Changes in vascular density in the macula after pars plana vitrectomy for idiopathic macular hole with macular peeling and one type of flap

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Background and Aims. The aim of this study was to evaluate changes in vascular density in the macula after pars plana vitrectomy for idiopathic macular hole (IMD) with macular peeling and flap.
Methods. A prospective study of 35 eyes in 34 patients who had undergone standard surgery. Evaluated parameters were best-corrected visual acuity (BCVA), intraocular pressure (IOP), central macular thickness (CRT), macular volume (TMV) and vascular density of the superficial and deep capillary plexus. The follow-up period was one year.
Results. We divided the total group into two: temporal and circular flap and total group. We compared the values after surgery with the preoperative values. In the total group, BCVA increased from 48.38 to 71.44 letters ($P \leq 0.05$). IOP changed from 15.24 to 14.76 mmHg ($P > 0.05$). CRT decreased from 432.27 to 323.64 µm ($P \leq 0.05$). TMV changed from 0.26 to 0.25 mm3 ($P > 0.05$). The vascular density of the superficial plexus decreased from 32 to 28% ($P \leq 0.05$). The intercapillary space of the superficial plexus increased from 68 to 72% ($P \leq 0.05$). The vascular density of the deep plexus increased from 17 to 23%. The intercapillary space of the deep vascular plexus decreased from 83 to 77%. Changes in vascular density and intercapillary space of the deep plexus were statistically significant for certain months after operations ($P \leq 0.05$). There were no significant differences between subgroups.
Conclusion. The superficial plexus vascular density is almost the same in the temporal flap and in the foveal-sparing flap is decreased, and the deep plexus vascular density increased statistically significantly during the follow-up period after surgery.

Key words: macular hole, pars plana vitrectomy, foveal-sparing flap, temporal flap, deep vascular plexus, superficial vascular plexus

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INTRODUCTION

An idiopathic macular hole (IMD) is a full-thickness defect in the retinal neurosensory tissue that involves the fovea and thus affects central visual acuity[1].

Posterior vitreous detachment (PVD) is a common phenomenon in the aging eye. However, this can be complicated by persistent symptomatic vitreomacular adhesions that exert traction forces on the macula (vitreomacular traction; VMT). VMT itself can be associated with epiretinal membrane formation and the development of idiopathic macular holes[2]. Rarely, macular holes can occur with higher myopias or after injuries[3].

The condition can cause visual disturbances, including metamorphopsia, photopsia, blurred vision, and reduced visual acuity all of which affect the individual's quality of life. It can also progress to central scotoma with increasing IMD (ref.[2,4]).

The first clinical findings on this disorder were published by Knapp in 1869 in connection with an injury[5]. Since then, our understanding of the development and pathogenesis of macular holes has greatly increased[6].

In 1988, Gass was the first to describe the biomicroscopic classification of macular holes and hypothesized that tangential vitreous traction may play a role. He divided IMD into four stages (ref.[7]).

After the introduction of OCT into clinical practice, a second, newer classification (The International Vitreomacular Traction Study Group - IVTS) was created in 2013. This divides holes based on the OCT findings into three groups (ref.[8]).

Optical coherence tomography angiography (OCT-A) provides a non-invasive (without the use of intravenous dye) three-dimensional imaging of the microvasculature of the retina and choroid[9]. It is a novel imaging platform that uses motion contrast to visualize the retinal microvasculature in a rapid, non-invasive manner with depth resolution[10]. It provides a combination of vascular and structural information. Unlike conventional fluorescein angiography, dye injection is not required to image choroidal neovascularization[11].

Until 1991, when Kelly and Wendell published the first pilot study, where pars plana vitrectomies (PPV) with membrane limitans interna (MLI) peeling led to successful closure of macular holes, the disorder was considered incurable[12]. Today, this procedure has become the standard for improving or at least stabilizing the visual acuity of affected eyes.

MLI peeling is the most technically demanding part of the surgical procedure. As protection against iatrogenic damage to the macula, visualization agents (indocyanine blue and trypan blue) are used. The techniques used are: circular (foveal sparing flap) or temporal flap. The temporal flap is most often used for large holes[13].

In this study, we investigated retinal microvasculature characteristics in the foveal region of eyes with IMH before and after 25-gauge (25-G) PPV with MLI peeling using OCT-A (Fig. 1, 2).

