

# The Role of Choroidal Vascular Structures in Vitreomacular Interface Disorders: Clinical Relevance and Importance Across Different Stages

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## ABSTRACT

**Objective:** This study aimed to evaluate the impact of pars plana vitrectomy (PPV) on the choroidal vascularity index (CVI) in patients with unilateral idiopathic epiretinal membrane (IERM) and full-thickness macular hole (FTMH), according to disease stages.

**Material and Method:** This retrospective study analyzed data from 100 patients (50 IERM, 50 FTMH) diagnosed between September 2020 and September 2023. Comprehensive ophthalmologic examinations and swept-source optical coherence tomography (SS-OCT) were performed preoperatively and at postoperative months 1, 3, and 6. CVI was calculated using binarization methods, and values of affected eyes were compared with healthy fellow eyes.

**Results:** In the IERM group, baseline CVI values ( $0.67 \pm 0.05$ ) were similar to those of fellow healthy eyes ( $0.68 \pm 0.027$ ) ( $p > 0.05$ ). However, in the FTMH group, baseline CVI values ( $0.65 \pm 0.03$ ) were significantly lower compared to fellow healthy eyes ( $0.67 \pm 0.03$ ) ( $p = 0.031$ ). Both groups demonstrated significant improvements in visual acuity following PPV ( $p < 0.001$ ). Nevertheless, there was no statistically significant difference in CVI between different disease stages in both IERM and FTMH groups before and after surgery ( $p > 0.05$ ).

**Conclusion:** Our findings demonstrate that vitrectomy surgery significantly improves visual outcomes in vitreomacular interface disorders. However, the absence of clinically significant differences in CVI values suggests the need for further prospective studies with larger sample sizes to clarify the clinical relevance and prognostic value of CVI in vitreomacular interface diseases.

**Key words:** Choroidal vascular index, epiretinal membrane, macular hole.

## INTRODUCTION

Posterior vitreous detachment is a natural aging process characterized by the liquefaction and separation of the vitreous from the inner limiting membrane (ILM) of the retina. However, abnormal detachment can result in vitreomacular traction syndrome, macular hole, epiretinal membrane, and other vitreomacular interface disorders.<sup>1-3</sup> Epiretinal membrane (ERM) refers to an abnormal membrane that develops on the surface of the ILM.<sup>4</sup> Full-thickness macular hole (FTMH) presents as a tissue defect in the foveal region, extending from the ILM to the outer

segment of the photoreceptor layer.<sup>5</sup> The prevalence of these vitreomacular interface disorders has been observed to increase over time.<sup>6</sup>

The choroid, lying between the retinal pigment epithelium (RPE) and sclera, consists of vascular and stromal tissues.<sup>7</sup> Choroidal thickness (CT), measured by swept-source optical coherence tomography (SS-OCT), varies with eye conditions but is influenced by factors like axial length and diurnal changes.<sup>8-13</sup> Choroidal vascularity index (CVI), a ratio of luminal to total choroidal area, offers a more

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reliable assessment by separately evaluating vascular and stromal areas and is less affected by systemic and ocular variables, providing insight into choroidal changes.<sup>10-16</sup>

The aim of this study is to evaluate the effects of pars plana vitrectomy (PPV) performed at different stages in patients with idiopathic ERM (IERM) and FTMH on CVI during the preoperative and postoperative periods. In this study, we also aimed to assess the impact of the disease on CVI by comparing the affected eye with the healthy eye in the same patient.

## METHODS

### Study participants

In this study, we retrospectively reviewed the medical records of patients who had IERM or FTMH in one eye between September 2020 and September 2023. The study was conducted in accordance with the Declaration of Helsinki. Ethics approval was obtained from the Clinical Research Ethics Committee of Başakşehir Çam and Sakura City Hospital (Approval Number: E-96317027-514.10-231671622). Due to the retrospective nature of the study and the use of anonymized data, the requirement for informed consent was waived by the committee.

