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The effect of changes in retinal perfusion on postoperative recovery of foveal function in full-thickness macular holes

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ABSTRACT

BACKGROUND: Data on the effect of changes in retinal perfusion on retinal functional recovery at surgical treatment of full-thickness macular holes are limited.

AIM: To investigate the effect of changes in retinal perfusion on postoperative recovery of fovea function in full-thickness macular holes.

MATERIALS AND METHODS: A prospective study included data of 93 patients (93 eyes) with full-thickness macular holes. Optical coherence tomography-angiography (OCT-A), visual acuity testing, microperimetry, and multifocal electroretinography were performed before surgical treatment, after 1 and 6 months. We studied the relationship between changes in foveal avascular zone area, vessel density in the superficial capillary plexus (SCP) and deep capillary plexus (DCP) with changes in best corrected visual acuity (BCVA), retinal sensitivity (RS) at the fixation point and P1 amplitude in the fovea at different periods after treatment.

RESULTS: After surgical hole closure, a significant decrease in foveal avascular zone area, increase in vascular density in SCP and DCP was found within 1 month after treatment ($p < 0.001$). Significant increase in BCVA, RS and P1 amplitude was observed 1 and 6 months after hole closure ($p < 0.001$). The most pronounced correlation was found in the long-term postoperative period between the change in vessel density in the SCP and the change in BCVA, RS and P1 amplitude ($r = 0.42$, $r = 0.26$ and $r = 0.3$, $p < 0.05$), as well as between the change in vessel density in the DCP and the change in BCVA, RS and P1 amplitude ($r = 0.41$, $r = 0.34$ and $r = 0.43$, $p < 0.05$).

CONCLUSIONS: In the treatment of patients with full-thickness macular holes, there is a significant relationship between changes in retinal perfusion and the recovery of visual acuity, retinal sensitivity and bioelectrical activity in the foveal area, and it is more pronounced in the period from 1 to 6 months after macular hole closure. The obtained results suggest a possible prognostic role of OCTA results in the surgical treatment of full-thickness macular holes.

Keywords: retina; macular hole; perfusion; optical coherence tomography-angiography; multifocal electroretinography.

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Влияние изменения перфузии сетчатки на послеоперационное восстановление функций фовеа при сквозных макулярных разрывах

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АННОТАЦИЯ

Актуальность. Данные о влиянии изменения перфузии сетчатки на её функциональное восстановление при проведении хирургического лечения сквозных макулярных разрывов ограничены.

Цель — изучить влияние изменения перфузии сетчатки на послеоперационное восстановление функций фовеа при сквозных макулярных разрывах.

Материалы и методы. В проспективное исследование включили данные 93 пациентов (93 глаза) со сквозными макулярными разрывами. До хирургического лечения, через 1 и 6 мес. проводили оптическую когерентную томографию-ангиографию, визометрию, микропериметрию и мультифокальную электроретинографию. Изучали взаимосвязь изменения площади фовеальной аваскулярной зоны, плотности сосудов в поверхностном и глубоком капиллярных сплетениях с изменением максимальной корригированной остроты зрения (МКОЗ), световой чувствительности (СЧ) в точке фиксации и амплитуды P1 в зоне фовеа в различные периоды после лечения.

Результаты. После закрытия разрыва выявлено значимое уменьшение площади фовеальной аваскулярной зоны, увеличение плотности сосудов в поверхностном и глубоком капиллярных сплетениях в течение 1 мес. после лечения ($p < 0,001$). Значимое увеличение МКОЗ, СЧ и амплитуды P1 наблюдали через 1 и 6 мес. после закрытия разрыва ($p < 0,001$). Наиболее выраженная корреляция выявлена в отдалённом послеоперационном периоде между изменением плотности сосудов в поверхностном капиллярном сплетении и изменением МКОЗ, СЧ и амплитуды P1 ($r = 0,42$, $r = 0,26$ и $r = 0,3$ соответственно, $p < 0,05$), а также между изменением плотности сосудов в глубоком капиллярном сплетении и изменением МКОЗ, СЧ и амплитуды P1 ($r = 0,41$, $r = 0,34$ и $r = 0,43$ соответственно, $p < 0,05$).

Выводы. При лечении пациентов со сквозными макулярными разрывами между изменением перфузии сетчатки и восстановлением остроты зрения, СЧ и биоэлектрической активности в зоне фовеа существует значимая взаимосвязь, при этом она более выраженная в период от 1 до 6 мес. после закрытия разрыва. Полученные результаты свидетельствуют о возможной прогностической роли данных оптической когерентной томографии-ангиографии при проведении хирургического лечения сквозных макулярных разрывов.