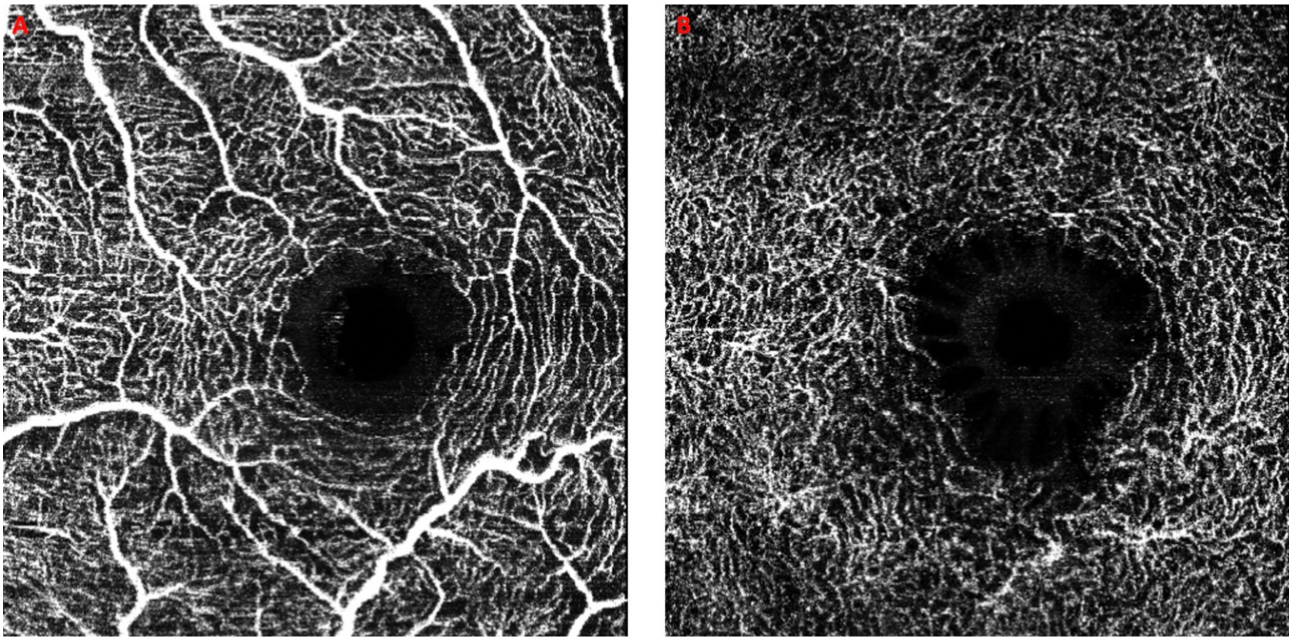

Fig. 1. Preoperative findings of the retinal microvasculature in the superficial and deep vascular plexus in the macula in a patient the day before pars plana vitrectomy with macular peeling and foveal-sparing flap; **A.** Superficial vascular plexus; **B.** Deep vascular plexus.

