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Optical coherence tomography angiography features of the chorioretinal complex and choriocapillaris perfusion before and after vitrectomy with conventional versus fovea-sparing internal limiting membrane peeling for idiopathic macular hole

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Purpose: *To assess optical coherence tomography angiography (OCTA)-measured changes in the chorioretinal complex and choriocapillaris perfusion density in the macula before and after vitrectomy with fovea-sparing versus conventional internal limiting membrane (ILM) peeling for idiopathic macular hole (IMH).*

Material and Methods: *Eyes with stage-2 to stage-4 holes as per the classification by Gass received 25-G vitrectomy with conventional or fovea-sparing ILM peeling and gas tamponade with 20% SF6 or 15% C3F8. IMH diameter, foveal avascular zone (FAZ) area in the deep retinal plexus and choriocapillaris perfusion density (CPD) were assessed before and 1 month after surgery.*

Results: ***T****otally, 70 patients had an IMH surgery in 71 eyes. The mean age ± standard deviation (SD) was 65.7 ± 6.8 years, median IMH duration (interquartile range or IQR), 3.0 (1.0-6.0) months, median best-corrected visual acuity or BCVA (IQR), 0.19 (0.1-0.25), and median maximum IMH diameter (IQR), 673.5 (549.5–1010.5) µm. In eyes with IMH and fellow eyes, the median FAZ area (IQR) was 0.51 (0.15–0.53) mm2, and 0.46 (0.10–0.74) mm^2, respectively (p = 0.49), and mean CPD ± SD, 0.11 ± 0.06, and 0.29 ± 0.13 (p = 0.0001), respectively. Thirty-four eyes received conventional ILM peeling and 37 eyes, fovea-sparing ILM peeling, and there was no significant intergroup difference in baseline characteristics. One month after surgery, IMH closure was achieved in 63/71 eyes (i.e., the closure rate was 88.7% for total operated eyes, and 88.2% and 89.2%, respectively, for eyes in conventional ILM peeling and fovea-sparing ILM peeling groups), and median BCVA (IQR) improved to 0.60 (0.4–0.8) (p = 0.00001). After IMH closure, in operated eyes, median FAZ area (IQR) decreased to 0.30 (0.12–0.6) mm2, but the difference was not significant, whereas mean CPD ± SD increased significantly from 0.11 ± 0.06 to 0.25 ± 0.10 (p = 0.0001). No significant difference in OCTA-based retinal microcirculation and choriocappillaris characteristics was observed between the conventional ILM peeling and fovea-sparing ILM peeling groups.*

Conclusion: *The presence of macular hole is accompanied by abnormal perfusion in the choriocapillaris, but the CPD recovers after IMH closure. Postoperative CPD recovery is not influenced by the type (conventional or fovea-sparing) of ILM peeling***.**

Keywords:

vitrectomy, optical coherence tomography, optical coherence tomography angiography, idiopathic macular hole, internal limiting membrane, retina

Introduction

An idiopathic macular hole (IMH) is a disease accompanied by a partial or total loss of central vision. It occurs almost three times more often in women than in men and develops usually in elderly individuals [1-3]. The disease requires surgical treatment, vitrectomy with internal limiting membrane (ILM) peeling and air-gas tamponade, with the patient having to maintain a face-down positioning for at least a 24-h period postoperatively [5-9]. In recent years, some authors [10, 11] have begun to prefer using fovea-sparing rather than conventional ILM peeling, since they believe that the former is a less traumatic treatment option for MH.

The use of optical coherence tomography angiography (OCTA) allows improving our understanding of the pathogenesis of IMH and whether macular hole closure will occur. A recent study [12] has reported that vitrectomy with temporal ILM peeling technique for full-thickness macular holes resulted in lower density of vessels in the deep retinal plexus in the area where ILM was peeled as compared to the rest of the fovea. Others, however, believe that it is the presence of an IMH that causes vascular changes in the retina and choriocapillaries [13-14].

