· Clinical Research ·

Post-operative visual outcomes based on morphological staging of idiopathic epiretinal membranes on OCT

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Abstract

● **AIM:** To evaluate the recently described optical coherence tomography (OCT) based classification of epiretinal membrane (ERM) and its usefulness in predicting the functional outcome.

● **METHODS:** A retrospective observational review of OCT scans of patients with the diagnosis of idiopathic ERM was carried out from January 2016 to June 2021. All consecutive images diagnosed with any stage of idiopathic ERM and fulfilled the eligibility criteria were included in the analysis. ERM was identified on OCT scans as a thin hyperreflective layer over the inner layers of retina. OCT scans of patients with ERM who underwent vitrectomy, were independently staged as per the new classification by two independent retinal surgeons to form a consensus on stage. Best corrected visual acuity (BCVA) in logMAR scale and central subfield thickness (CST) on pre- and post-operative spectral domain OCT scans were the variables noted for all patients at the time of diagnosis and at 6 and 12mo follow up visit after undergoing intervention. Partial correlation coefficient was computed between BCVA (logMAR) and CST by ERM stage adjusting by baseline measures.

● **RESULTS:** Clinical charts of 74 patients with idiopathic ERM were assessed. Clinically significant improvement in BCVA overtime was observed with significant difference in median visual acuity of patients with Stage II-IV ERM with $P<0.001$. The median CST of all patients with stage II-IV ERM showed similar consistent improvement with $P<0.001$ from baseline to 12th month. Our results showed not only gain in visual acuity but also shift from baseline to anatomical normalization of CST in stage II. We found a decrease in CST with difference of 166 μm and 151 μm in stage III and stage IV respectively. Our results remained consistent with the hypothesis of improved visual outcomes with all stages of ERM with adjusted moderate linear correlation between visual acuity and CST in stage II-IV ($r>0.3$).

● **CONCLUSION:** Equally significant visual outcomes of patients with ERM staged II-IV and therefore can be counselled for improved visual acuity after surgical removal of ERM with improvement up to 5 lines on Snellen's chart from the baseline.

● **KEYWORDS:** optical coherence tomography; epiretinal membrane; cotton ball sign; vitreoschisis; vitrectomy

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INTRODUCTION

Epiretinal membrane (ERM) is a fibro cellular growth on or adjacent to the inner retinal layers. ERM can be completely asymptomatic at times, but it can also lead to moderate or severe decline in visual acuity and metamorphopsia[1]. ERM can be idiopathic or secondary to other pathologies that may include inflammatory processes, retinal vascular disorders, tumours, or trauma. The precise mechanism of idiopathic ERM is hypothesized by various researchers and the most common relation is noted with posterior vitreous detachment (PVD)[2]. One of widely accepted theories is that breaks in internal limiting membrane (ILM) occur at the time of PVD that cause proliferation of glial cells on the inner retinal surface and lead to ERM formation. Glial cells are thought to originate from Müller cells whereas hyalocytes have also been identified in idiopathic ERMs. Another view suggests that PVD leads to vitreoschisis which is followed by proliferation of vitreous cortical cells in the macular area. The exact origin of these cells is unclear due to the ability of these cells to transdifferentiate[3].

