



Development of Classification Criteria for Neuroretinal Ischemia in Arterial Hypertension

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Annotation: Most researchers consider retinal vessels to be a unique object for studying the characteristics of systemic microcirculation. Changes in the fundus provide information about risk factors and the presence of vascular diseases of the heart, brain, kidneys and eyes.

Key words: consider retinal vessels, ocular fundus, ophthalmologist, biomicroscopy, ophthalmic.

Introduction. According to T. Y . Wong et al., CVD retinopathy accounts for 34.7–54.9% of the total number of vascular diseases of the retina and optic nerve, which leads to a significant increase in visual disability. For the first time, hypertensive retinopathy was described in 1898 by the English ophthalmologist R. M. _ Gunn in patients with hypertension and kidney disease. In 1939 N. Keith et al showed that these symptoms are a predictor of death in patients with hypertension. In recent years, the CIS countries use the classification of M.L. Krasnov, who identifies three stages in the development of changes in the ocular fundus in arterial hypertension, gradually turning one into another. It should be noted that none of the listed ones fully affects the changes in blood vessels in arterial hypertension, especially in the early period of the disease, when the target organs are still unaffected and cardiovascular complications that threaten the life of the patient have not developed.

Purpose . To improve the classification of retinal changes in arterial hypertension, taking into account the data of biomicroscopy , ophthalmic

scopy, static perimetry and optical coherence tomography with angiography.

Material and Methods . The material of the study was 180 patients. After a standard ophthalmological examination, all patients underwent a study on an optical coherence tomography with angiography (OCTA) RTVue-100 XR Avanti (Optovue , USA, Version 2019). Determination of the content of ET-1 was carried out using the enzyme immunoassay method (" Biomedica ", Austria). Determination of the level of homocysteine in the blood serum was carried out by enzyme immunoassay using a set of the firm " Human ".

Results and Discussion . The analysis of OCT -angiography indicators, the study of correlations between visual functions, parameters of retinal photosensitivity and Doppler parameters of the vessels of the organ of vision, as well as comparison with ophthalmoscopic and clinical data, made it possible

to classify 3 degrees of severity of retinal and optic nerve ischemia, according to perfusion disorders in various areas.

Registration of OCTA parameters in the control group showed the density of capillaries of the vascular networks in the superficial and deep layers of the retina and optic nerve, as well as choriocapillaries, were within 47.81 ± 2.17 ($p < 0.05$). At the same time, areas of hypoperfusion in the superficial layers of the retina of the paramacular region revealed an avascular area within 1.07 ± 0.014 mm² ($p < 0.05$).

There was a decrease in the density of capillaries of the choroid plexus of the superficial layers of the retina and optic nerve by 21% in 2 patients, which amounted to 45.21 ± 2.62 ($p < 0.05$), deep layers of the retina and optic nerve by 17% in 4, which was 45.89 ± 2.71 ($p < 0.05$), superficial and deep layers of the retina and optic nerve by 32% in 2 patients, 45.89 ± 2.71 ($p < 0.05$). It should be noted that in patients of this group, the density of vascular plexus choriocapillary layers was within the normal range and amounted to 47.13 ± 2.41 ($p < 0.05$). When registering areas of hypoperfusion in the superficial layers of the retina of the paramacular region, the avascular area was within 1.07 ± 0.014 mm² ($p < 0.05$). In the peripapillary region, areas with impaired perfusion in these patients in the superficial and deep layers of the vascular plexus were not found. In the study of visual functions of patients in this group, the indicators were within normal values, in particular, visual acuity with the best correction was 0.81 ± 0.019 , but there was a decrease in retinal photosensitivity, which decreased by 11-14%, which was within MD - 1.21 ± 0.019 dB, PSD - 1.67 ± 0.031 dB.

During ophthalmoscopy, the shape of the optic disc (ON) was round in 4 cases, and vertically oval in 4 cases, the color of the optic disk in all patients was pale pink, the boundaries were clear, no pathological changes were detected when visualizing the level, the number of vessels passing through through the edge of the ONH was within normal limits and amounted to 12 ± 0.09 ; the caliber of arteries and veins, as well as their ratio, were recorded without pathological changes. The macular and peripheral areas of the retina were without pathological changes.