All patients received comprehensive eye exams including best-corrected visual acuity (BCVA) on the logarithm of the minimum angle of resolution scale (logMAR), intraocular pressure (IOP) via Goldmann applanation tonometry, slit-lamp biomicroscopy, axial length (AL) using optical biometer OA-2000 (Tomey, Japan), dilated fundus exams, and OCT (DRI Triton, Topcon, Tokyo, Japan) at baseline and postoperative months 1, 3, and 6. Fellow eyes served as controls.

The Inclusion Criteria are as follows: (1) aged 18 years and above; (2) patients with only one eye affected by IERM or FTMH; (3) patients who underwent uncomplicated cataract surgery at least 1 year ago; (4) patients followed up for at least 6 months after PPV surgery.

The exclusion criteria were as follows: (1) patients with any signs of retinopathy other than IERM or FTMH; (2) patients with a history of previous intraocular surgery, trauma, uveitis, or glaucoma; (3) patients with refractive error exceeding  $\pm 6$  diopters (as spherical equivalent); (4) patients with systemic diseases such as hypertension and diabetes mellitus; (5) Patients with a history of systemic

medication use; (6) patients with IERM and/or FTMH in both eyes; (7) patients with media opacity affecting OCT image quality; (8) patients with axial length greater than 26 mm; (9) patients with other pathologies affecting the posterior segment of the fellow eye.

### SS-OCT image acquisition and analysis

OCT imaging utilized SS-OCT device, with a 1050 nm wavelength and 100,000 A-scans/s speed. Each eye underwent a 6-line radial scan across the central fovea. OCT was performed after BCVA assessment and before pupil dilation, to reduce choroidal vascular effects from dilation drops<sup>17</sup>, adhering to a protocol considering circadian impacts on choroidal structures; thus, all scans were done between 10:00 AM and 12:00 AM. Two independent researchers analyzed each measurement. IERMs were classified by a 4-grade OCT system by Govetto et al. while FTMHs were sorted by size: small ( $\leq 250$  microns), medium (250-400 microns), and large ( $>400$  microns), forming three respective groups for FTMH patients.<sup>18,19</sup>

To calculate the CVI, OCT scans passing through the central foveal region were subjected to image binarization. This involved segmentation following the protocol outlined by Agrawal et al. using Image J software (version 1.51; <https://imagej.nih.gov/ij/>).<sup>20</sup> Recent advances include automated 3D CVI segmentation and AI-based choroid delineation with high accuracy using deep learning models, further supporting the robustness and reproducibility of our quantitative approach.<sup>16,21</sup> An area measuring 1,500  $\mu\text{m}$  in width, perpendicular from the RPE to the choroidal-scleral junction in the subfoveal choroid, was analyzed. The TCA was selected using the polygon selection tool, and ROIs were added to the regions of interest (ROI) manager. After converting the image into 8 bits, a Niblack auto local threshold tool was applied to provide the mean pixel value with the standard deviation (SD) for all points. Subsequently, the color threshold tool highlighted the stromal area (SA), which was then added to the ROI manager. Both the initially chosen polygonal TCA and the highlighted SA underwent selection and merging through an “AND” operation in the ROI manager. This merged area was appended to the ROI manager as a third area. The determination of the LA within the polygon involved subtracting the third composite area (SA) from the total polygon area. The ratio of LA to TCA was designated as the CVI. The Choroidal Stromal index

(CSI) is calculated as the ratio of SA to TCA, while the Choroidal Stromal Luminal Ratio (CSLR) is calculated as the ratio of SA to LA.

### **Surgical procedure**

Surgical procedures, all performed by surgeon S.A.O., utilized standard 25-gauge 3-port PPV with Alcon's Constellation Visualization System (Fort Worth, TX, USA). Techniques included posterior hyaloid membrane removal, ERM peeling with diluted triamcinolone, and ILM peeling with membrane blue-dual (DORC, Zuidland, Netherlands) and forceps (Grieshaber Revolution DSP, ILM Forceps, Alcon) for FTMH, creating an superior inverted flap. Surgeries concluded with a fluid-air exchange, air and sulfur hexafluoride 20% gas tamponade, and sclerotomies closure. Postoperatively, patients were instructed to maintain prone positioning for 5-7 days and prescribed antibiotic (1.5% moxifloxacin) and anti-inflammatory (1% prednisolone acetate) eye drops for 4 weeks, with no reported effects on CVI.

