoma [45].

The OCTA technology has a number of advantages. The examination is non-invasive and safe, quick to perform, precise and standardized. In addition, OCTA provides three-dimensional assessment of microcirculation, capacity for imaging and measuring the decrease in the number of capillaries, high image contrast, archiving of results, and broad availability of the examination procedure. The main limitations of OCTA examinations include the lack of a normative basis and the effect of pupillary width, haze of the optical media, saccadic movements and unstable patient fixation on reflected signal strength and examination artifacts.

Another technique enabling a quick, non-invasive, relative evaluation of retinal microcirculation in real time is laser speckle flowgraphy (LSFG). LSFG systems consist of a fun-

dus camera, a diode laser with a wavelength of 830 nm, and a digital camera. A total of 118 images (30 frames per second) are captured during a four-second measurement. The quantitative parameter in LSFG is the mean blur rate (MBR), which is calculated for the total area of the optic disc, for the large vessels within it, and for the tissue area occupied by capillaries. Kiyota *et al*. argue that [46] the latter parameter may be a useful hemodynamic marker in early glaucoma.

CONCLUSIONS

Patients with glaucoma have an impaired ocular blood flow, and the assessment of ocular circulation in these patients has been in the focus of interest of scientists and clinicians for many decades. Consequently, a number of advanced diagnostic technologies have been developed for measuring ocular perfusion. However, so far they have turned out to be primarily research tools used for scientific purposes. This is because published clinical studies have failed to provide reliable scientific evidence that blood flow measurement contributes to better clinical outcomes in patients with glaucoma [9]. Only properly designed clinical trials, with standardized measurement techniques and normative databases, can bring researchers closer to establishing the relationship between ocular hemodynamics, metabolism, and glaucoma progression, and to determining the clinical usefulness of measuring ocular blood flow in glaucoma patients. Studies conducted over the past decade have shown that optical coherence tomography angiography is an imaging technique with a great scientific and clinical potential, which may contribute to expanding the knowledge about the pathogenesis of glaucoma and lead to its earlier detection.

DISCLOSURE

The author declares no conflict of interest.

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