When assessing the state of hemodynamics in the brachiocephalic arteries in these patients, hemodynamically insignificant asymmetry of the velocity parameters of blood flow in the internal carotid artery, no increase in the linear velocity of blood flow was noted, but a thickening of the intima-media complex was visualized, which amounted to 0.97 ± 0.012 mm. The indicators of markers Hz and ET-1 in this contingent of patients in the blood serum were within normal values and amounted to 0.092 ± 0.01 µg/l, and in the lacrimal fluid were slightly increased and amounted to 0.112 ± 0.021 µg/l.

Assessment of the somatic status of patients revealed the absence of any pathological changes in the general condition - blood pressure values, MRI and EchoCG parameters, and no cognitive impairment was detected. In this regard, this category of patients was included in the group with initial hypertension.

When calculating the blood circulation of the organ of vision, values were obtained that were slightly lower than normal parameters. So, using the formula of a mathematical model for calculating the ischemia of the organ of vision, which takes into account not only the parameters of the hemodynamics of the vessels of the eyeball, but also the indicators of hydrodynamics, in patients of this category, a result of 35.8 was obtained, with a norm of at least 36. This indicates that despite high visual acuity, ischemic processes associated with hypertensive vascular disease developed in the eyeball. This, in turn, led to a decrease in the photosensitivity of the retina, a decrease in the density of the capillaries of the vascular plexus, and an increase in the resistivity index of the main vessels of the eyeball with a good somatic status of the patient. This circumstance indicates that visual acuity cannot be a differentiating parameter in the development of the hypertensive process, while a decrease in the photosensitivity of the retina and a decrease in the density of capillaries of the choroid plexus of the

superficial and deep layers of the retina and optic nerve are pathognomonic in hypertensive lesions of the retina and optic nerve.

Hemodynamic parameters and perfusion status of the vascular plexus paramacular and peripapillary zones of this category of patients in dynamics after the therapy were normalized and amounted to 45.82 ± 2.58 ($p > 0.001$). area of hypoperfusion paramacular retina in dynamics decreased and amounted to 1.02 mm^2 . Given the above changes in hemodynamic parameters and hemoperfusion of the tissues of the organ of vision in hypertensive vascular lesions in patients of this group, they were classified as arterial hypertension - associated *mild* neuroretinal ischemia.

Analysis of the data obtained revealed a decrease in the density of capillaries of the vascular plexus of the superficial layers of the paramacular area of the retina by 47% in 3 patients, which amounted to 43.47 ± 2.81 ($p < 0.05$), deep layers of the paramacular and peripapillary area by 54% in 4, which amounted to 43.21 ± 2.09 ($p < 0.05$), superficial and deep layers of the paramacular, peripapillary areas, as well as choriocapillaries by 69% in 2 patients, which were within 43.61 ± 2.16 and 45.21 ± 2.17 , respectively ($p < 0.05$). When registering areas of hypo- and aperfusion in the superficial layers of the retina of the paramacular region, the avascular area was within $1.67 \pm 0.019 \text{ mm}^2$ ($p < 0.05$). In the peripapillary region, areas of hypoperfusion in these patients in the superficial layers of the vascular plexus amounted to 0.054 ± 0.0089 , and in the deep layers 0.054 ± 0.0089 (quadrants). The results of the study of visual functions revealed a decrease in central vision acuity to varying degrees, so in patients with predominant localization of the pathological process according to angio-OCT data in the central zone of the retina, in particular in the perifoveolar and paramacular zones, they were reduced by 53% and with the best correction amounted to on average 0.48 ± 0.011 ($p < 0.05$). But, with the location of the ischemic process and areas of hypoperfusion in the peripapillary region, the central visual acuity was reduced by 49%, which amounted to 0.54 ± 0.011 ($p < 0.05$), but scotomas, narrowing and loss of peripheral vision were noted. In cases where areas of hypoperfusion and aperfusion were noted both in the macular region and in the peripapillary zones of the fundus, as well as a decrease in the density of vascular capillaries plexus were noted both in the superficial, in the deep layers of the retina and in the choriocapillaries, the decrease in central visual acuity was significant and averaged 0.21 ± 0.017 ($p < 0.05$).

In the study of retinal light sensitivity, a decrease in indicators by 38% was found, which was within the limits of MD - $-4.17 \pm 0.012 \text{ dB}$, PSD - $4.51 \pm 0.026 \text{ dB}$ ($p < 0.05$). There were also negative arcuate scotomas in the lower (3 eyes) and upper quadrants (4 eyes) of the paramacular region, an increase in the size of the blind spot (4 eyes).