### **Statistical Analysis**

In the study, descriptive statistics for continuous variables were reported with mean  $\pm$  standard deviation and median (first (Q1) and third (Q3) quartiles), while descriptive statistics for categorical variables were reported with counts and percentages. Normality of continuous variables was assessed using the Kolmogorov-Smirnov test. For independent comparisons between two groups, independent-samples t-test was used for variables showing normal distribution, while the Mann-Whitney U test was used for variables not showing normal distribution. For comparisons among more than two independent groups, one-way analysis of variance (ANOVA) and Kruskal-Wallis tests were used depending on the distribution structure. For comparisons between preoperative and postoperative means, either paired-samples t-test or Wilcoxon signed-rank test was used depending on the distribution structure. For comparisons of more than two repeated measurements, repeated measures ANOVA or Friedman tests were used. Relationships between variables were examined using Pearson correlation coefficient. The statistical analysis was conducted using the Statistical Package for the Social Sciences (SPSS) software version 22 (SPSS Inc., Chicago, IL, USA). A significance level of 95% was considered, and results with a p-value less than 0.05 were interpreted as statistically significant.

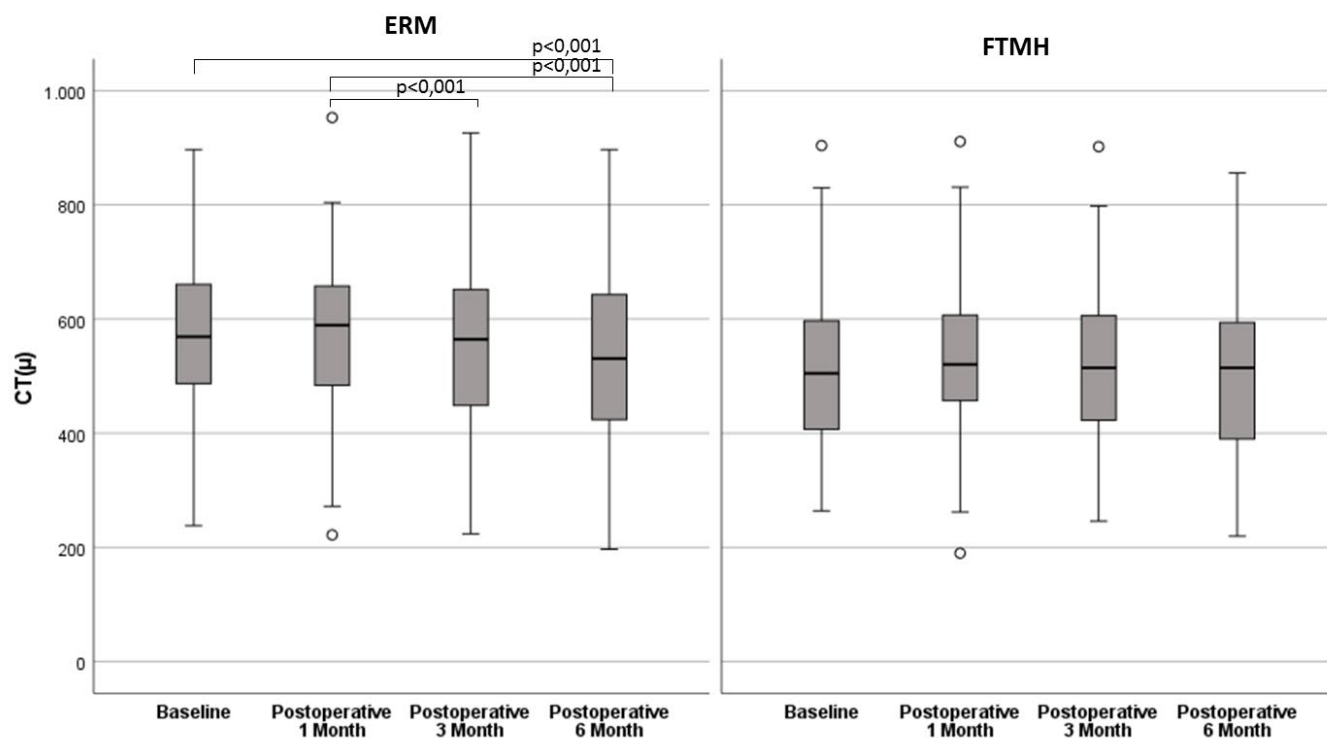