The purpose of this study was to assess OCTA-measured changes in the chorioretinal complex and choriocapillaris perfusion density in the macula before and after vitrectomy with fovea-sparing versus conventional ILM peeling for IMH.

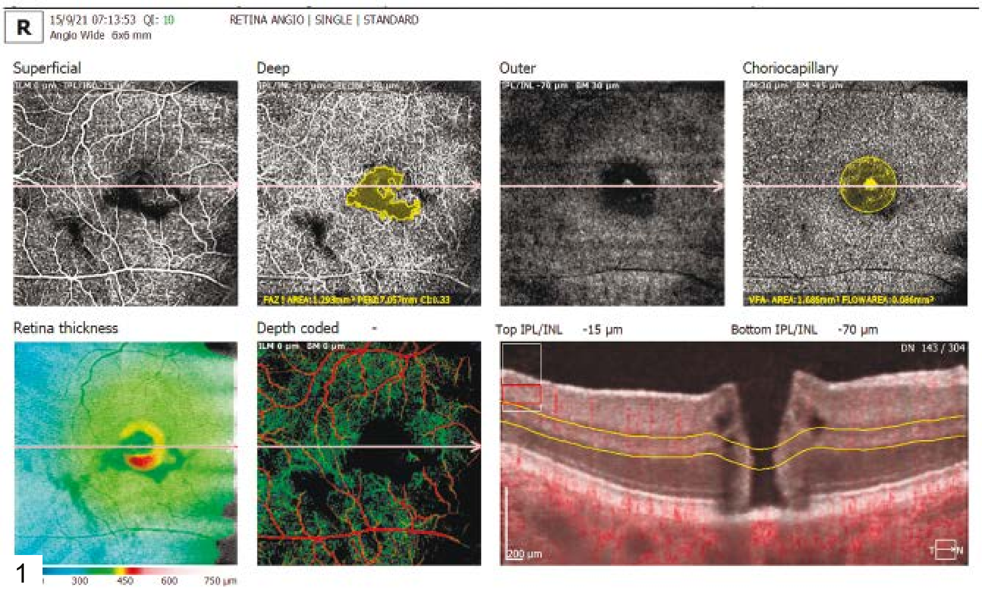
Material and Methods

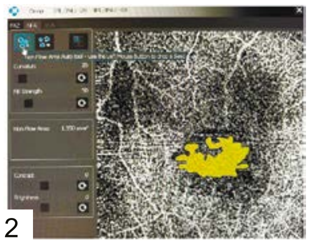
This prospective, open-label, interventional study was conducted at the Vitreoretinal and Laser Pathology Department of the Filatov Institute and conformed to the Declaration of Helsinki. Written informed consent to surgery (vitrectomy) was obtained from all study subjects. Inclusion criteria were stage-2 to stage-4 holes as per the classification by Gass [15]. Exclusion criteria were history of vitrectomy, myopia exceeding -6 diopters, wet age-related macular degeneration, glaucoma, diabetic retinopathy or other vascular choroidal and retinal disorders.

A preoperative examination included visual acuity assessment, refractometry, tonometry, biomicroscopy, dilated fundus examination with a slit-lamp and 90 D lens, binocular indirect ophthalmoscopy with a 20 D lens, and macular optical coherence tomography (OCT; OPTOPOL Technology, Zawiercie, Poland) with the estimation of the maximal and minimal diameters of the macular hole and foveal retinal thickness (FRT). OCTA Retina Angio Wide mode was used to measure foveal avascular zone (FAZ) area in the deep capillary plexus (DCP). Measurements were performed twice after setting up a target point either in the foveal zone or in the center of macular hole; the scanning time was 2.4 sec. Choriocapillaris perfusion area was measured in the macular site of a one-disc-diameter area. Choriocapillaris perfusion density (CPD) was calculated as the ratio of choriocapillaris perfusion area with the area under examination. The area under examination in each eye was equal to a one-disc-diameter area. An Angio OCT-A device from Optopol Technology (Zawiercie, Poland) was used in the study (Fig. 1-3).