Ophthalmoscopy revealed the following changes in the optic nerve and retina: the shape of the optic disc was round in 4 cases, and vertically oval in 5 cases; prominence of the ONH, the number of vessels passing through the edge of the ONH was reduced and amounted to 10 ± 0.09 ($p < 0.05$), arteries of uneven caliber, narrowed in places, there are accompaniment bands, a pathological reflex is noted, veins are unevenly dilated in places. Macular and foveolar reflexes are smoothed, the peripheral area of the retina is without pathological changes.

When assessing the state of hemodynamics in the brachiocephalic arteries in these patients, hemodynamically insignificant asymmetry of the velocity parameters of blood flow through the internal carotid artery was noted, an increase in the linear velocity of blood flow was recorded up to 120 cm/s, and a thickening of the intima-media complex was also visualized, which amounted to $1.21 \pm 0.061 \text{ mm}$ ($p < 0.05$). When analyzing the content of Hz and EN-1 markers in this category of patients, an increase in the amount of the latter in the lacrimal fluid was found, which amounted to $2.412 \pm 0.041 \text{ } \mu\text{g/l}$ ($p < 0.05$), and in the blood serum the values did not exceed the norm and were within $0.931 \pm 0.018 \text{ } \mu\text{g/l}$ ($p < 0.05$).

Examination of the general condition of patients revealed the presence of arterial hypertension of the I degree in 3 patients, obesity in 5 patients of this group. When assessing MRI parameters, indirect signs of vascular and dyscirculatory encephalopathy were noted. However, it should be noted that no impairment of cognitive functions was detected in these patients. In this regard, this category of patients was included in the group with the clinical course of arterial hypertension.

When calculating the blood circulation of the organ of vision, there was a decrease in indicators to 34.12 ± 0.017 ($p < 0.05$), with a norm not lower than 36. This indicates the development of an ischemic process in the tissues of the eye associated with atherosclerotic vascular lesions at the time of the patient's examination. This, in turn, led to a decrease in the photosensitivity of the retina by %, a decrease in the density of capillaries of the vascular plexus by %, an increase in the resistivity index of the main vessels of the eyeball by %.

The indicators of the density of capillary perfusion of the choroid plexus and hemocirculation in patients of this group improved after the therapy, so the density of capillaries in the paramacular region was, and in the peripapillary region it was within ($p > 0.005$). area of hypoperfusion paramacular retina in dynamics decreased and amounted to mm^2 . Taking into account the above changes in hemodynamic parameters and hemoperfusion of the tissues of the organ of vision in hypertensive vascular lesions in patients of this group, they were classified as arterial hypertension - associated *moderate* neuroretinal ischemia.

vascular capillaries was revealed. plexus of the superficial layers of the paramacular area of the retina by 75% in 4 patients, which amounted to 38.91 ± 2.09 ($p < 0.05$), deep layers of the paramacular and peripapillary area by 81% in 4, which amounted to $37.11 \pm 2, 42$ ($p < 0.05$), superficial and deep layers of the paramacular, peripapillary areas, as well as choriocapillaries by 89% in 2 patients, which were within 33.01 ± 2.12 and 35.01 ± 2.09 , respectively ($p < 0.05$). When registering areas of hypo- and aperfusion in the superficial layers of the retina of the macular region, the avascular area was within $2.14 \pm 0.013 \text{ mm}^2$ ($p < 0.05$). In the peripapillary region, the areas of hypoperfusion in these patients in the superficial layers of the choroid plexus were 0.054 ± 0.0089 , and in the deep layers 0.054 ± 0.0089 (quadrants). In the study of visual functions, the following results were obtained: the decrease in the acuity of central vision depended on the clinical manifestations of hypertensive lesions of the vessels of the organ of vision. Thus, with the development of the clinic of anterior ischemic neuropathy of hypertensive origin, a decrease in visual acuity to 0.061 ± 0.011 was noted with the best correction. Accordingly, in this category of patients, altitudinal, sectoral loss of visual fields was noted. With the development of occlusion of the central retinal artery, there was also a decrease in visual acuity to 0.057 ± 0.038 with the best correction, visual field disturbances were in the form of sectoral loss, concentric narrowing and residual eccentric field of vision. With computer perimetry, there was a sharp decrease in retinal photosensitivity by more than 75%, which was within the limits of MD - $17.0 \pm 0.97 \text{ dB}$, PSD - $5.7 \pm 0.31 \text{ dB}$ ($p < 0.05$).

