

Choroidal vascularity index changes with phacovitrectomy for vitreoretinal interface disorders

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Purpose: Vitreomacular interface disorders have long been argued to change choroidal structure. The aim of this study was to determine the choroidal vascularity index (CVI) changes following internal limiting membrane peeling for epiretinal membrane (ERM) and full thickness macular hole (FTMH). **Methods:** Fifty-nine patients with unilateral ERM and 56 with unilateral FTMH were included in the study. Axial length, pre- and post-surgery intraocular pressure, baseline and post-phacovitrectomy CVI were calculated and compared with the normal fellow eyes. To compare the baseline and the final measurements, Wilcoxon test was used. Mann–Whitney *U* test was used for independent data comparisons. Median and standard deviations were compared. **Results:** Axial length, pre- and post-surgery intraocular pressure differences were insignificant between study and fellow eyes within all groups. CVI were significantly lower in post-vitrectomy study eyes of all groups compared with pre-surgery ($P < 0.001$). There were no significant changes before and after the surgeries in fellow eyes. Baseline CVI of ERM study eyes (median 65.90%) and FTHM study eyes (median 65.59%) did not differ significantly between groups ($U = 1336$, $P = 0.07$, $r = 0.16$). **Conclusion:** There are conflicting results of vitreoretinal interface disorders CVI in the literature. In this study, both FTMH and ERM eyes showed reduced CVI postoperatively compared with the baseline. Preoperatively, there were no difference between study eyes and the fellow eyes.

Key words: Choroidal vascular index, epiretinal membrane, macular hole, optical coherence tomography, vitreomacular surgery

Posterior vitreous detachment is the normal aging process of the vitreous. However, in the event of an anomalous detachment, vitreomacular interface disorders start to form. When focal vitreous traction is exerted at the interface, a full thickness macular hole (FTMH) can occur. If the traction force is distributed to a broad area, it may result in an epiretinal membrane (ERM).^[1] Epiretinal membrane is an abnormal membrane formation on the surface of the internal limiting membrane (ILM) of the retina. A full thickness macular hole is a full-thickness tissue loss in the central macula, including the ILM and photoreceptor layers.^[2] Vitrectomy is the preferred method of treatment, especially in decreasing visual acuity or in the presence of metamorphopsia.

Choroid is the main oxygen and nutrient provider to the outer retina and the retinal pigment epithelium. It is known to be affected by various diseases, including FTMHs.^[3–5] Choroidal vascular index (CVI) has been recently identified and found to be a better index than choroidal thickness due to the separate assessment of vascular and stromal layers.^[6] In this method, image binarization of optical coherence tomography (OCT) image scans show the luminal area and the total choroidal area, allowing us to calculate the vascular and stromal area ratios. There are previous studies that show CVI changes between before and after vitrectomy in vitreomacular interface disorders. Baseline CVI was found to be greater in these disorders

compared with their fellow eyes in one study.^[7] However, a later study with more participants found no difference between eyes with vitreoretinal disorders and their fellow eyes.^[8] It is possible that the blood flow in the outer retina and the choroid is affected by the changes in nutrient demands of retinal pathologies. In this study, vitreoretinal disorders were divided into ERM and FTMH groups to see whether different disorders have different effects on the choroid.

The aim of this study was to study the changes in CVI following combined phacovitrectomy for ERM or FTMH.

Methods

We retrospectively reviewed the medical records of patients with ERM in one eye and patients with FTMH in one eye from January 2014 to September 2021 at Baskent University University Hospital. This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Baskent University ethics committee.

The inclusion criteria were patients with ERM or FTMH in one eye on whom combined phacovitrectomy was performed. The exclusion criteria were: (1) Eyes with any previous ocular

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surgery, trauma, or diseases such as glaucoma, diabetic retinopathy or age-related macular degeneration; (2) eyes with spherical equivalent of ± 6 diopters (D); (3) systemic diseases other than diabetes and hypertension; and (4) patients with ERM or FTHM in both eyes. Patients that had media opacities that disturbed the OCT quality were not included. Patients with previous cataract surgeries that solely underwent vitrectomy were not included, and not compared in this study due to insufficient number of patients. Patients with ERM or FTHM in both eyes were not included in order to be able to use the opposite eye as control group. Macular holes were medium (diameter 250 to 400 μ m) or large (diameter > 400 μ m), primary, full-thickness holes.

