Optical coherence tomography biomarkers as predictive factors for postoperative visual acuity in patients with epiretinal membrane treated with vitrectomy

Irini Chatziralli1, Eleni Dimitriou1, Tina Xirou2, Stamatina A. Kabanarou2, George Theodossiadis1, Panagiotis Theodossiadis1

Abstract:
BACKGROUND: The purpose of this retrospective study was to evaluate potential predictive factors of postoperative visual outcome in patients with idiopathic epiretinal membrane (iERM), treated with pars plana vitrectomy (PPV).

METHODS: Participants in the study were 46 patients diagnosed with iERM, who underwent PPV. Best-corrected visual acuity measurement and spectral domain-optical coherence tomography (OCT) were performed at baseline (preoperatively), and at months 6 and 12 postoperatively. Demographic characteristics and OCT parameters were assessed as potential predictive factors for postoperative visual outcome.

RESULTS: Increasing age, retinal thickness, presence of disorganization of inner retinal layers, ellipsoid zone disruption, and presence of vitreomacular traction were found to be negatively associated with postoperative visual acuity. Gender, presence of subretinal fluid, cysts in the inner or outer nuclear layer, and hyperreflective foci were not found to affect visual acuity. There was statistically significant improvement in visual acuity and central retinal thickness between baseline and months 6 and 12 in the study sample.

CONCLUSIONS: It is important to determine predictive factors for visual outcome, so as to inform patients about prognosis and help in the decision-making of patients’ management.

Keywords: Epiretinal membrane, optical coherence tomography, predictive factors, vitrectomy

Introduction

Epiretinal membrane (ERM) refers to fibroglial cellular proliferation at the vitreoretinal interface, above the internal limiting membrane (ILM) mainly at the macular area.1,2 The prevalence of ERM has been estimated to be about 2.2%–28.9%, which increases with age, while the 5-year incidence has been found to be 5.3% in the Blue Mountains Eye Study.3-6 ERM can be idiopathic or associated with ocular abnormalities, such as retinal vascular disease, intraocular inflammation, retinal detachment, or trauma.1,2 Idiopathic ERM (iERM) at the early stages is mostly asymptomatic and becomes symptomatic progressively, being a common cause of visual impairment and metamorphopsia in patients over the age of 50 years.3,4

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The gold standard for the treatment of iERM is pars plana vitrectomy (PPV), while the decision on the necessity of ERM removal has been mainly based on patients’ symptoms and visual acuity. Previous studies have shown that preoperative visual acuity, central macular thickness, patient’s age, integrity of ellipsoid zone, and external limiting membrane are prognostic factors for visual outcome after PPV.

Advances in optical coherence tomography (OCT) have led to the introduction of new anatomic measures on spectral-domain OCT (SD-OCT), such as precise evaluation of individual layers, qualitative and quantitative assessment of fluid distribution, existence of hyperreflective foci (HF), inner retinal irregularity, and disorganization of inner retinal layers (DRIL), which may predict more precisely the treatment success or failure after treatment. In light of the above, the purpose of this study was to investigate if characteristics identified on SD-OCT may serve as biomarkers to predict postoperative visual outcome in patients with iERM, treated with PPV.

Methods

Participants in this retrospective study were 46 patients (46 eyes) with iERM, who underwent PPV at Red Cross Hospital and 2nd Department of Ophthalmology, University of Athens, Greece. The study was in adherence with the Tenets of Helsinki Declaration and no institutional review board approval was needed, since it was a retrospective study.

Patients’ charts were reviewed for demographic data and best corrected visual acuity (BCVA). All participants had undergone SD-OCT (Spectralis; Heidelberg Engineering, Heidelberg, Germany). Retinal thickness was measured using the retinal thickness map analysis protocol with nine Early Treatment Diabetic Retinopathy Study subfields. For each study eye, a raster of 6 radial scans was also performed. Qualitative and quantitative evaluations of SD-OCT images were performed at baseline, assessing the presence of various morphologic features, including capillary refill time (CRT) measurement (defined as average retinal thickness of the circular area with 1 mm diameter around the foveal center), presence of subretinal fluid (SRF), presence of cystoid changes in the outer nuclear layer (ONL) and in the inner nuclear layer (INL), presence of DRIL, presence of HF, integrity of ellipsoid zone (defined as intact or disrupted), presence of VMT. OCT features were evaluated preoperatively (baseline) as well as at months 6 and 12 postoperatively. OCT images were graded by two independent assessors (IC, ED) and the interobserver agreement was almost perfect (k > 0.86).

Statistical analysis

For the description of patients’ characteristics at baseline, mean ± standard deviation was used for continuous variables and counts with percentages for categorical variables. For the longitudinal comparisons of BCVA and CST between baseline and each time point, the Wilcoxon matched-pairs signed-ranks test was used; given that two comparisons were done, the level of statistical significance was set at 0.05/2 = 0.025, according to the Bonferroni correction.

For the assessment of factors that may determine the visual acuity, since there was marked deviation from normality, Generalized Least Squares (GLS) linear regression analysis was performed, as appropriate for longitudinal data, given the intercorrelation of observations in such datasets. Visual acuity was the dependent variable. Factors that were assessed as potential predictors for visual acuity were: age, gender, the CST, the presence of SRF, the presence of cysts in ONL and INL, the presence of DRIL, the presence of HF, the status of EZ, and the presence of VMT. The aforementioned factors were set as independent variables, in models always adjusted for time (in months). The beta coefficients with their 95% confidence intervals (CIs) are provided in the manuscript.