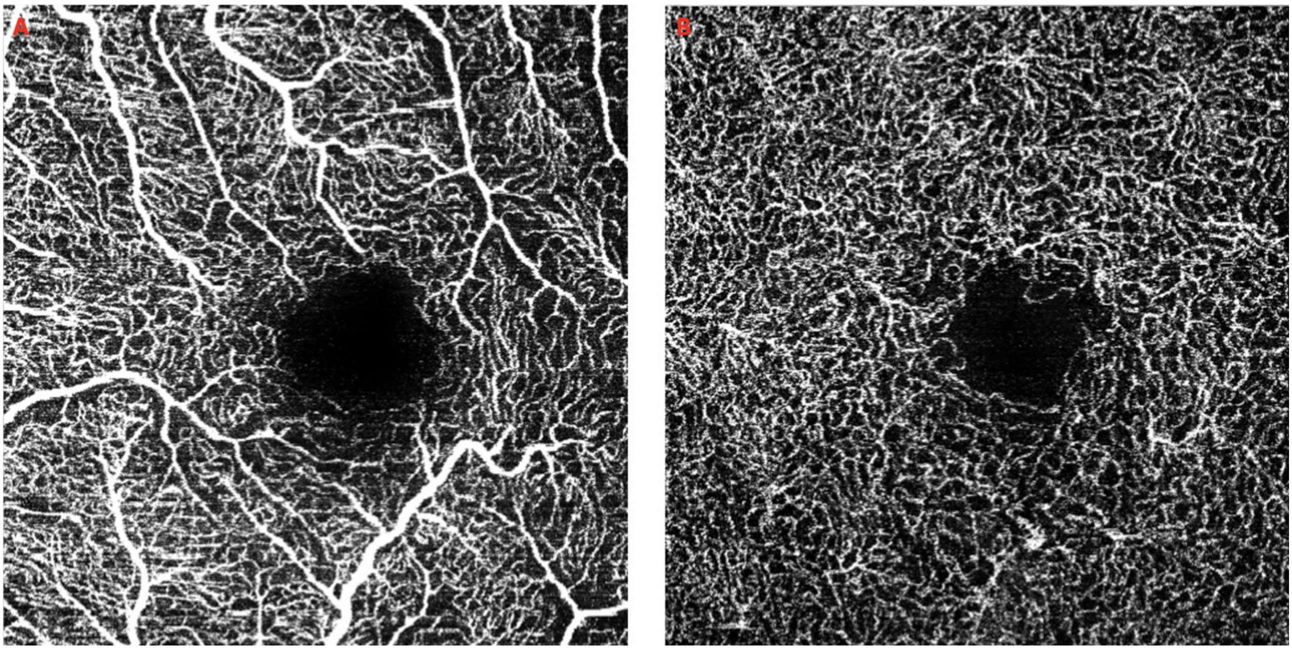

Fig. 2. Postoperative findings of retinal microvasculature in the superficial and deep vascular plexus in the macula in a patient at an annual check-up after pars plana vitrectomy surgery with macular peeling and foveal-sparing flap; **A.** Superficial vascular plexus; **B.** Deep vascular plexus.

MATERIALS AND METHODOLOGY

This was a prospective study including 35 eyes of 34 patients who had undergone standard 25-G PPV surgery for IMD with macular peeling. The operations were performed at the Ophthalmology Department of the Faculty Hospital, Hradec Králové (FNHK) in the years 2019–2021. All patients signed an informed consent before participating in the study. The research was approved by the FNHK ethics committee. During the follow-up period, two patients died in association with COVID-19 and one patient died of disseminated tumor spread.

The main entry criteria for inclusion in the sample were the presence of IMD and undergoing PPV with one type of flap (temporal or foveal-sparing flap). Subsequent medical examinations of the patient took place on 1st, 3rd, 6th and 12th months after the operation. Exclusion criteria were the coincidence of other diagnoses (age-related macular degeneration or diabetic retinopathy with diabetic macular edema) with starting anti-VEGF treatment or having other eye diseases that could affect the change in visual acuity.

The evaluated parameters were: best-corrected visual acuity (BCVA), intraocular pressure (IOP), central macular thickness (CRT), macular volume (TMV) and assessment of superficial and deep capillary plexus vascular density on OCT-A. For each patient, we took a photo of the fundus and OCT images, including OCT-A.

The PPV procedure was performed using the CONSTELLATION® Vision System from Alcon. OCT was performed on a Spectralis device, Heidelberg Engineering. We used the ImageJ program to calculate the density of the capillary and vascular plexus. ImageJ is a Java-based image processing program developed at the National Institutes of Health and the Laboratory for Optical and Computational Instrumentation, University of Wisconsin. Rha et. al. in their publication, refer to the program as a cost-effective, simple and easily accessible method of volume measurement using Image J software (ref.[14,15]). From the program, we converted the images into a binary map (white – blood vessels and black – background) and then converted the numerical data into percentages.

BCVA was evaluated by ETDRS boards. IOP was measured non-contact, in case of discrepancies, applanation. CRT and TMV were automatically measured on the OCT unit. The diameter of the macular hole was measured manually on the OCT device (in the narrowest place and the widest place – at the bottom of the macula).