Medical and ophthalmologic history including noncontact pneumatic tonometry (IOP), axial length measure (IOLMaster 700 PCI device, Carl Zeiss Meditec AG), slit-lamp biomicroscopy and dilated fundus examination and OCT imaging (Spectralis, Heidelberg Engineering Germany) of initial and postoperative 8-week visit recordings were examined.

Surgical procedures were performed by the same surgeon (G.Y.): 2.4 mm clear corneal incision phacoemulsification followed by 23-gauge transconjunctival sutureless vitrectomy.

In all cases, monofocal hydrophilic intraocular lenses (Acrysof IQ, Alcon Laboratories, Inc.) were implanted in the bag by using a cartridge introduction system without incision enlargement. Membrane dual blue dye and a sulfur hexafluoride 18.0% gas tamponade were used in all patients. The same postoperative antibiotic (moxifloxacin 1.5%, 4 weeks) and anti-inflammatory (prednisolone acetate 1%, 6 weeks) eye drops were used for all the study patients.

Horizontal OCT scans centered on the central foveal region were selected for measurements. Image processing was performed using Fiji image processing package via the method previously described by Agrawal *et al.*^[9] 1500 micron, with its center being the fovea, was selected for measurement. The polygon selection tool was used to select the total choroidal area (TCA) and added to the Regions of Interest

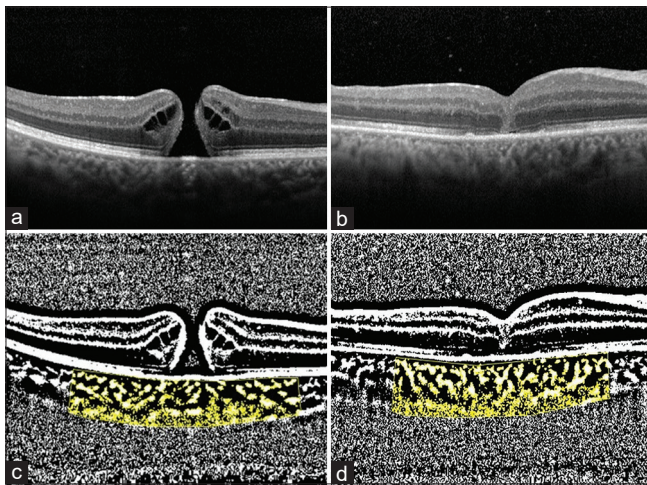


Figure 1: Preoperative (a) and postoperative (b) 8-week OCT of full thickness macular hole. Preoperative (c) and postoperative (d) 8-week choroidal segmented OCT images of the same patient

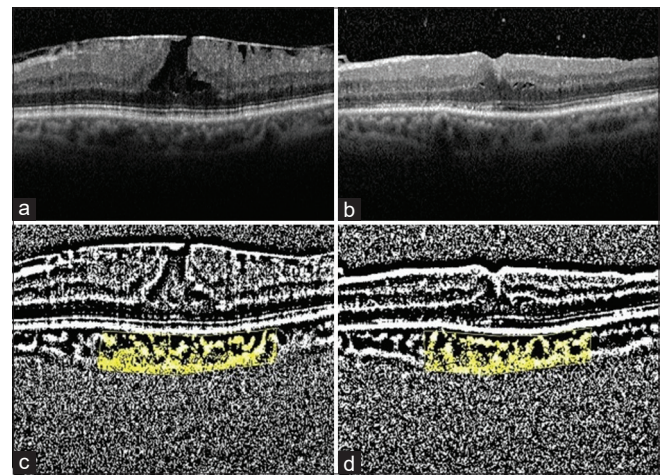


Figure 2: Preoperative (a) and postoperative (b) 8-week OCT of epiretinal membrane. Preoperative (c) and postoperative (d) 8-week choroidal segmented OCT images of the same patient