Ключевые слова: сетчатка; макулярный разрыв; перфузия; оптическая когерентная томография-ангиография; мультифокальная электроретинография.

Как цитировать

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BACKGROUND

A full-thickness macular hole (FTMH) is one of the most common conditions in vitreoretinal surgery [1]. Modern technologies allow achieving 100% anatomical closure of FTMHs [2–4]. However, surgical techniques do not ensure high functional results, therefore studies of various predictors of success in FTMH treatment are ongoing [5, 6].

While FTMH is developing, secondary retinal changes occur around the hole, including intraretinal edema with cystic lesions, sensory retinal detachment, and disruption of the outer retinal layers [7]. Such anatomical signs as minimal sensory retinal defect at the ellipsoid zone, minimal damage to the external limiting membrane, and preserved normal foveal morphology on optical coherence tomography (OCT) images after hole closure are important predictors of functional retinal recovery [8]. However, several studies noted a change in retinal perfusion in FTMH, although the effect of changes in retinal perfusion both before and after FTMH surgery on functional recovery of the fovea remains poorly understood [9–12].

The *study aimed* to investigate the effect of changes in retinal perfusion on the postoperative recovery of foveal function in FTMH.

METHODS

A prospective study was performed at the St. Petersburg branch of the National Medical Research Center “S.N. Fedorov MNTK Eye Microsurgery” of the Ministry of Health of the Russian Federation and included 93 patients (93 eyes, mean age: 64.5 ± 6.5 years) with stage 1–4 idiopathic FTMH (according to D. Gass) after their first surgery. The study was performed in 2022–2024 and complied with the requirements of the Declaration of Helsinki (as amended in 2003). All participants signed an informed consent form for diagnostic examination and surgery.

Inclusion criteria were confirmed and previously untreated idiopathic FTMH.

Non-inclusion criteria were ocular opacities challenging visualization and functional examination, concomitant macular condition, glaucomatous optic neuropathy, inflammatory and vascular diseases, refractive errors greater than 6 D, silicone oil tamponade performed during a surgical procedure, and pre-operative retinal pigment epithelium atrophy in the hole area.

The patients were examined using a multimodal approach pre-operatively, 1 and 6 months postoperatively (Fig. 1).

Macular structural features and perfusion were studied using optical coherence tomography angiography (OCTA), Solix (Optovue, USA), and AngioVue Retina (6.4 × 6.4 mm) with an automated perfusion analysis using the device software (AngioVue Analysis SW, version: 11.0.0.29946). The foveal avascular zone (FAZ) area and foveal vessel density in the superficial and deep capillary plexuses (SCP and DCP) were evaluated by the ETDRS grid. OCT images of Q8 quality or higher were used for the analysis, and segmentation of the retinal layers was automated.

Functional examination included assessment of best corrected visual acuity (BCVA) using Huvitz CCP3100 chart projector (Huvitz, Korea). Light sensitivity (LS) was assessed at the fixation point using a microperimeter (Compass, CenterVue, Italy) and 10-2 test (68 points and 1 fixation point, 4-2 threshold strategy, achromatic Goldmann III stimulus). The electrical activity of the foveal retina was measured using multifocal electroretinography (ERG) with Neuro-ERG (Neurosoft, Russia) with an assessment of the P1 response amplitude in the central hexagon of the multifocal ERG pattern corresponding to the fovea (61 hexagons, retinal area of 17.9°).

FTMH surgery was performed according to a standard protocol with removal of the internal limiting membrane, hole closure with platelet-rich plasma or autologous conditioned plasma, and combined air-gas tamponade.

Statistical analysis of the results was performed in Statistica 12.0 (StatSoft Inc., USA). The quantitative results are shown as $M \pm SD$. Normality of distribution in the analyzed samples was assessed using the Kolmogorov–Smirnov test. The parameters at different follow-up time points were compared using the Student’s t-test for related samples. The Pearson correlation coefficient was calculated to determine the relationship between the parameters in the groups. To study the relationship between changes in functional and structural parameters, the differences between pre-operative and 6-month postoperative (overall changes from the baseline), pre-operative and 1-month postoperative, 1- and 6-month postoperative parameters were calculated (early and long-term postoperative changes), then a correlation analysis of the obtained data was performed. The results were considered statistically significant at $p < 0.05$.