## **RESULTS**

A total of 200 eyes were included in the study, comprising 50 eyes of 50 patients with IERM, 50 healthy eyes, 50 eyes of 50 patients with FTMH, and 50 healthy eyes. Of the patients included in the study, 61% were female, with a mean age of  $64.59 \pm 9.7$  years. Table 1 presents the demographic data and baseline clinical characteristics of the IERM and FTMH patient groups. Visual acuity was significantly lower in the affected eyes compared to fellow eyes in all groups ( $p < 0.05$ ). In the FTMH group, the baseline CVI averages of the affected eyes were significantly lower than those of the fellow eyes ( $p = 0.031$ ).

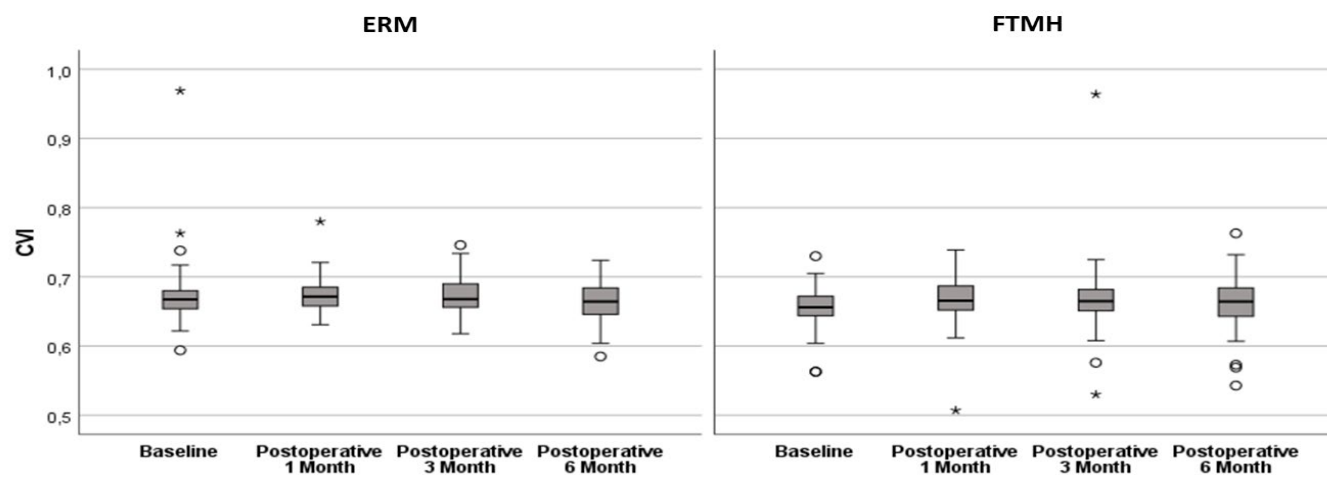
In both the IERM and FTMH groups, a decrease in BCVA (LogMAR) is observed, and this change is statistically significant ( $p < 0.001$ ). When examining the change in CT, it is observed that in the IERM group, at least one of the repeated measurements differs from the others. The change in CT over time was not found to be statistically significant in the FTMH group ( $p > 0.05$ ) (Figure 1). In both the IERM and FTMH groups, there was no significant difference found between the measurements of CVI at different time points before and after surgery ( $p > 0.05$ ) (Figure 2).

Table 2 presents the mean values of BCVA, CT, and CVI according to IERM grades. The IERM stage was classified as Grade 2 in 22 eyes (44%), Grade 3 in 17 eyes (34%), and Grade 4 in 11 eyes (22%). No patient was classified as Grade 1. In all three grade groups, the decrease in BCVA (logMAR) averages at 6 months postoperatively compared to preoperative values was statistically significant ( $p < 0.05$ ). The postoperative 6-month CT measurements of IERM patients in Grade 2 were also significantly lower compared to preoperative values ( $p < 0.05$ ). However, baseline BCVA, CT, and CVI variables were found to be similar among the grades.