Table 1: Age, axial length, intraocular pressure, and preoperative and postoperative choroidal vascular index comparisons between the groups

	ERM		FTMH		Total	
	Study Eye	Fellow Eye	Study Eye	Fellow Eye	Study Eye	Fellow Eye
Age (years)	67 (62-74)	67 (62-74)	67 (62-73)	67 (62-73)	67 (62-74)	67 (62-74)
Axial Length	23.49 mm	23.40 mm	23.48 mm	23.28 mm	23.48 mm	23.34 mm
	$P=0.65$		$P=0.34$		$P=0.57$	
Pre IOP (mmHg)	16 (14-19) $Z = -0.020, P=0.98$	16 (13-22)	17.5 (14-21) $Z = -0.283, P=0.77$	16.5 (12-20)	16 (14-20) $Z = -0.226, P=0.82$	16 (12-21)
Post IOP (mmHg)	16 (13-20) $Z = -1.515, P=0.13$	17 (14-22)	17 (13-21) $Z = -0.474, P=0.63$	17 (14-22)	17 (13-21) $Z = -1.395, P=0.16$	17 (14-22)
Pre CVI (%)	65.90 (64.63-69.16) $Z=0.611, P=0.54$	66.90 (64.30-68.90)	65.59 (63.03-67.67) $Z = -0.228, P=0.81$	65.65 (62.95-68.05)	66.10 (64.20-68.80) $Z = -0.352, P=0.725$	65.52 (63.81-68.61)
Post CVI (%)	65.71 (64.17-69) $Z = -0.679, P=0.49$	66.20 (64.40-69)	65.39 (62.85-67.40) $Z = -1.305, P=0.19$	65.75 (63.10-68.77)	65.52 (63.80-68.80) $Z = -1.395, P=0.16$	66.10 (63.81-68.61)

(ROI) manager. Niblack auto-local threshold was applied to the 8-bit image separating the luminal area (LA) and the stromal area (SA); it was then converted back to red, green, blue image. Color threshold was applied and added to the ROI manager. Both areas previously added in the ROI manager were selected and combined in order to measure LA [Figs. 1 and 2]. The CVI was then measured by calculating the ratio of LA to TCA.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 22; IBM Corp). The normality of the distribution of each of the parameters was checked using the Kolmogorov–Smirnov normality test which showed that the data did not follow a normal distribution. To compare the baseline and the final measurements, Wilcoxon test was used. Mann–Whitney *U* test was used for independent data comparisons. Median (Mdn) and standard deviations (SD) were compared. *P* values < 0.05 were considered statistically significant.

Results

This study included 115 patients (59 single-eye ERM and 56 single-eye FTMH). Median age was 67 years (IQR 62–74).

In the ERM group, there were 31 male and 28 female patients. Of those, 12 of them diabetes mellitus and hypertension, while 12 had only diabetes mellitus and 15 had hypertension. In the FTHM group, there were 24 male and 32 female patients. Of those, nine of them diabetes mellitus and hypertension, while 11 had only diabetes mellitus and 20 had hypertension. Median values are given in Table 1. Axial length, pre- and post-surgery IOP differences were insignificant between study and fellow eyes within all groups [Table 1]. The age difference between ERM and FTHM group was insignificant ($U = 1615$, $P = 0.83$, $r = 0.019$).

CVIs were significantly lower in post-vitreotomy study eyes of all groups compared with pre-surgery. For the ERM group, the *Z* value was -6.68 with $P < 0.001$. For the FTHM group, the *Z* value was -6.51 with $P < 0.001$. There were no significant changes before and after the surgeries in fellow eyes of the ERM group ($Z = -0.234$, $P = 0.83$) or the FTHM group ($Z = -0.82$, $P = 0.41$). Baseline CVI of ERM study eyes (median 65.90%) and FTHM study eyes (median 65.59%) did not differ significantly between groups ($U = 1336$, $P = 0.07$, $r = 0.16$).

Discussion

In this study, we investigated CVI changes in vitreomacular diseases before and after vitrectomy.