A 25-G three-port pars plana vitrectomy (Constellation, Alcon, Switzerland) was performed with the use of a wide-angle observation system (BIOM, Oculus, Weltzer, Germany). Surgical stages included induction of posterior hyaloid detachment, 360-degree excision of the posterior hyaloid, and trypan blue ILM staining. Patients had either conventional ILM peeling around a 1.5-2.0 disc diameter macular hole or fovea-sparing peeling using our previously-reported technique [16]. The surgery was completed with gas tamponade with 20% SF6 or 15% C3F8. Patients were asked to maintain a face-down position for one to two weeks following surgery depending on the type of gas tamponade. Re-examination was performed at one month after surgery.

Statistical analyses were conducted using Statistica 8.0 (StatSoft, Tulsa, OK, USA) software and spreadsheets. Nominal data are presented as absolute numbers and percentages. The normal distribution of data was tested using the Kolmogorov–Smirnov test. Mean (M), standard





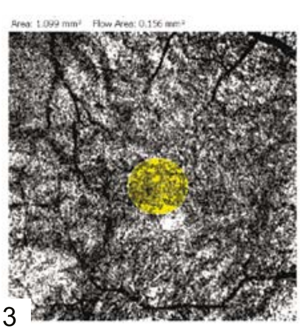


Fig. 1. Measuring the foveal avascular zone area in the deep retinal plexus and choriocapillaris perfusion area in the 1 disc diameter (DD) area (general view of tomography software interface)

Fig. 2. Measuring the foveal avascular zone area in the deep retinal plexus (magnified view of tomography software interface)

Fig. 3. Measuring the choriocapillaris perfusion density in the 1 disc diameter (DD) area (magnified view of tomography software interface)

Table 1. Best-corrected visual acuity (BCVA) and optical coherence tomography (OCTA)-measured foveal avascular zone (FAZ) area and choriocapillaris perfusion density (CPD) in eyes with idiopathic macular holes (IMHs) versus apparently normal fellow eyes

	BCVA		FAZ area (mm²)		CPD
	Median	(IQR)	Median	(IQR)	M±SD
Eyes with macular holes, n=50	0.17	0.1 - 0.25	0.51	0.15-0.53	0.11±0.06
Apparently normal fellow eyes, n=40	0.92	0.7 – 1.0	0.46	0.10-0.74	0.29±0.13
Significance of difference between groups	p=0.00001		p=0.49		p=0,0001

Note: n, number of eyes; IQR, interquartile range; FAZ, foveal avascular zone; CPD, choriocapillaris perfusion density

deviation (SD), and 95% confidence interval (CI) values were calculated for normally distributed data. Student's t test was used to compare mean values of normally distributed data. The median (interquartile range (IQR)) values were calculated for non-normally distributed data. Mann-Whitney U test was used for the comparison of two samples when the underlying distributions were not normal. Spearman or Pearson correlation coefficients were calculated to assess correlations. Diagnostic performance was determined with area under the receiver operating characteristic curve (ROC AUC) with 95% CI. A model with an AUC > 0.5 was considered satisfactory. In addition, the cut-off value from the ROC curve was obtained for highest possible sensitivity and specificity.

Results

Totally, 70 patients (15 males and 55 females) had an IMH surgery in 71 eyes. The mean age (SD) was 65.7 (6.8) years. The median IMH duration (IQR) was 3.0 (1.0-6.0) months, and, preoperatively, the median BCVA (IQR) in eyes with IMH was significantly lower than that in fellow eyes (0.19 (0.1-0.25) versus 0.92 (0.7-1.0). The median minimum diameter of the IMH (IQR) was 377.0 (281.0–530.0) µm, and the maximum diameter IMH (IQR), 673.5 (549.5–1010.5) µm. Significant differences in BCVA and CPD, but not in FAZ area in the deep retinal plexus, were observed between the eyes with IMH and fellow eyes (Table 1).