Two classifications were used to assess the stage of hole size. The original classification according to Gass, which divided holes into 4 classes: stage 0 – physiological finding, stage 1A and 1B – present elevation of the sensory epithelium (foveolar detachment) until the depression disappears, stage 2 – small hole with VMT, stage 3 – larger hole with VMT, operculum may or may not be present and stage 4 – complete retinal defect without VMT but with PVD (ref.[7]).

The second, more recent classification (The International Vitreomacular Traction Study Group – IVTS) divides holes based on OCT findings into: stage 0 – VMA, stage 1 – VMT, stage 2 – small or medium hole with VMT, stage 3 – medium or large hole with VMT and stage 4 – hole of all sizes, without VMT calculated according to the narrowest point of the defect (ref.[8]).

Our intent was to operate on each patient under local anaesthesia. In one patient, due to the implantation of an ICD cardiodefibrillator, we performed the operation under local anaesthesia with anesthesiological supervision. One patient had retrobulbar bleeding during operations under local anaesthesia and the operation had to be performed under general anaesthesia. A 25-G PPV was used in all patients.

The surface of the macula was stained with MembraneBlueDual® dye, which contains both brilliant and membrane blue, sinks down well, does not swirl in the vitreous space and reliably stains the macula. After washing out the dye, MLI peeling was performed with disposable 25G microtweezers. The MLI removal area was 5x3 mm, in the case of reoperation the peeling was extended up to the arcades which are 6x4 mm. A pronated head position was used, as each patient received endotamponade (air or gas) after PPV. All patients were instructed to be positioned one week after surgery.

The data were processed using an Excel program. Normality of the distributions was tested with the Shapiro-Wilk test and the medians assessed using the two-sample paired Wilcoxon test. The level of significance was alpha 0.05.

RESULTS

In total the number of procedures was 37. Two patients had reoperation in the same eye during the follow-up period due to a persistent macular hole (one female and one male). There were 26 (76%) women in the total group, 8 (24%) men. 3 patients (2 women and 1 man) had an affected second eye before inclusion in the group. In one patient both eyes were involved. The average age was 69 (52–80 years).

Of 35 eyes, cataracts were removed before PPV in 11 eyes (31%), of the remaining 24 eyes (69%) at the time of PPV surgery, 1 eye (4%) had cataracts. One patient had cataract surgery with PPV surgery at the same time. Of 24 eyes, 23 patients had cataract surgery in 23 eyes, 22 patients during the follow-up period. On average, in 24 eyes (which had not undergone cataract surgery in the past), a cataract was diagnosed within 4 months after PPV (in one patient, the indication was immediately upon admission). On average, the length from diagnosis to the time of cataract surgery was 5 months (0.5–9).

0. and IA./IB. no patients had gass hole stage before the PPV procedure. II. and III. 3 patients had the hole stage. Most patients had an IV before the PPV procedure (31 patients). The distribution of eyes according to IVTS stage in our group was: VMA and VMT no patients, small or medium hole with VMT 3 patients, medium or large hole with VMT 3 patients and the last group: small, medium or large without VMT 31 patients.

Before surgery, CRT averaged 432 µm (281 – 580). The width of the macula at the narrowest point was an average of 382 µm (86 – 720). The width of the macula at the widest point (calculated at the bottom of the macula) averaged 936 µm (172 – 1698). The TMV was on average 0.26 mm^3 (0.09 – 0.48).

Patients with a circular flap made up the most represented percentage in the group: 25. A temporal flap was performed in 10 patients. In two patients who underwent reoperation, lateral extension of the MLI peeling area was performed.

Patients with tamponade were divided into 4 groups. One patient had air tamponade, 6 patients received 15% C_3F_8 tamponade, 2 patients received 15% SF_6 tamponade, and the largest percentage consisted of patients with 20% SF_6 tamponade. Two eyes that had to undergo reoperation first received SF_6 gas tamponade (once 20% SF_6 and the second time 15% SF_6).

Four patients (12%) had transient IOP elevation after surgery. All were given local anti-glaucoma treatment and their IOP normalized within a month. One patient (3%) was found to have an eccentric hole in the upper temporal arcade one month after surgery. In macula was attached at the centre and there were no subjective visual problems. The findings were stable throughout the follow-up period. In one patient (3%), occlusion of the lower macular branch of the central retinal vein on the left occurred 9 months after the operation with macular oedema and deterioration in vision, where intravitreal administration of growth factor blockers was also planned. We subsequently discharged the patient. One patient (3%) had a persistent macular hole with signs of healing and reoperation was not indicated. Two patients (6%) had reoperation for persistent macular hole.