Table 3 also includes the mean values of BCVA, CT, and CVI according to FTMH grades. There was no statistically significant difference found among the grade groups of hole patients in terms of these variables ( $p > 0.05$ ). However, within each grade group, it is observed that the BCVA averages at 6 months postoperatively are statistically significantly decreased compared to preoperative values ( $p < 0.05$ ). Additionally, all eyes had FTMH closure following vitrectomy.



**Figure 1.** The choroidal thickness of the IERM and FTMH patients at the four visits.



**Figure 2.** The choroidal vascularity index of the ERM and FTMH patients at the four visits.

**Table 1.** Demographic and clinical characteristics of the study populations

|                              | IERM          |              | p         | FTMH          |              | p         |
|------------------------------|---------------|--------------|-----------|---------------|--------------|-----------|
|                              | Study Eyes    | Fellow Eyes  |           | Study Eyes    | Fellow Eyes  |           |
| Number of eyes               | 50            | 50           | -         | 50            | 50           | -         |
| Age, years                   | 65,62±7,83    | 65,62±7,83   | -         | 63,56±11,25   | 63,56±11,25  | -         |
| Gender, male/<br>female      | 18/32         | 18/32        | -         | 21/29         | 21/29        | -         |
| BCVA, logMAR                 | 0,82±0,45     | 0,21±0,13    | <0,001‡,* | 1,25±0,46     | 0,18±0,19    | <0,001‡,* |
| IOP, mmHg                    | 16,16±3,63    | 15,76±3,41   | 0,572 †   | 15,5±3,16     | 15,14±3,49   | 0,591†    |
| AL, mm                       | 23,32±0,81    | 23,13±0,65   | 0,674‡    | 23,53±1,02    | 23,01±0,87   | 0,881‡    |
| CT, µm                       | 564,56±138,21 | 564,3±138,77 | 0,993†    | 514,02±144,61 | 522,4±136,56 | 0,766†    |
| Minumum hole<br>diameter, µm | -             | -            | -         | 469,62±187,21 | -            | -         |
| LA, mm <sup>2</sup>          | 0,86±0,16     | 0,87±0,17    | 0,683†    | 0,83±0,20     | 0,86±0,20    | 0,509†    |
| TCA, mm <sup>2</sup>         | 1,29±0,25     | 1,30±0,25    | 0,754†    | 1,27±0,29     | 1,27±0,28    | 0,876†    |
| CVI                          | 0,67±0,05     | 0,68±0,027   | 0,874‡    | 0,65±0,03     | 0,67±0,03    | 0,031†,*  |
| CSI                          | 0,33±0,026    | 0,33±0,027   | 0,962‡    | 0,343±0,031   | 0,327±0,038  | 0,030†,*  |
| CSLR                         | 0,495±0,057   | 0,494±0,06   | 0,917†    | 0,525±0,076   | 0,491±0,097  | 0,004‡,*  |

Continuous variables are presented as the mean ± standard deviation. Categorical variables are presented as number (%)

\* p<0,05, † Independent-samples t test, ‡ Mann Whitney U test.

IERM, idiopathic epiretinal membrane; FTMH, full thickness macular hole; BCVA, best-corrected visual acuity; IOP, intraocular pressure; AL, axial length; CT, choroidal thickness; LA, luminal area; TCA, total choroidal area; CVI, choroidal vascularity index; CSI, choroidal stromal index; CSLR, choroidal stromal luminal ratio.