Because this comparison includes only fellow eyes that were deemed to be healthy, the number of fellow eyes is lower than that of eyes with IMH. Since the baseline FAZ area was assessed in 50 eyes with IMH (33 eyes and 15 eyes that had conventional ILM and fovea-sparing peeling, respectively), the baseline BCVA for these eyes differs from that for a study sample of 71 with IMH. The baseline CPD was assessed in 48 eyes with IMH (31 eyes and 17 eyes that had conventional ILM and fovea-sparing peeling, respectively).

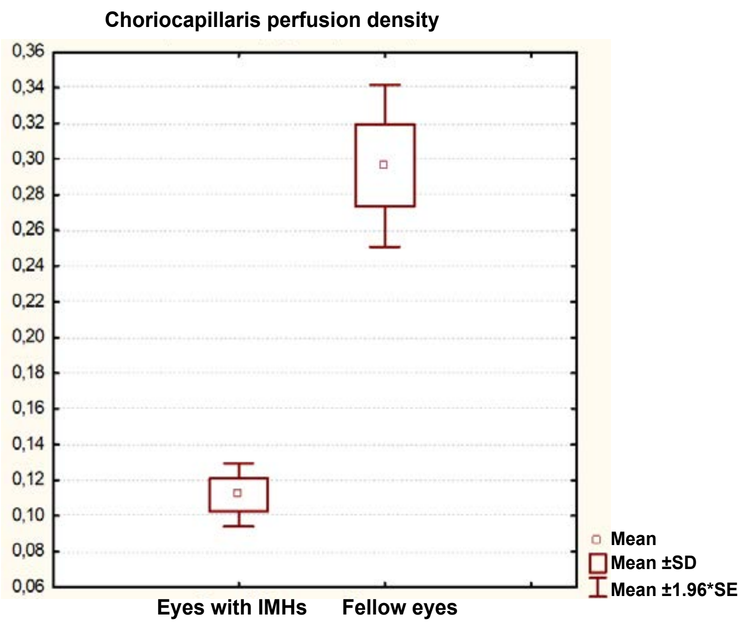


Fig. 4. Choriocapillaris perfusion density in eyes with idiopathic macular holes (1) and apparently normal fellow eyes (2)

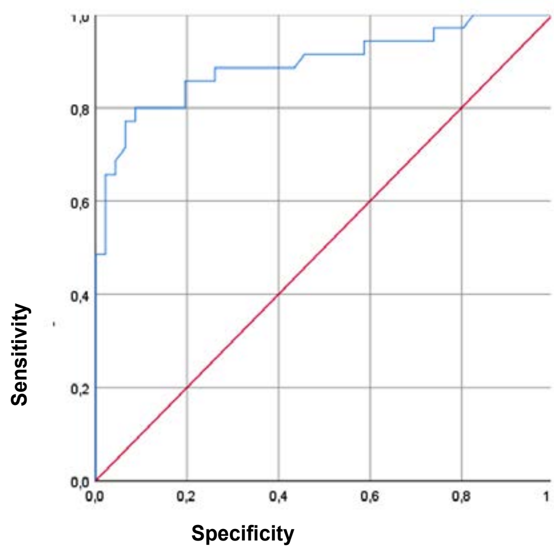


Fig. 5. Receiver Operating Characteristic (ROC) curve for choriocapillaris perfusion density

Baseline CPD was significantly lower in eyes with IMH than in fellow eyes. A moderate positive correlation was observed between the minimum IMH diameter and CPD ($r = 0.63$, $p < 0.05$) and a weak positive correlation, between the CPD and BCVA ($r = 0.41$, $p < 0.05$). Figure 4 demonstrates a statistically significant decrease in choriocapillaris flow density in the fovea.