We divided the results into three groups. The first was the total set, the second was temporal flap (TF) patients, and the third was foveal-sparing flap (CF) patients.

Total set of results

The average duration of visual problems before surgery was 5 months (1–28 months). We found a statistically significant correlation between the duration of symptoms and the resulting BCVA ($P \leq 0.05$).

The results of the BCVA are shown in Table 1 where it is clear that the number of letters in the postoperative monitoring increased. The increase is statistically significant throughout the follow-up period compared to the preoperative value ($P \leq 0.05$).

The results of the IOP (mmHg) measurements are best shown in the table where it is clear that the IOP increased in the 1st month (M) after the operation. Subsequently, 3 M after the surgery, they returned to approximately the IOP value before the surgery. This remained stable throughout the follow-up period. Changes in IOP during follow-up were not statistically significant compared to the preoperative value (P>0.05).

The results of CRT (um) are shown in the same table. Postoperative CRT values throughout the follow-up period were statistically significantly lower ($P \leq 0.05$) than the preoperative value.

The results of TMV (mm3) are shown in Table 1. The TMV values did not change or changed minimally during the entire follow-up period. Changes in TMV during the follow-up compared to the initial values were not statistically significant (P>0.05).

The vascular density values for the superficial vascular plexus are shown in Fig. 3. The postoperative values throughout the follow-up were statistically significantly lower ($P \leq 0.05$) than the preoperative value.

The results for the intercapillary space of the superficial plexus are shown in Fig. 4. The postoperative values throughout the follow-up were significantly higher ($P \leq 0.05$) than the preoperative value.

Fig. 5. shows the results that the density of the deep vascular plexus increased during the follow-up period compared to the preoperative value. This was statistically significant in the 3rd and 12th months after surgery ($P \leq 0.05$).

Fig. 6. shows the results for the intercapillary spaces of the deep plexus. It is obvious that the inter capillary space of the deep vascular plexus in the follow-up period decreased compared to the preoperative value. This reduction was statistically significant in the 3rd and 12th months after surgery ($P \leq 0.05$).

We found a statistical significance between the duration of symptoms and changes in the microvasculature

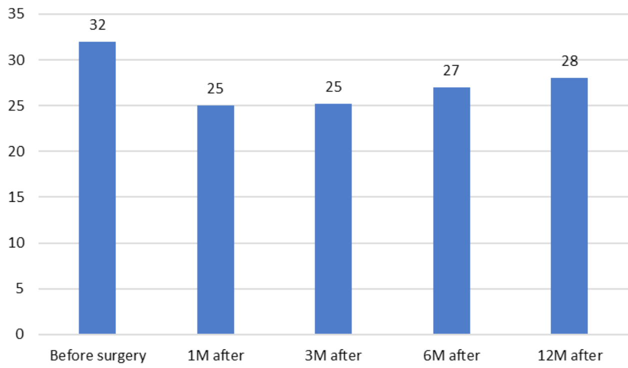

Fig. 3. Changes in the vascular density of the superficial vascular plexus in percentage.
Percentages were calculated from vascular density and intercapillary space of the superficial plexus. M, Month after surgery.

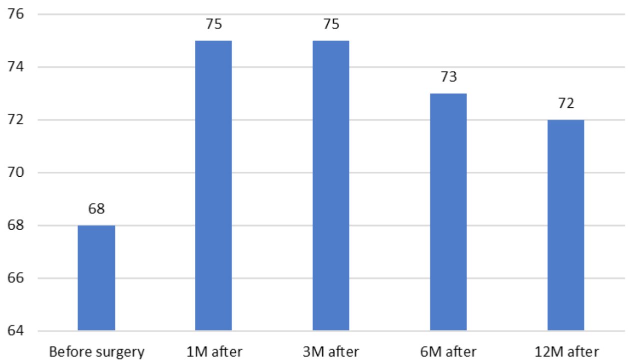

Fig. 4. Changes in the intercapillary space of the superficial plexus in percentage.
Percentages were calculated from intercapillary space and vascular density of the superficial plexus. M, Month after surgery.

in the macula in the superficial and deep vascular plexus ($P\leq0.05$).