The prevalence of ERM ranges between 2.2% and 28.9% as reported in various epidemiological studies and the incidence has been found to increase with age. Among Asians, the incidence is estimated to be 3.8%[4-5]. ERM was initially classified by Fung *et al*[6], which included cellophane maculopathy, crinkled cellophane maculopathy and macular pucker. This classification has been in use until optical coherence tomography (OCT) based classifications gave a better insight into the architecture of ERM, its relationship with vitreomacular interface and its influence on the vital retinal layers. OCT has now become instrumental in diagnosing, managing, and monitoring the ERM and its role in visual impairment[7]. One of the landmark studies published about vitreomacular interface included the findings of International Vitreomacular Traction Study Group which changed the understanding of macular hole formation and the role of vitreomacular interface abnormalities. It identified and classified vitreomacular adhesion, vitreomacular traction (VMT) and macular hole into further subclassifications and gradings but did not specify the role of ERM in the pathogenesis[8]. Various other OCT based classifications of ERM have been published where authors have correlated the ERM structure and its progression with macular morphology. Hwang *et al*'s[9] classification includes fovea involving ERM with outer retinal layer thickening (1A), fovea involving ERM with outer and inner retinal layer thickening (1B) and fovea involving ERM with inner retinal layer thickening (1C); the other arm of this classification involves fovea sparing ERMs with retinal schisis and macular pseudo hole. Konidaris *et al*[10] classified ERM based on OCT characteristics and divided the ERM as; with and without PVD and ERM with and without VMT. Both arms of classification were further subclassified in subgroups based on the presence of ERM contraction, macular pseudo hole, retinal oedema, retinal schisis, retinal folding, cystoid macular oedema (CME) and retinal detachment (RD). Although, it has explained the morphology of ERM and macula extensively, its functional relevance with impact on vision after intervention remains unclear.

Newer ERM classifications have focused more on identifying the reason of loss of vision. This has included the disrupted ellipsoid zone and outer segments of photoreceptors (PR), central subfield thickness (CST) and inner segment/outer segment line disruption[11-12]. Researchers have also found that the morphology of inner retinal layers contributes to visual function. The research group led by Govetto *et al*[13] has recently reclassified ERM based on OCT morphology. They have shown morphologic features that are more closely associated with visual function and explained the role of inner retinal layer morphology and its impact on vision. They have divided ERM into 4 stages; stage I has intact foveal pit with identifiable retinal layers, stage II has loss of foveal pit with identifiable retinal layers, stage III has loss of foveal pit with ectopic inner retinal layers that are individually identifiable. Lastly, stage IV includes loss of foveal pit with ectopic foveal layers that are also disrupted and not identifiable[14].

In this study we have evaluated the correlation of recent morphological based Govetto *et al*[13,15] classification of ERM with post-operative visual acuity and CST change. OCT is the most readily accessible and non-invasive imaging modality to identify retinal pathology. Therefore, correlation of ERM stages with visual outcomes was calculated which helped determine its impact on functional visual outcomes in our population. To our knowledge, this is the first study in our region (low to middle income countries) to correlate the latest classification of ERM and its role in determining the prognosis after surgical intervention.

SUBJECTS AND METHODS

Ethical Approval Data was collected from the medical records on a structured proforma. Access to medical records was sought after written approval from the Ethic Review Committee (ERC # 2021-6502-18464) of the Aga Khan University Hospital and our study followed the principles of The Declaration of Helsinki. Written informed consent was obtained from the patients.

A retrospective observational review was conducted at The Aga Khan University Hospital, Karachi. Medical records and OCT scans of patients with the diagnosis of idiopathic ERM from January 2016 to June 2021 were reviewed. OCT images were obtained using the Spectralis spectral domain (SD)-OCT (Heidelberg Engineering GmbH, Heidelberg, Germany) and reviewed with the Heidelberg Eye Explorer (version 1.10.2.0) using the HRA/ Spectralis Viewing Module (version 6.9.5.0).

All consecutive images diagnosed with any stage of idiopathic ERM and fulfilled the eligibility criteria were included in the analysis. Those patients aged 18 or more with at least 12mo follow up post operatively were included in the initial review. History of acquired or inherited retinal disorders, RD, choroidal neovascularization, central serous chorioretinopathy, advanced glaucoma, or optic neuropathy, endophthalmitis or any other intraocular infection, ocular trauma and history of retinal lasers or intravitreal injections were used as exclusion criteria. ERM was identified on OCT scans as a thin hyperreflective layer over the inner layers of retina. OCT scans of patients with ERM who underwent vitrectomy, were independently staged as per the Govetto *et al*[13,15] classification by two retinal surgeons to form a consensus as shown in Figure 1.