A significant difference in the CPD between the eyes with IMH and healthy fellow eyes allowed developing a model for predicting the odds of the presence of a macular hole based on the value of the CPD. Diagnostic performance of the choriocapillaris flow area in the projection of the macula in predicting the presence of macular hole was determined with ROC AUC with 95% CI (Fig. 5).

The ROC AUC for CPD was 0.89 (95% CI, 0.81–0.97), with a high AUC value indicating that CPD has a high performance for predicting the presence of macular hole. A cut-off value of 0.156 for CPD was calculated using ROC curve for the diagnosis of macular hole which gave a sensitivity of 83% and specificity of 80% for differentiating the presence of IMH from the absence of IMH.

One month after surgery, IMH closure was achieved in 63/71 eyes (i.e., the closure rate was 88.7%). Of the eight eyes in which IMH closure was not achieved after primary surgery, six received an additional gas tamponade with 15% C3F8, and two, re-vitrectomy with additional ILM peeling and gas tamponade with 15% C3F8. Thereafter, IMH was achieved in all these eyes. A post-operative OCTA was, however, performed only in the eyes in which IMH closure was achieved after primary surgery. Postoperatively, FAZ area and CPD were assessed in 33 eyes (19 eyes and 14 eyes that had conventional ILM and fovea-sparing peeling, respectively).

In the eyes that received macular hole surgery, median BCVA (IQR) improved from 0.19 (0.1-0.25) to 0.60 (0.4-0.8) ($p = 0.000000$), with a significant increase in the CPD, but the difference in FAZ area was not significant (Table 2).

One month after surgery, mean CPD in the eyes that received macular hole surgery increased, but was significantly lower than that in the fellow eyes (0.20 ± 0.13 versus 0.29 ± 0.13, respectively; $p = 0.001$). A statistically significant correlation was observed between the postoperative CPD and postoperative BCVA ($r = 0.27$, $p < 0.05$).

After IMH closure, OCT-measured FRT (SD) was significantly greater for the eyes that underwent surgery than for the fellow eyes (325 (98) µm versus 260 (68.5)

Table 2. Best-corrected visual acuity (BCVA) and optical coherence tomography (OCTA)-measured foveal avascular zone (FAZ) area in the deep retinal plexus and choriocapillaris perfusion density (CPD) before and after successful vitrectomy with primary idiopathic macular hole (IMH) closure

BCVA Median (IQR)		FAZ area (mm^2) Median (IQR)		CPD M ± SD	
Before surgery	After surgery	Before surgery	After surgery	Before surgery	After surgery
n=70	n=70	n=50	n=33	n=48	n=33
0.17 0.1 - 0.25	0,60 0.4 - 0.8	0.51 0.15-0.53	0.30 0.12-0.6	0.11±0.06	0.20±0.13
p=0.000000		p=0.46		p=0.005	

Note: n, number of examined eyes; IMH, idiopathic macular hole; IQR, interquartile range; FAZ, foveal avascular zone; CPD, choriocapillaris perfusion density

Table 3. Baseline best-corrected visual acuity (BCVA), minimum IMH diameter, maximum IMH diameter, foveal avascular zone (FAZ) area and choriocapillaris perfusion density (CPD) in eyes that underwent vitrectomy with conventional ILM peeling versus fovea-sparing ILM peeling

Group of patients	BCVA	Minimum IMH diameter (µm)	Maximum IMH diameter (µm)	FAZ area (mm^2)	CPD
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	M ± SD
Conventional ILM peeling n=34	0.14 (0.07-0.25)	421 (287-459)	805 (520-1048)	0.39 (0.18-0.67)	0.12±0.06
Fovea-sparing ILM peeling n=37	0.17 (0.1-0.25)	376 (261-520)	654 (568-806)	0.50 (0.12-0.88)	0.09±0.04
Difference between groups	p=0.89	p=0.68	p=0.36	p=0.72	p=0.14