Division of patients into temporal and foveal-sparing flap sets

Foveal-sparing flap (CF) consisted of 24 patients, 25 eyes, 25 procedures. Temporal flap (TF) consisted of 10 patients, 10 eyes, 12 procedures.

The results for the BCVA are shown in the Table 1. BCVA TF values: It is obvious that BCVA values increased during the whole follow-up period compared to the preoperative value. The increase was statistically significant in the 1st, 3rd and 12th M after operations ($P<0.05$). BCVA CF values: Postoperative BCVA values throughout the follow-up period were statistically significantly higher ($P<0.05$) than the preoperative value.

The IOP results are shown in Table 1. The IOP values in CF and TF changed minimally ($P>0.05$) during the follow-up period compared to the initial value.

The CRT results are shown in the attached Table 1. CRT TF values: It is obvious that the CRT values decreased in the entire follow-up period compared to the preoperative value. This reduction was statistically significant in the 3rd, 6th and 12th M after operations ($P<0.05$). CF CRT values: Postoperative CRT values throughout the follow-up period were statistically significantly lower ($P<0.05$) compared to the preoperative value.

The TMV results are shown in the attached Table 1. TMV TF values: It is clear that the TMV values changed minimally in the follow-up period compared to the preoperative value. This change was statistically significant only in the 1st M after operations ($P<0.05$). TMV CF values: Postoperative CRT values changed minimally ($P>0.05$) during the entire follow-up compared to the preoperative value.

The results for the surface intercapillary space are shown in Table 2. Values of the surface intercapillary space in TF: It is obvious that the values of the surface intercapillary space increased in the follow-up period compared to the preoperative value. This change was statistically significant only in the 1st M after operations ($P<0.05$). Values of surface intercapillary space in CF: Postoperative values of surface intercapillary space increased throughout the follow-up compared to the preoperative value ($P<0.05$).

The results of the superficial vascular plexus are shown in the attached Table 2. Values of the superficial vascular plexus in TF: It is obvious that the values of the superficial vascular plexus decreased in the follow-up period compared to the preoperative value. This change was statistically significant only in the 1st M after operations ($P<0.05$). Superficial vascular plexus values in CF: Postoperative values of superficial vascular plexus decreased throughout the follow-up compared to the preoperative value ($P<0.05$).

The results of the deep intercapillary plexus are shown in the attached Table 2. The values of the deep intercapillary plexus in TF: It is obvious that the values have decreased in the follow-up period compared to the preoperative value. This change was statistically significant only in the 3rd M and 12th M after operations

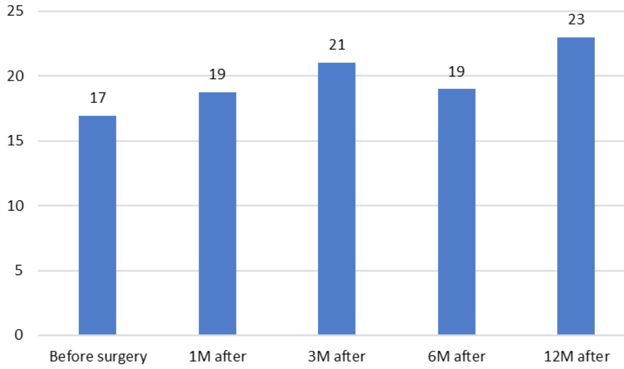

Fig. 5. Changes in the vascular density of the deep vascular plexus in percentage.
Percentages were calculated from vascular density and intercapillary space of the deep vascular plexus. M, Month after surgery.

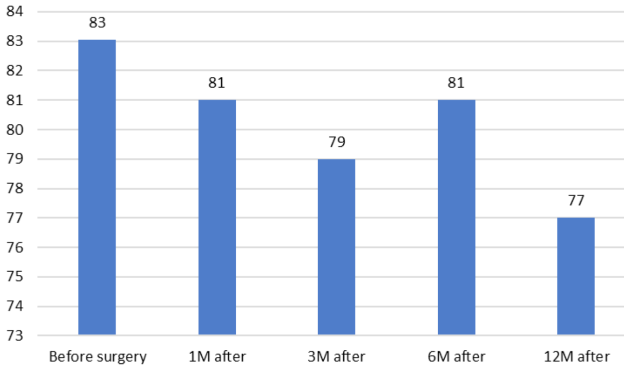

Fig. 6. Changes in the intercapillary space of the deep plexus in percentage.
Percentages were calculated from intercapillary space and vascular density of the deep vascular plexus. M, Month after surgery.