In case of disagreement between the two, a third retinal surgeon analysed the scans. Images from the Govetto *et al*[13,15] study were used as reference to stage the ERM. Best corrected visual acuity (BCVA) in logMAR scale and CST on pre- and post-operative SD-OCT scans were the variables noted for all patients at the time of diagnosis and at 6 and 12mo follow up visit after undergoing the vitrectomy procedure.

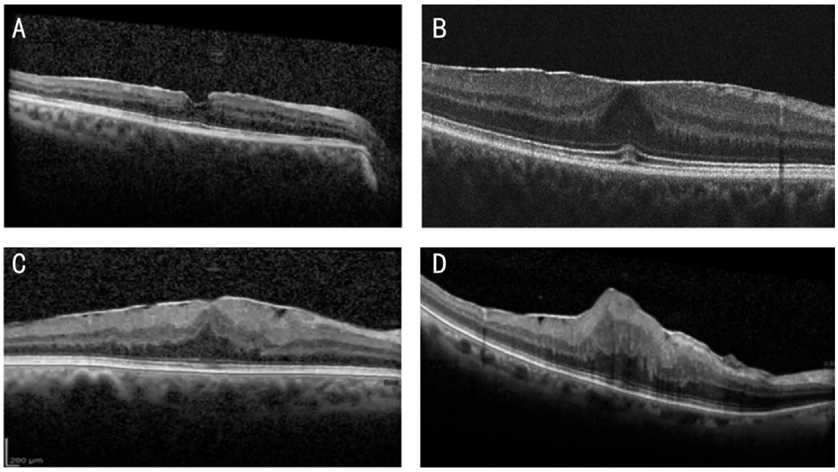

Figure 1 Pre-operative OCT scans of ERM (stage I-IV) as described by the new classification A: Stage I ERM: Intact foveal pit with identifiable retinal layers; B: Stage II ERM: Loss of foveal pit wth identifiable retinal layers and cotton ball sign; C: Stage III ERM: Loss of foveal pit wth identifiable ectopic inner retinal layers; D: Stage IV ERM: Loss of foveal pit wth unidentifiable ectopic foveal layers.

Data was analysed on SPSS version 22 (SPSS Inc., Chicago, Illinois, USA). Normality of continuous data was assessed by Shapiro-Wilk test. Mean±standard deviation or median (interquartile range; IQR) is presented for continuous data and frequency and percentages are presented for qualitative data. Partial correlation coefficient was computed between BCVA (logMAR) and CST by ERM stage adjusting by baseline measures. Non-paramatric Friedman repeated measure ANOVA was applied to assess change in variables over time. A *P* value of 0.05 was considered as significant.

RESULTS

Clinical charts of 74 patients with idiopathic ERM were assessed in which 35 were females. A total of 68 patients had documented visual acuity whereas, 58 patients had CST measured on OCT scans that were available at the time of review. ERM was staged according to Govetto *et al*[13,15] classification and post operative visual acuity and CST was analysed at 6th and 12th month post operatively. The demographics and clinical characteristics are shown in Table 1. We observed a significant improvement in visual acuity overtime with significant difference in median visual acuity of patients with stage II-IV with *P*-values on Friedman Chi-square of <0.001 that remained consistent on post hoc Dunn's test. Median visual acuity at 12th month for stage II, III, IV was 0.00 (0.00-0.10), 0.20 (0.10-0.20), 0.60 (0.50-0.70). Difference in visual acuity of patients with stage I ERM showed *P*-value of 0.037 which analysed total of 4 patients (Table 2).

Table 1 Demographics and clinical characteristics of study population *n* (%)

Variables	Data
Age, y	60.4±8.0
Gender	
Female	35 (47.3)
Male	39 (52.7)
Side of eye	
Left	33 (44.6)
Right	41 (55.4)
ERM stage	
Stage-I	5 (6.8)
Stage-II	22 (29.7)
Stage-III	31 (41.9)
Stage-IV	16 (21.6)
Concomitant cataract surgery	
Yes	33 (44.6)
No	41 (55.4)
Cotton ball sign	
Yes	9 (12.2)
No	65 (87.8)
Dye used	
Yes	70 (94.6)
No	4 (5.4)
ILM peel	
Yes	69 (93.2)
No	5 (6.8)

ILM: Internal limiting membrane.