Note: n, number of examined eyes; ILM, internal limiting membrane; IMH, idiopathic macular hole; IQR, interquartile range; FAZ, foveal avascular zone; CPD, choriocapillaris perfusion density

Table 4. Foveal avascular zone (FAZ) area and choriocapillaris perfusion density (CPD) in eyes with macular hole closure after vitrectomy with conventional ILM peeling versus fovea-sparing ILM peeling

Group of patients	FAZ area (mm²)		CPD	
	Before surgery	After surgery	Before surgery	After surgery
	Median (IQR) n	Median (IQR) n	M±SD n	M±SD n
Conventional ILM peeling	0.39 (0.18-0.67) 33	0.34 (0.15-0.67) 19	0.12±0.06 31	0.19±0.16 19
	p=0.8		p=0.05	
Fovea-sparing ILM peeling	0.50 (0.12-0.88) 17	0.22 (0.12-0.46) 14	0.09±0.04 17	0.18±0.08 14
	p=0.08		p=0.002	

Note: n, number of examined eyes; ILM, internal limiting membrane; IMH, idiopathic macular hole; IQR, interquartile range; FAZ, foveal avascular zone; CPD, choriocapillaris perfusion density

Table 5. Choriocapillaris perfusion density CPD in eyes with IMH closure and fellow eyes after vitrectomy with conventional ILM peeling versus fovea-sparing ILM peeling

Group of patients	CPD		ЩПХ	
	Eyes with macular hole closure		Fellow eyes	
	n	M±SD	n	M±SD
Conventional ILM peeling	19	0.19±0.16	35	0.29±0.13
	p=0.003			
Fovea-sparing ILM peeling	14	0.18±0.08	35	0.29±0.13
	p=0.0001			

Note: n, number of examined eyes; ILM, internal limiting membrane; IMH, idiopathic macular hole; IQR, interquartile range; FAZ, foveal avascular zone; CPD, choriocapillaris perfusion density

μm, n = 22, p = 0.015). A negative correlation was observed between the FRT and FAZ area in the eyes that exhibited IMH closure after IMH surgery (r= -0.69; n = 24, $p < 0.05$).

Preoperatively, there was no significant difference in minimum IMH diameter, maximum IMH diameter, FAZ area or CPD between the conventional peeling group and the fovea-sparing group (Table 3).

Postoperatively, the median BCVA (IQR) improved to 0.55 (0.35 – 0.7) in the fovea-sparing peeling group, and to 0.43 (0.35 – 0.6) in the conventional peeling group, and the difference between the groups was significant (p = 0.039). In addition, the mean FRT (SD) was 357.4 ± 103.2 for the conventional peeling group, and 291.8 ± 42.7 for the fovea-sparing peeling group (i.e., eyes in the latter group tended to have a FRT more similar to that in healthy fellow eyes), but the difference between the groups was not significant (p = 0.08).

Postoperatively, changes in FAZ area and CPD in the former group were similar to those in the latter group as well as in total eyes that underwent surgery (Table 4).

In the fovea-sparing peeling group, the CPD significantly improved, and there was a tendency to a decrease in the FAZ area. The CPD also significantly improved in the conventional peeling group. Moreover, postoperatively, there was no significant difference in the FAZ area or CPD between the fovea-sparing peeling group and the conventional peeling group, and FAZ area and CPD in the eyes that underwent surgery were lower than in the fellow eyes (Table 5).

Discussion

Most studies of the retinal and choroidal vascular plexuses in the macula before and after IMH surgery are related to the assessment of the FAZ area in the superficial and deep capillary plexuses of the retina. All authors note that, preoperatively, when macular hole is open, both in the superficial and deep plexuses, FAZ area is expanded compared to healthy eyes due to retinal edema at the macular hole margin. The FAZ area in the operated eye decreases and becomes smaller than that in the fellow eye after macular hole closure. In addition, in studies in which the ILM was peeled only at one side of the macular holes, retinal capillary density in the deep retinal plexus was lower in the ILM peeling region than in the region of the preserved ILM. This may indicate that ILM peeling alters parafoveal capillary perfusion. Some studies found a correlation between the FAZ area and the BCVA before and after IMH closure. Others observed a correlation between the macular tear size and the FAZ area and between the FAZ area and FRT after IMH closure [12–14, 17, 18].