**Table 2.** Changes in Visual Acuity, Choroidal Thickness and Choroidal Vascularity Index According to Epiretinal Membrane Stages

|                                      |                       | IERM                   |                        |                        | P       |
|--------------------------------------|-----------------------|------------------------|------------------------|------------------------|---------|
|                                      |                       | Grade 2 (n=22)         | Grade 3 (n=17)         | Grade 4 (n=11)         |         |
|                                      |                       | Mean±SD (quartile)     | Mean±SD (quartile)     | Mean±SD (quartile)     |         |
| BCVA, logMAR                         | Baseline              | 0,85±0,46(0,5-1)       | 0,77±0,44(0,5-1)       | 0,85±0,47(0,4-1)       | 0,725** |
|                                      | Postoperative 6 Month | 0,38±0,2(0,2-0,5)      | 0,43±0,18(0,4-0,5)     | 0,58±0,32(0,5-0,7)     | 0,052** |
| p (Baseline x Postoperative 6 Month) |                       | <0,001†,*              | <0,001†,*              | 0,023†,*               |         |
| CT, µm                               | Baseline              | 554,23±140,53(483-678) | 550,41±123,04(500-628) | 607,09±159,22(537-678) | 0,469** |
|                                      | Postoperative 6 Month | 506,18±140,61(410-620) | 511,29±142,3(424-618)  | 589±199,31(510-714)    | 0,323†† |
| p (Baseline x Postoperative 6 Month) |                       | 0,028‡,*               | 0,079‡                 | 0,598‡                 |         |
| CVI                                  | Baseline              | 0,68±0,07(0,66-0,67)   | 0,67±0,03(0,65-0,68)   | 0,68±0,03(0,65-0,68)   | 0,775** |
|                                      | Postoperative 6 Month | 0,66±0,03(0,64-0,68)   | 0,67±0,02(0,65-0,69)   | 0,66±0,04(0,64-0,68)   | 0,607†† |
| p (Baseline x Postoperative 6 Month) |                       | 0,284†                 | 0,503‡                 | 0,062†                 |         |

Values are presented as the mean ± standard deviation (quartiles (q1-q3)). q1: first quartile (25th percentile), q3: third quartile (75th percentile) \* p<0,05, † Wilcoxon signed ranks test, ‡ Paired-samples t test, \*\* Kruskal Wallis, †† One way ANOVA.  
IERM, idiopathic epiretinal membrane; BCVA, best-corrected visual acuity; CT, choroidal thickness; CVI, choroidal vascularity index

**Table 3.** Changes in Visual Acuity, Choroidal Thickness and Choroidal Vascularity Index According to Full Thickness Macular Hole

|                                                                                                                                                                                                                                                                                                                                                                                                    |                       | FTMH                  |                       |                        | P       |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|-----------------------|-----------------------|------------------------|---------|
|                                                                                                                                                                                                                                                                                                                                                                                                    |                       | Grade 1 (n=7)         | Grade 2 (n=10)        | Grade 3 (n=33)         |         |
|                                                                                                                                                                                                                                                                                                                                                                                                    |                       | Mean±SD (quartile)    | Mean±SD (quartile)    | Mean±SD (quartile)     |         |
| BCVA, logMAR                                                                                                                                                                                                                                                                                                                                                                                       | Baseline              | 1,27±0,59(0,8-1,3)    | 1,11±0,41(1-1,3)      | 1,3±0,46(1-1,3)        | 0,475** |
|                                                                                                                                                                                                                                                                                                                                                                                                    | Postoperative 6 Month | 0,58±0,33(0,3-1)      | 0,66±0,37(0,4-1)      | 0,74±0,33(0,5-1)       | 0,428** |
| p (Baseline x Postoperative 6 Month)                                                                                                                                                                                                                                                                                                                                                               |                       | <0,018†,*             | 0,010‡,*              | <0,001†,*              |         |
| CT, µm                                                                                                                                                                                                                                                                                                                                                                                             | Baseline              | 518,43±107,9(474-602) | 574,8±147,62(477-678) | 504,67±148,89(400-586) | 0,313†† |
|                                                                                                                                                                                                                                                                                                                                                                                                    | Postoperative 6 Month | 502±109,78(390-584)   | 553,8±151,84(485-595) | 501,64±141,73(375-594) | 0,579†† |
| p (Baseline x Postoperative 6 Month)                                                                                                                                                                                                                                                                                                                                                               |                       | 0,627‡                | 0,172‡                | 0,633‡                 |         |
| CVI                                                                                                                                                                                                                                                                                                                                                                                                | Baseline              | 0,67±0,03(0,64-0,7)   | 0,66±0,02(0,65-0,67)  | 0,66±0,03(0,64-0,67)   | 0,365** |
|                                                                                                                                                                                                                                                                                                                                                                                                    | Postoperative 6 Month | 0,67±0,04(0,64-0,69)  | 0,66±0,21(0,66-0,68)  | 0,66±0,04(0,64-0,68)   | 0,488** |
| p (Baseline x Postoperative 6 Month)                                                                                                                                                                                                                                                                                                                                                               |                       | 0,933†                | 0,481‡                | 0,354†                 |         |
| Values are presented as the mean ± standard deviation (quartiles (q1-q3)). q1: first quartile (25th percentile), q3: third quartile (75th percentile)<br>* p<0,05, † Wilcoxon signed ranks test, ‡ Paired-samples t test, ** Kruskal Wallis, †† One way ANOVA.<br>FTMH, full thickness macular hole; BCVA, best-corrected visual acuity; CT, choroidal thickness; CVI, choroidal vascularity index |                       |                       |                       |                        |         |