RESULTS

General characteristics of patients are presented in Table 1. D. Gass stage 4 holes were the most common, with apical and basal hole diameters of 411.6 ± 126.5 and 819.8 ± 287.8 μm, respectively. In all cases, cystic sensory retina changes were observed around the hole at the inner nuclear and outer plexiform/Henle layers. Preoperative BCVA was 0.28 ± 0.13. The duration of symptoms by admission for FTMH surgery was 5.7 months (2 weeks to 14 months); however, patients could not remember when the symptoms occurred in some cases.

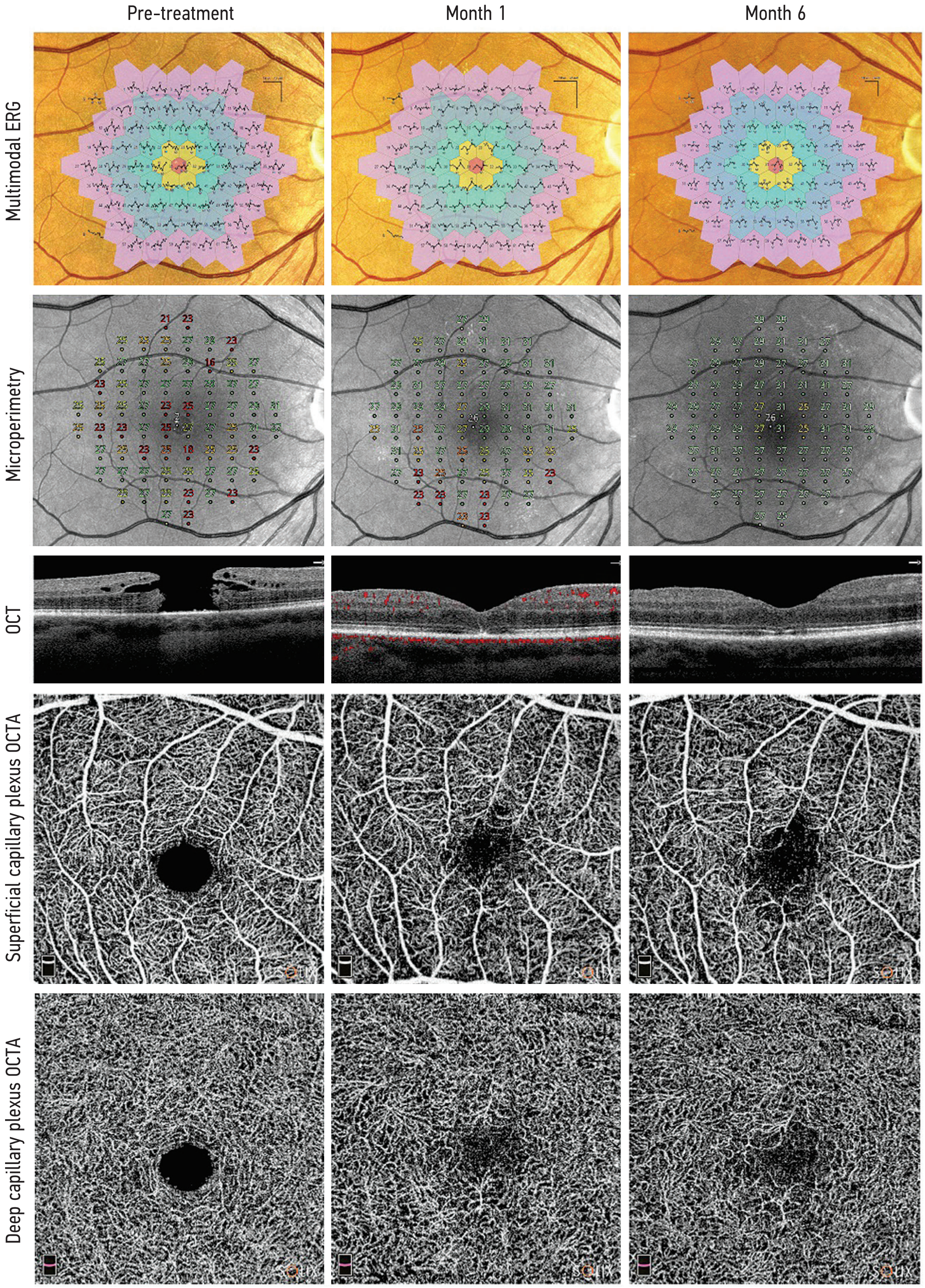

Fig. 1. An example of multimodal imaging in a patient with full-thickness macular hole during the observation period: patterns of multifocal electroretinography and microperimetry, linear scans and en face images of the studied structural changes of the fovea by OCT and OCT-A