Ophthalmoscopy revealed the following changes in the optic nerve and retina: the shape of the optic disc was round in 4 cases, and vertically oval in 6 cases, the color of the optic disc was pale, the borders were fuzzy, there was some prominence of the optic disc, the number of vessels passing through the edge of the optic disc was reduced and was 7 ± 0.12 ($p < 0.05$), the arteries are narrowed, there are accompaniment bands, a pathological reflex is noted, the veins are uneven. Macular and foveolar reflexes are absent, dystrophic changes in the peripheral region of the retina are noted.

When assessing the state of hemodynamics in the brachiocephalic arteries in these patients, a hemodynamically significant asymmetry of the velocity parameters of blood flow in the carotid arteries was noted, an increase in the linear velocity of blood flow was recorded by more than 120 cm/s, and a thickening of the intima-media complex was also visualized, which amounted to $1.68 \pm 0.061 \text{ mm}$ ($p < 0.05$). There were also changes in the course of the carotid arteries in the form of a C -

shaped bend, kinking and coiling . When analyzing the content of Hz and ET-1 markers in this category of patients, an increase in the amount of the latter in the lacrimal fluid was found, which amounted to $5.23 \pm 0.06 \mu\text{g/l}$ ($p < 0.05$) and in the blood serum within $2.312 \pm 0.018 \mu\text{g/l}$ ($p < 0.05$).

Examination of the general condition of patients revealed the presence of II degree arterial hypertension in 5 patients, obesity in 6 patients of this group. When evaluating MRI parameters, signs of vascular and dyscirculatory encephalopathy were noted. In this regard, this category of patients was included in the group with the clinical course of arterial hypertension.

When calculating the blood circulation of the organ of vision, there was a decrease in indicators to 27.71 ± 0.034 ($p < 0.05$), with a norm not lower than 36, which indicates the development of an ischemic process in the tissues of the eye associated with atherosclerotic vascular lesions at the time of the patient's examination. This, in turn, led to a decrease in the photosensitivity of the retina, a decrease in the density of the capillaries of the vascular plexus , and an increase in the resistivity index of the main vessels of the eyeball.

When registering the density of capillary perfusion of the choroid plexus and hemocirculation in patients of this group after the therapy, no improvement was observed, so the density of capillaries in the paramacular region was, and in the peripapillary region it was within ($p > 0.005$). area of hypoperfusion paramacular retina decreased in dynamics and amounted to $2.01 \pm 0.01 \text{ mm}^2$. Given the above changes in hemodynamic parameters and hemoperfusion of the tissues of the organ of vision in hypertensive vascular lesions in patients of this group , they were classified as arterial hypertension - associated *severe* neuroretinal ischemia .

During the correlation, a direct correlation was noted with a decrease in the density of capillaries and a decrease in visual functions; an inverse correlation was also noted with a decrease in the density of the vascular network and an increase in the resistivity index of the ophthalmic artery. With a decrease in the density of capillaries of the surface layers of the retina, an increase in the resistivity index of the central retinal artery was noted, and with a rarefaction of the deep layers of the vascular plexus , an increase in the resistance index of the posterior short ciliary arteries was recorded. There was also a lesion of the vascular plexus of the optic nerve, the cause of which was also a hypertonic lesion of the posterior short ciliary arteries. Violation of the hemodynamics of the ophthalmic artery led to a decrease in the density of capillaries of the vascular plexus and superficial and deep layers of the retina, as well as the vasculature of the optic nerve. This circumstance proves the expediency of angiography in case of vascular pathology of the organ of vision, even in the initial stages of the disease, which will allow early diagnosis of the disease in the absence of clinical or ophthalmic symptoms.

Thus, the use of optical coherence tomography with the function of angiography makes it possible to diagnose the development of ischemia of the retina and optic nerve not only in the early period of the disease, when the target organs are still not affected, but also contributes to the differentiation of the level of ischemic tissues, the area and depth of damage to the layers of the retina and optic nerve for a more differentiated approach and

by 20%, retinal photosensitivity by 40%, vascular capillary density plexus by more than 45%, *severe* - a significant decrease in visual functions, up to light perception , retinal photosensitivity by 80%, vascular capillary density plexus on disease prediction.

Conclusion. Thus, the multifunctional study of hypertensive vascular lesions of the organ of vision makes it possible to distinguish 3 main degrees of development of ischemia in the tissues of the eyeball: *a mild degree* - with high visual acuity, a decrease in retinal light sensitivity by 15%, a decrease in the density of vascular capillaries plexus more than 15%; *the average degree* - a decrease in visual acuity of more than 75%.

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