## DISCUSSION

CVI is considered a more stable and consistent marker of choroidal diseases, less affected by systemic events.<sup>20</sup> Our findings regarding postoperative CVI dynamics are in line with recent studies showing transient decreases in CVI following vitrectomy for IERM and FTMH.<sup>22</sup> In this study, we investigated the effects of vitrectomy on choroidal vascular components in pseudophakic eyes with vitreomacular diseases such as IERM and FTMH.

Our study, like many others in the literature, found that the baseline CT characteristics of eyes with IERM and FTMH were similar to healthy eyes.<sup>23,24</sup> However, in the IERM group, progressive thickening and anteroposterior traction of the ERM and ILM may lead to choroidal involvement. Conversely, in the FTMH group, choroidal

involvement may occur through different mechanisms such as vitreomacular traction.<sup>24-27</sup> Following vitrectomy, a decrease in CT was observed only in stage 2 of the IERM group, possibly due to an imbalance in patient distribution among the groups. In contrast, no significant changes were observed in total or stage-based CT after vitrectomy in the FTMH group. These findings suggest that postoperative inflammation may initially increase CT, followed by a gradual reduction due to decreased mechanical forces and inflammation over follow-up periods. Similarly, recent clinical evidence supports minimal CVI changes in eyes with vitreomacular traction, indicating that the impact of tractional forces may differ across VMI pathologies.<sup>28</sup>

Preoperative CVI values were found to be similar to healthy eyes in patients with IERM, while they were lower in the FTMH group compared to healthy eyes (p=0.031).



Our results are consistent with a study conducted in both IERM and FTMH groups.<sup>23</sup> Additionally, there are studies indicating no difference in CVI between healthy and affected eyes in patients with IERM and FTMH.<sup>25,29,30</sup> These differences suggest that changes in the choroid due to vitreomacular disease may affect the choroid in healthy eyes as well, indicating a need for further research.

Although a decrease in CVI was observed in the IERM group at all visits after vitrectomy, no significant differences were found.<sup>23,25,27</sup> In contrast to our study, many studies related to IERM employed combined surgeries, which led to an increase in CVI compared to our findings.<sup>31,32</sup> The reason for this could be attributed to a higher amount of inflammatory cytokines resulting from combined vitrectomies with cataract surgery, leading to more pronounced changes in choroidal vascular structures. Therefore, understanding and interpreting data regarding CVI in combined surgeries may be more challenging than for patients undergoing PPV alone. Consequently, we believe that including only pseudophakic patients in the study will provide more consistent data. Additionally, the robustness of our CVI analysis is supported by recent validations of 3D segmentation and deep-learning based choroidal analysis techniques.<sup>16</sup>

As far as we know, although there are numerous studies evaluating choroidal vascular structures in patients with IERM, there is a lack of literature providing detailed information on choroidal vascular structures according to the stages of the disease. No differences in CVI values between groups were observed during both baseline and after vitrectomy follow-ups across various stages of IERM. It is understood that as the stages of IERM progress, anteroposterior traction increases. Therefore, the relationship between the decrease in CVI after PPV and the elimination of anteroposterior traction is not clear, and further research is needed to investigate this issue.