Рис. 1. Пример мультимодальной визуализации у пациента со сквозным макулярным разрывом в течение периода наблюдения: паттерны мультифокальной электроретинографии (ЭРГ) и микропериметрии, линейные сканы и анфас-изображения изучаемых структурных изменений фовеа при проведении ОКТ и ОКТА

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Table 1. General characteristic of subjects with full-thickness macular holes
Таблица 1. Общая характеристика пациентов со сквозными макулярными разрывами

Parameter	Value
Age, years	64.5 ± 6.5
Sex, women/men (*n*)	74/19
Mean refraction, D	0.12 ± 1.85
Anterior-posterior axis, mm	23.54 ± 1.12
Best corrected visual acuity	0.28 ± 0.13
Pseudophakia/cataract (*n*)	18/75
Full-thickness macular hole stage, 1–4 (*n*)	I (10). II (18). III (19). IV (46)
Duration of symptoms, months	5.7 (0.5–14)
Apical diameter, μm	411.6 ± 126.5
Basal diameter, μm	819.8 ± 287.8

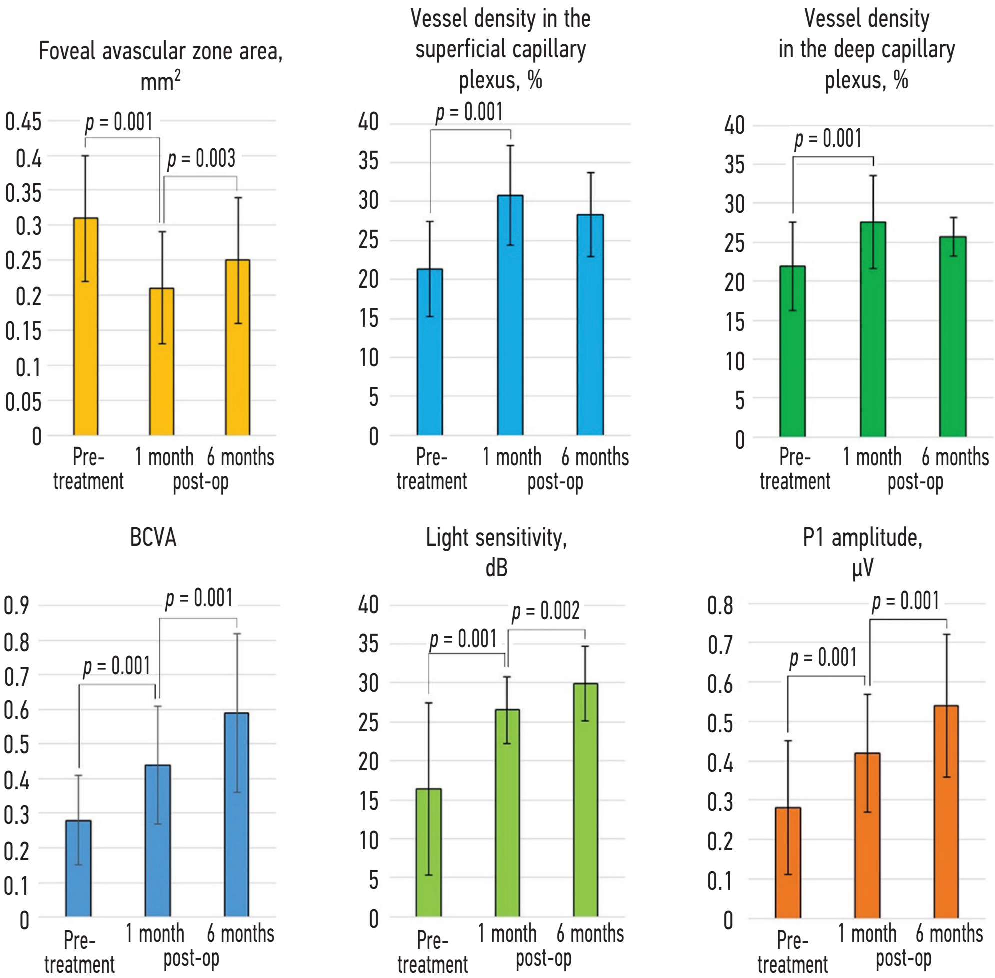

Fig. 2. Changes in the studied perfusion parameters and functional parameters of the fovea during the observation period
Рис. 2. Изменение исследуемых показателей перфузии и функциональных показателей фовеа в течение периода наблюдения

Type 1 and 2 FTMH closures were reported in 67 and 26 cases, respectively, with no intra- or postoperative complications and no recurrences of macular holes during follow-up.