Table 1. Changes in the total group and the temporal and foveal-sparing flap.

	Foveal-sparing flap					Temporal flap					Total file				
	Before surgery	1M	3M	6M	12M	Before surgery	1M	3M	6M	12M	Before surgery	1M	3M	6M	12M
BCVA (letter score)	46	58	62	68	70	52	63	61	58	74	48	60	62	66	71
IOP (mmHg)	17	18	16	20	16	14	16	14	13	14	15	17	15	14	15
CRT (um)	415	334	317	338	326	468	400	388	330	320	432	359	339	335	324
TMV (mm^3)	0.27	0.30	0.24	0.30	0.26	0.23	0.30	0.28	0.30	0.30	0.26	0.26	0.30	0.30	0.25

BCVA, Best-corrected visual acuity; IOP, Intraocular pressure; CRT, Central retinal thickness; TMV, Total macular volume; M, Month after surgery.

(P<0.05). Values of the deep intercapillary plexus in CF: Postoperative values decreased throughout the follow-up compared to the preoperative value (P>0.05).

The results for the deep vascular plexus are shown in Table 2. The values of the deep vascular plexus in TF: it is obvious that the values increased in the follow-up period compared to the preoperative value. This change was statistically significant only in the 3rd M and 12th M after operations (P<0.05). Values of the deep vascular plexus in CF: Postoperative values increased throughout the follow-up compared to the preoperative value (P>0.05).

DISCUSSION

Surgical treatment of PPV with tamponade has become the gold standard in the treatment of IMD from its introduction into practice in 1991, when Kelly and Wendell published the first pilot study results where PPV with MLI peeling resulted in successful closure of MD (ref.[12]). It happens that the most common surgical complication is progressive clouding of the lens in phakic patients. There were 24 phakic patients in our group, 95.8% of whom had cataract surgery during the follow-up period.

MLI peeling has become a standard step in IMD surgery, and most authors confirm the importance of MLI peeling for IMD closure (ref.[16-25]).

Kwok et al. reported better postoperative results in patients with macular peeling compared to those without macular peeling. Anatomical IMD closure occurred in 88.9% of patients with macular peeling versus 59.1% without macular peeling. Removal of MLI not only increases the chance of a better anatomical outcome it also improves the functional results[16]. Other authors have also had similar results[17-20]. In our series, all patients underwent MLI peeling with an anatomical success rate of 91.4%.

Ghassemi et al. described 72 eyes in 72 patients with large (>400 μm) full-thickness IMD who were randomly assigned to three groups: A: hemicircular peeling MLI with temporal flap, B: circular peeling MLI with temporal flap, and C: MLI circular peeling with a foveal-sparing flap. They focused on the change in BCVA and anatomical closure of the hole. In all groups, the mean BCVA significantly improved in all three 6 months after surgery, with no statistically significant difference between groups. At the same time, they concluded that MLI peeling with a foveal-sparing flap is a highly effective procedure for the treatment of a large, full-thickness macular hole. Different flap techniques have comparable results, suggesting that the technique can be chosen based on surgeon preference[26]. In our group, we compared the results of the circular and temporal flap, which is a subgroup of the foveal-sparing flap. We selected several parameters for measuring outcome namely BCVA, IOP, CRT and TMV. The results were comparable between the two groups. We had similar results to Ghassemi et al.[26]. Hirata et al. achieved a similar outcome with the temporal flap, where there was a significant improvement in BCVA and TMV (ref.[27]). Bleidißel et al. also found a significant improvement in BCVA with a foveal-sparing flap[28].

Fluorescein angiography does not show well the radial peripapillary or deep capillary networks. However, OCT angiography can image all layers of the retinal vasculature without the intravenous application of fluorescein. For this reason, OCT angiography is to be preferred for clinical evaluation of the retina in general[29].