In the current study, we found no such changes in the FAZ area before and after vitrectomy. It should be, however, noted that a tendency to a decrease in the FAZ area after IMH closure was observed in the fovea-sparing peeling group, but not in the conventional peeling group. In addition, a negative correlation was observed between the FRT and FAZ area in the eyes that exhibited IMH closure after IMH surgery. Moreover, because most FAZ area-related studies found in the literature had a small study sample of only 15 to 28 eyes, the findings in these studies vary considerably.

We found the CPD to have a higher diagnostic performance for predicting the presence of macular hole. CPD was significantly smaller in eyes with IMH than in eyes without IMH. After IMH closure, CPD significantly increased in all operated eyes irrespective of the type of ILM peeling. In the current study, a cut-off value of 0.156 for CPD was calculated using ROC curve for the diagnosis of macular hole and gave a sensitivity of 83% and specificity of 80% for differentiating the presence of IMH from the absence of IMH. After IMH closure, CPD in the eyes that underwent surgery significantly increased, but remained lower than in the fellow eyes.

Wilczyński and colleagues (2019) [14] reported a finding similar to ours, with an increased fovea vessel density after vitrectomy. In addition, Ahn and colleagues [22] noted that vascular density of choriocapillaris in surgically closed full-thickness macular holes was similar to that of fellow eyes but lower than that of controls.

Changes in FAZ area may be explained by capillary compression due to retinal edema at the macular hole margin, but changes in choriocapillary perfusion cannot be explained by the mechanical compression of choriocapillaries. Why does choriocapillary perfusion density decreases in the presence of IMH? The results of this study suggest that choriocapillary perfusion may have a role in the development of IMH, whereas vitrectomy with ILM peeling for IMH results in improved perfusion in the macular choriocapillary layer. The mechanism of this phenomenon, however, is not well understood and requires further research.

Other researchers [19–21] hypothesized that altered choriocapillary perfusion does not develop in the presence, but precedes the development of IMH and, along with vitreomacular and tangential tractions, plays a role in the development of IMH. This somewhat explains why it is choriocapillaries which perfusion improves after IMH closure. The recovery of choriocapillary blood flow is likely to be associated with the recovery of both the retinal structure in the fovea and photoreceptor function. This may be indicated by the fact that, in the presence of lamellar macular holes, no change in choriocapillaries was found, and the choriocapillary density correlated with preoperative area of disrupted ellipsoid zone [22]. Retinal photoreceptors and pigment epithelial cells are extremely metabolically active, and the choriocapillaris is the major source of oxygen and nutrients for them [23]. It is likely that the recovery of photoreceptor function contributes to increased choriocapillaris performance, with an increase in choriocapillaris flow density.

Conclusion

First, the presence of macular hole is accompanied by abnormal circulation in the choriocapillaris, which is manifested by a reduced density of choriocapillaris perfusion in the macula. A CPD below 0.126 may indicate the presence of IMH. Second, after IMH closure, choricapillaris function recovered, but, at 1 month after surgery, it was still lower than that in the fellow eye. Finally, postoperative CPD recovery is not influenced by the type (conventional or fovea-sparing) of ILM peeling.

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Disclosures

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Abbreviations: *BCVA, best-corrected visual acuity; CCA, choriocapillaris area; CCFA, choriocapillaris flow area; ILM, internal limiting membrane; IMH, idiopathic macular hole; OCT, optical coherence tomography; OCTA, optical coherence tomography angiography; FAZ, foveal avascular zone; FRT, foveal retinal thickness*