OCTA showed that the FAZ area was 0.31 ± 0.09 mm^2 pre-operatively, significantly decreased to 0.21 ± 0.08 mm^2 1 month postoperatively (p = 0.001), and then significantly increased to 0.25 ± 0.09 mm^2 6 months postoperatively (p = 0.003, Fig. 2). Foveal SCP vessel density was 21.3 ± 6.1% pre-operatively, increased to 30.8 ± 6.4% 1 month postoperatively (p = 0.001), and then did not significantly change (28.3 ± 5.4%) 6 months postoperatively.

Table 2. Correlation of perfusion parameters and functional parameters recorded in the fovea after full-thickness macular holes' closure at different examinations periods

Таблица 2. Корреляция показателей перфузии и функциональных показателей, регистрируемых в фовеа после закрытия сквозных макулярных разрывов (СМР) в разные временные периоды

OCTA data	Changes in functional parameters		
	BCVA	Light sensitivity, dB	P1 amplitude
Time period: pre-operatively and 6 months postoperatively			
Foveal avascular zone area	0.05	–0.18	–0.07
SCP vessel density	0.32*	0.17	0.18
DCP vessel density	0.38*	0.18*	0.32*
Time period: pre-operatively and 1 month postoperatively			
Foveal avascular zone area	0.07	–0.19	–0.11
SCP vessel density	0.21*	0.06	0.14
DCP vessel density	-0.04	0.05	0.19*
Time period: 1–6 months postoperatively			
Foveal avascular zone area	0.11	–0.15	–0.12
SCP vessel density	0.42*	0.26*	0.3*
DCP vessel density	0.41*	0.34*	0.43*

Note. ПКС, superficial capillary plexus; ГКС, deep capillary plexus. *$p < 0.05$.
Примечание. ПКС — поверхностное капиллярное сплетение; ГКС — глубокое капиллярное сплетение. *$p < 0,05$.

DCP vessel density was 21.9 ± 5.7% pre-operatively, increased to 27.6 ± 6.0% 1 month postoperatively ($p = 0.001$), and did not significantly change (25.7 ± 2.5%) 6 months postoperatively.

Functional examination showed that pre-operative BCVA was 0.28 ± 0.13 and increased significantly to 0.44 ± 0.17 and 0.59 ± 0.23 1 and 6 months postoperatively, respectively ($p = 0.001$; Fig. 2). Pre-operative LS at the fixation point was 16.4 ± 11.1 dB, increased to 26.5 ± 4.3 dB1 month postoperatively ($p = 0.001$), and reached 29.9 ± 4.8 dB6 months postoperatively ($p = 0.002$). The foveal P1 amplitude before hole closure was 0.28 ± 0.17 μV and increased significantly to 0.42 ± 0.15 and 0.54 ± 0.18 μV 1 and 6 months postoperatively, respectively ($p = 0.001$).

In the early postoperative period, changes in SCP vessel density significantly correlated with BCVA changes ($r = 0.21$, $p = 0.005$), and changes in DCP vessel density significantly correlated with the P1 amplitude based on multifocal ERG data ($r = 0.19$, $p = 0.01$; Table 2). In the long-term period after hole closure, significant moderate correlation was noted between changes in the assessed functional parameters and changes in SCP and DCP vessel density (Table 2). Comparison of the parameter changes throughout follow-up (from baseline to postoperative month 6) revealed significant correlation between DCP vessel density and changes in BCVA ($r = 0.38$, $p = 0.001$), LS ($r = 0.18$, $p = 0.01$), and P1 amplitude ($r = 0.32$, $p = 0.001$). Moreover, changes in SCP vessel density also correlated with BCVA changes over 6 months after hole closure ($r = 0.32$, $p = 0.002$; Table 2).

DISCUSSION

Changes in retinal perfusion play an important role in the pathogenesis of various macular vascular diseases, such as diabetic retinopathy or vascular occlusion, and quantitative perfusion parameters determined using OCTA may have prognostic value for recovery of the retinal function [13]. Previously, retinal perfusion was shown to change around the hole area in FTMH, as the FAZ area was increased and SCP and DCP vessel density was decreased [10, 14]. These changes are suggested to be induced not only by a mechanical tissue defect, but also by edema with intraretinal cystic lesions, which displace and compress vessels in the capillary plexuses, with more pronounced changes at the deep plexus [10, 15, 16].