In our study, we aimed to investigate morphological and vascular changes (in the superficial and deep vascular zone) using OCT-A in patients after PPV with MLI peeling for IMD before and after surgical treatment. Quantitative evaluation of vascular and cystic changes after IMD surgery demonstrates recovery potential due to neuronal and vascular plasticity and suggests that the healing process after IMD surgery may involve anatomical and hemodynamic changes in the layers of the retina[30-32]. We had the same results as the authors cited. During the follow-up period, there was a statistically significant reduction in CRT and an improvement in the anatomical conditions in the central retinal area.

We also focused on comparing the results for BCVA during the follow-up period where there was a statistically significant improvement at all time intervals. In the compared forms of flap methods, we noted the difference as have others[30,32,33].

The most important part of our follow-up was the change in superficial and deep vascular plexus before and after surgery. Rizzo et. al. report that based on OCT and OCT-A examinations, images of cystoid cavities show very similar features and are complementary for the evaluation of the disease[34]. Dusová et al. describe OCT-A images that showed "vascular shifts" at the border of the cystoid cavities in full-thickness IMH, indicating preservation of the

Table 2. Changes in the vascular pattern in the macula with a temporal and foveal-sparing flap.

	Temporal flap					Foveal-sparing flap				
	Before surgery	1M	3M	6M	12M	Before surgery	1M	3M	6M	12M
PPIP	69	76	72	73	70	67	75	76	73	74
PPVP	31	24	28	27	30	33	25	24	27	26
PHIP	84	80	77	80	75	83	82	80	82	78
PHVP	16	20	23	20	25	17	18	20	18	22

PPIP, Percentage of superficial intercapillary space; PPVP, Percentage of superficial vascular space; PHIP, Percentage of deep intercapillary space; PHVP, Percentage of deep vascular space; M, Month after operations.

microvasculature surrounding the cystoid spaces during the disease process[35].

Kim et. al. caution that the deep vascular plexus is at risk in the case of a long-lasting large IMD (ref.[33]). In our group, regeneration and restoration of the deep vascular plexus was visible, while in the group with a circular flap, statistically significant changes occurred throughout the follow-up.

During this period, we had two patients who underwent re-PPV for a persistent macular hole. After reoperation, the IMD closed with an improvement in the anatomical proportions in the central region, which was objectified by an improvement in BCVA. This is in agreement with others[36].

In our group, we concluded that in the superficial vascular plexus, the intercapillary space increased and the vascular plexus decreased after operations in the foveal-sparing flap and in the temporal flap is almost the same. While in the deep plexus, the intercapillary space was reduced, the vascular density increased. We observed no difference in the flap methods in the deep plexus. Changes in the superficial vascular plexus are attributed to peeling during the operation and traction stress and foveal shift occurring after the operation[37]. This may also have an effect on the change in vascular and intercapillary density before and after PVV surgery for IMD with macular peeling.

A note about OCT-A

In concluding, we would like to emphasize the advantage of evaluating macular capillary plexuses with OCT-A which can be useful in monitoring the structural and functional changes of the retina in various eye conditions OCT-A showing vascular changes and, their quantitative and morphological characteristics may be a useful tool for evaluation not only in IMD before and after surgical treatment but also showing the potential for recovery due to vascular and neuronal plasticity.

As with any other imaging method, artifacts occur in OCT-A images as well. Nevertheless, qualitative evaluation of OCT-A images is almost always possible and provides essential findings about the morphology and perfusion status of the retina and choroid. A good knowledge of possible artifacts and critical analysis of the complete OCT-A data set allows for correct interpretation and is essential for making an accurate clinical diagnosis.

CONCLUSIONS

The goal of our study was to focus on changes in the vascular density of the superficial and deep plexus. The vascular density of the deep plexus increased during the one-year follow-up period in both group and the vascular density of the superficial plexus is almost the same in the temporal flap and in the foveal-sparing flap is decreased during the one-year follow-up period after PPV surgeries with macular peel and flap. The results are also confirmed by the significant improvement of BCVA and reduction of CRT after the operations. We also demonstrated a statistical dependence between the duration of symptoms and changes in the microvasculature in the macula in both superficial and deep vascular plexus. We found no differences between the different forms of the flap method in PPV.

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Author contribution: AT: manuscript writing; NJ, JS: supervising; JD, JM: operated patients.

Conflict of interest statement: None declared.

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