The major blood supply to the retina is the choroid with its immense blood flow necessary due to the high photoreceptor activity. The continuous flow of ions and water across the retina into the choroid has been suggested to be a major dependent in choroidal vascularity modulation, especially in the homogeneous foveomacular zone.^[10,11]

Our results showed that CVI difference was insignificant in vitreoretinal diseased eyes and their healthy counterparts (median 66.10 for ERM and 65.52 for FTHM). This is in contrast to Rizzo *et al.*'s^[7] study of twenty-six patients that found their study eye group's CVI to be greater than their fellow eyes at baseline. This might be due to the difference of participant numbers. This study's results are in agreement with Chun

et al.'s^[8] study of 132 eyes that also found no difference between ERM and FTHM eyes and their fellow eyes. Other studies have also showed that fellow eyes of FTHM have similar choroidal characteristics with the affected eyes.^[12,13] In contrast, FTHM eye choroidal thicknesses were found to be significantly lower than that of completely healthy subjects.^[14]

FTMH recover after vitrectomy with the connection of the inner retina and formation of a bridge-like glial proliferation, slowly followed by outer retina. Müller cell gliosis is the most important factor in this, possibly induced by ILM peeling.^[15] Postoperative healing starts with gliosis over the macular hole followed by filling of the space underneath. The process of outer retina reformation may take up to twelve months after the surgery. During this time, it is thought that swelling glial cells push the health photoreceptor together, decreasing the size of the photoreceptor defect improving the visual acuity.^[15] Optical coherence tomography angiography (OCTA) studies have shown increase of macular choriocapillaris flow postoperatively.^[15,16] Restoration of metabolic flow from the previous defect area may explain the restoration of choriocapillaris after the closure of FTHM.^[16] In this study, CVI was found to be lower postoperatively compared with FTHM baseline calculations. This is dissimilar to Rizzo *et al.*'s^[7] previous study that found that phacovitrectomy increases CVI in the early postoperative period while vitrectomy alone decreases it. This may be due to differences in the OCT timelines and postoperative inflammation differences.

ERM was shown to affect the choroid, depending on its tractional force in previous studies.

Macular choroidal thickness was found to be elevated in ERM with retinal folding or with macular edema, whereas no significant difference was found in those without traction.^[17] It was hypothesized that the altered retinal blood flow caused by traction may induce choroidal vessels to compensate for the increased oxygen and nutrient needs.^[17] Michalewska *et al.*,^[18] in contrast, found no significant difference between eyes with ERM and their fellow eyes but diminished choroidal thickness at three months post vitrectomy. Similar to our study, they also included all ERM patients regardless of traction presence. Kang *et al.*^[19] found decreased choroidal thickness at three months post vitrectomy with a sample size of 21 eyes. They also did not differentiate between ERM with or without traction. It is therefore possible that all these studies show reduced choroidal thickness due to the elimination of the anteroposterior traction. However, Gediz *et al.*^[20] found no significant change in CVI values with increasing stages of epiretinal membrane and increasing levels of contraction. If that is the case, the hypothesis of the CVI reduction post vitrectomy being affected by traction relaxation is debatable and would need further research. They also found no difference between healthy and ERM eyes which is similar to this study.

In this study, both FTHM and ERM eyes showed reduced CVI postoperatively compared with the baseline. On the whole, this may be due to decreasing choroidal thickness with higher oxygenation with vitrectomy.^[21] In FTHM, it is also possible that the restoration of the nutrient flow after hole closure is no longer necessary for choroidal vascular dilation resulting in vasoconstriction in the choroid. The CVI reduction in ERM eyes might be due to anteroposterior traction relaxation. One of the limitations in this study is that the ERM group was

not differentiated into traction and non-traction groups. The retrospective nature of the study was also a limitation, mainly in the fact that long-term follow up was not possible.

Conclusion

In conclusion, although vitreomacular interface disorders might affect the choroid in various ways we have found choroidal vascularity indexes of these affected eyes are not different from their healthy counterparts, but decrease with vitreomacular surgery.

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Conflicts of interest

There are no conflicts of interest.

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