After successful FTMH closure surgery, retinal microvascular structures undergo remodeling, with glial and Müller cell proliferation.<sup>33</sup> This proliferation supports the migration of healthy photoreceptors towards the hole area, promoting hole closure and improving visual prognosis. Changes in choroidal tissue vascular structures following FTMH closure serve as indicators of metabolic activity, supporting retinal and photoreceptor function.

In our study, we aimed to standardize surgical procedures by employing the same surgeon and method for all vitrectomy patients, reducing potential choroidal vascular variations. FTMH patients were categorized based on hole diameter: small, medium, and large. Despite significant differences in CVI values between FTMH eyes and fellow eyes across all groups, no variance was observed between FTMH stages pre- and post-vitrectomy. Although vitrectomy typically resolves traction and benefits retinal and choroidal vascular structures, our findings did not correlate disease stage with CVI. This suggests that surgical-induced inflammation may influence choroidal vasculature. Limited research exists on FTMH patients' choroidal vasculature, making our study, to our knowledge, the first to assess CVI according to FTMH staging.

Patients with choroidal damage in FTMH have been suggested to have a poorer visual prognosis after surgery, with choroidal vascular structures contributing to the recovery of RPE and retinal functions.<sup>34</sup> Contrary to studies demonstrating increased macular choroidal blood flow after macular hole surgery, we did not observe any difference in CVI among our patients.<sup>30-35</sup> Another study utilizing laser speckle flowgraphy in FTMH patients demonstrated no change in choroidal capillary flow before and after surgery, similar to our study where similar results were obtained based on CVI parameters.<sup>36</sup> The increase in choroidal capillary flow after FTMH closure may be attributed to the restoration of metabolic activity in the previous macular hole area with surgical closure.

This study has some limitations. Firstly, we used normal healthy eyes as a control group to analyze CVI differences in ERM or FTMH. While selecting healthy eyes as the control group, we aimed to minimize interindividual CVI variations, but it should be noted that there may be personal CVI differences, which could also affect the study results. In this study, the healthy fellow eye of each patient was used as the control group. This method minimizes the impact of inter-individual systemic and anatomical variability by eliminating potential confounding factors such as age, sex, and axial length. Additionally, since all patients were pseudophakic, optical variations related to the lens were also avoided. However, it should be considered that in some cases, subclinical involvement in the fellow eye may exist, which could limit the assumption that the control eye is



entirely “healthy.” Therefore, this methodological context should be taken into account when interpreting the findings. This statement was intended to emphasize a general methodological limitation of CVI studies, especially for readers who might apply different control designs, rather than indicating a specific weakness in our intra-individual comparison approach. Secondly, eyes were not classified as tractional or non-tractional based on the presence of vitreopapillary traction. Finally, due to the retrospective nature of patient data collection in this study, information on posterior vitreous detachment was not recorded, making it impossible to evaluate this aspect.

The strengths of our study include all eyes in the study group being pseudophakic and operated on with the same surgical method. Additionally, we performed stage-based evaluations in patients with IERM and FTMH. There were no differences in baseline CVI among all stages, contributing to more consistent CVI measurements during the follow-up assessments.

## Conclusion

In the IERM group, the baseline CVI measurements between patient and fellow eyes, as well as the difference in CVI measurements in patient eyes before and after vitrectomy in all stages, were not clinically significant. In the FTMH group, while the difference in CVI measurements between patient and fellow eyes was initially significant, the difference in before and after vitrectomy CVI measurements in patient eyes in all stages was not clinically significant. Therefore, our study has provided insight into potential vascular and structural changes in vitreomacular interface disorders and between stages. Further prospective studies with larger sample sizes and long-term follow-up are needed to determine the clinical relevance of CVI and its potential use as a prognostic biomarker across different stages of vitreomacular interface disorders, particularly through stage-based stratification and longitudinal assessment of pre- and postoperative CVI changes in relation to visual and anatomical outcomes.

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