Statistical analysis was performed using SPSS 22.0 (SPSS Inc., Chicago, Illinois, USA). A P < 0.05 was considered as statistically significant, apart from cases where the Bonferroni correction was adopted, as declared above.
Results

The study included 46 patients (46 eyes) with iERM, with mean age of 73.4 ± 7.2 years. Thirty-seven percent of patients in this study were male and 63% female. Table 1 shows the demographic and clinical baseline characteristics of our study sample.

The mean BCVA was 0.71 ± 0.15 logMAR and improved to 0.39 ± 0.17 logMAR at month 6 and to 0.29 ± 0.18 logMAR at month 12 postoperatively, which differed significantly compared to baseline (P < 0.001 for both time points).

The mean CRT was 529 ± 48 μm and decreased to 432 ± 57 μm at month 6 and to 412 ± 39 μm at month 12 postoperatively, which differed significantly compared to baseline (P < 0.001 for both time points).

Results of the GLS linear regression analysis, examining the factors associated with BCVA (in letters) are presented in Table 2. Increasing age (coefficient = −4.01, 95%CI = −5.97–−2.05, P < 0.001), increasing crystal field theory (CFT) (coefficient = −5.20, 95%CI = −8.72–−1.52, P < 0.001), presence of DRIL (coefficient = −4.89, 95%CI = −6.82–−2.96, P < 0.001), EZ disruption (coefficient = −6.55, 95%CI = −9.19–−1.98, P < 0.001), and presence of VMT (coefficient = −3.78, 95%CI = −5.93–−1.74, P < 0.001), were significantly associated with worse BVCA. BCVA was not associated with gender, the presence of SRF, the presence of cysts in the ONL and INL and the presence of HF.

Discussion

The principal message of this study is that age, central foveal thickness, presence of DRIL, ellipsoid zone disruption, and co-existence of VMT were found to be independent predictive factors for final visual outcome, since they were negatively associated with postoperative visual acuity in patients with iERM treated with PPV.

Previous studies have investigated predictive factors for postoperative BCVA in patients with iERM treated with PPV, such as photoreceptors integrity,[14,15] macular volume[16] and changes in inner retinal layers.[13,17] Noticeably, inner segment/outer segment (OS) and cone OS tips integrity, as well as photoreceptor segments length, have been found to be the most promising predictive factors, but all of them refer to the outer retinal layers, although ERM is located on the inner retina.[10] Our study confirmed the already known fact that CFT and EZ have a significant role in the postoperative visual outcome in patients with iERM, but also demonstrated that inner retinal layers may be affected, since DRIL was found to be associated with worse visual acuity.

The poor visual outcome in cases of DRIL can be attributed to the irregularity of the inner retinal layers, probably caused by chronic tractional forces. Inner retinal layers, especially at the macular area, seem to be sensitive to tractional stress. Kim et al. hypothesized that ERM contraction leads to alteration of inner foveal microanatomy, stretching of the INL or edema, which may disorganize the cell bodies that comprise the INL.[18] The structural changes in inner retinal layers may consequently result in disconnection of synaptic junctions between photoreceptors and ganglion cells, while Mueller cells, bipolar, horizontal and amacrine cells may be also affected.[19,20] The latter has been also supported by electroretinogram studies, which have found that b-waves were more affected than a-waves, suggesting Mueller or bipolar cells dysfunction.[14,21]

Regarding the role of VMT, Chatziralli et al. have shown that the co-existence of VMT with ERM may lead to significantly greater EZ defect, causing parafoveal functional disturbances and affecting the visual acuity, compared to patients with VMT alone.[22] This may be explained, taking into account that the traction...
induced by VMT and co-existent ERM causes the loss of apposition between cone OS and retinal pigment epithelium.

It is also worthy to mention that the influence of age on postoperative visual acuity has been previously analyzed, but the results of the so far studies are controversial. Nitta et al. have found that younger age was significantly associated with visual improvement of 0.3 logMAR or more compared to baseline, but other studies did not confirm this association. Our results demonstrated that increasing age is a negative predictive factor for postoperative visual outcome, which was consistent with Nitta et al.

Potential limitation of this study pertains to its retrospective nature and the relatively small study sample. Moreover, the nature of the GLS regression models inherently precluded the incorporation of baseline BCVA as a separate covariate in the model; in this context, baseline values are simply predicted as linear combinations in the respective equations, as happens for any other time point assuming linearity during the study period.

**Conclusions**

Our study showed that age and OCT biomarkers, such as central foveal thickness, presence of DRIL, EZ disruption, and VMT, may predict postoperative visual acuity in patients with iERM treated with PPV. On the other hand, gender, the presence of SRF, cysts, or HF did not seem to affect postoperative visual outcome. Further studies with larger study sample are needed to verify our results and determine OCT biomarkers and other predictive factors for such patients, so as to inform patients about the postoperative prognosis and help us in the decision-making of patients’ management.

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**Conflicts of interest**
There are no conflicts of interest.

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