The functional results of macular hole surgical closure depend on recovery of the normal anatomical structure of the retina. For example, initial status and postoperative recovery of the photoreceptor ellipsoid zone, external limiting membrane, and retinal ganglion cell complex were found to be important [17, 18]. Previous several studies also revealed correlation of SCP and DCP vessel density with LS and retinal electrical activity, which was more pronounced in the areas of cystic changes and detached sensory retina [9, 12, 19].

In contrast to previous studies, we evaluated the effect of changes in retinal perfusion on its functional recovery at early and late postoperative periods of up to 1 month and 1–6 months after surgical hole closure.

In this study, type 1 hole closure was reported in 67 out of 93 cases with full restoration of the foveal layers [5]. In these cases, the FAZ area significantly decreased and SCP and DCP vessel density increased within 1 month after hole closure. These changes were caused by mechanical displacement of the hole edges and all vascular structures to the hole center, as well as by regression of intraretinal cystic lesions around the hole in the early postoperative period. In the long-term postoperative period, the FAZ area increased, and SCP and DCP vessel density did not change significantly compared with postoperative month 1 values, which indicates recovery of the layers and vessels of the macular sensory retina. Thus, foveal vascular plexuses recover during the postoperative period, and the most active remodeling and recovery of perfusion are noted in the early postoperative period. Later, the plexuses change little, but the degree of their recovery affects the sensory retina homeostasis and function.

Examination of patients revealed a significant increase in BCVA, LS, and the P1 amplitude in the fovea area both 1 month and 6 months after hole closure. Correlation with changes mainly in DCP vessel density supports the earlier assumption that pre-operative preserved blood flow in the capillary plexuses around the hole and reperfusion of capillaries compressed by cystic lesions may be favorable prognostic markers of functional retinal recovery [10].

An analysis of the relationship between perfusion and functional parameters found significant correlation and a higher correlation coefficient in the long-term postoperative period, 1–6 months after hole closure. This finding may be explained by both prolonged retinal recovery and more significant increased tissue perfusion in the long-term period, with other factors (e.g., a mechanical tissue defect) affecting the prognosis being less significant. Moreover, the observed correlation of changes in the P1 amplitude based on multifocal ERG data with changes in DCP vessel density demonstrates the effect of blood supply on electric activity of bipolar cells in the retinal Muller cells complex [20].

Notably, the limitation of this study was consecutive inclusion of all eligible FTMH cases of any hole closure type. Future specific study of different hole closure types may provide more information about the perfusion role in retinal recovery. In addition, another limitation was the fact that other structural retinal changes, including those related to the surgical procedure, were not evaluated.

CONCLUSION

In FTMH, there is a significant relationship between changes in retinal perfusion and visual recovery, LS, and foveal electric activity, which is more pronounced 1–6 months after hole closure. The obtained results suggest a possible prognostic role of OCTA data for FTMH surgery.

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: E.V. Boiko, significant contribution to the concept and design of the work, editing, final approval of the version to be published; T.A. Doktorova, significant contribution to the concept and design of the work, collection, analysis and processing of material, statistical data processing, writing; A.A. Suetov, significant contribution to the collection, analysis and processing of material, statistical data processing, writing; S.V. Sosnovskii, significant contribution to the editing, final approval of the version to be published.

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Competing interests. The authors declare that they have no competing interests.

Ethics approval. This study was approved by the local ethical committee of S. Fyodorov Eye Microsurgery Federal State Institution, Saint Petersburg Branch (Protocol No. 11 dated 2022 Feb. 08).

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: Э.В. Бойко — концепция и дизайн работы, редактирование текста и окончательное утверждение версии статьи; Т.А. Докторова — концепция и дизайн работы, сбор, анализ и обработка материала, статистическая обработка данных, написание текста; А.А. Суетов — сбор, анализ и обработка материала, написание текста; С.В. Сосновский — существенный вклад в редактирование текста и окончательное утверждение версии, подлежащей публикации.

Источник финансирования. Авторы заявляют об отсутствии внешнего финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

Этический комитет. Протокол исследования одобрен локальным этическим комитетом Санкт-Петербургского филиала ФГАУ НМИЦ «МНТК «Микрохирургия глаза» им. акад. С.Н. Фёдорова» Минздрава России 08.02.2022 (№ 11).

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