Our results showed equally significant visual outcomes of patients with ERM staged II-IV and therefore can be counselled for improved visual acuity after surgical removal of ERM with improvement up to 5 lines on Snellen's chart from the baseline. The median CST of all patients with stage II-IV that showed similar consistent improvement with *P*-value on Friedman Chi-square (P<0.001) from baseline to 12th month except at stage I that analysed total of 3 patients (P=0.94). Our results showed not only gain in visual acuity but also shift from baseline to anatomical normalization of CST in stage II. We found a decrease in CST with difference of 166 and 151 μm in stage III and stage IV respectively (Table 3).

Table 2 Median change in visual acuity overtime median (IQR), n=68

Follow-ups	Stage-I, n=4	Stage-II, n=20	Stage-III, n=28	Stage-IV, n=16
Baseline	0.15 (0.10, 0.35)	0.5 (0.33, 0.60)	0.70 (0.60, 0.88)	1.10 (0.90, 1.30)
6mo	0.05 (0.00, 0.25)	0.10 (0.00, 0.20)	0.30 (0.20, 0.50)	0.80 (0.60, 1.00)
12mo	0.00 (0.00, 0.15)	0.00 (0.00, 0.10)	0.20 (0.10, 0.20)	0.60 (0.50, 0.70)
Difference	$\chi^2(2)=6.62$, $P=0.037$	$\chi^2(2)=19.60$, $P<0.001$	$\chi^2(2)=46.62$, $P<0.001$	$\chi^2(2)=22.43$, $P<0.001$

Overall change over time: $\chi^2(2)=103.79$, $P<0.001$. IQR: Interquartile range.

Table 3 Median change in central subfield thickness overtime median (IQR), μm, n=58

Follow-ups	Stage-I, n=3	Stage-II, n=19	Stage-III, n=24	Stage-IV, n=12
Baseline	195.0 (190.0, 198.0)	342.0 (315.0, 410.0)	450.5 (361.0, 514.3)	526.5 (463.3, 650.3)
6mo	194.0 (188.0, 199.0)	330.0 (293.0, 376.0)	373.5 (328.8, 426.8)	455.5 (398.3, 563.0)
12mo	191.0 (190.0, 193.0)	231.0 (213.0, 245.0)	284.5 (255.5, 311.5)	375.5 (312.0, 394.5)
Difference	$\chi^2(2)=0.67$, $P=0.944$	$\chi^2(2)=30.63$, $P<0.001$	$\chi^2(2)=37.75$, $P<0.001$	$\chi^2(2)=16.17$, $P<0.001$

Overall change over time: $\chi^2(2)=82.17$, $P<0.001$. IQR: Interquartile range.

Our results remained consistent with the hypothesis of improved visual outcomes with all stages of ERM with adjusted moderate linear correlation between visual acuity and CST in stage II-IV ($r>0.3$).

DISCUSSION

This study determined the correlation between pre-operative OCT based ERM classification with post-operative visual and anatomic outcomes. The results show a clear predictive value of post-surgical outcomes based on the Govetto *et al*[13,15] classification. We found in our study population, those with ERM stages II to IV had consistent improvements in both BCVA and CST 6- and 12-month post-operatively. On the other hand, stage I showed no significant improvement in either BCVA or CST after surgery. Unfavourable results in stage I were seen but they need to be viewed in light of the small sample size of this group in our study. Four stage I patients out of total 68 were included in the analysis for BCVA and only 3 out of total of 58 for CST changes. Therefore, in case of stage I ERM our study could not reach a very strong conclusion and there is a need for further review of patients in the future to reach a good enough sample size. Adjusted correlation coefficients of change in BCVA and CST at 6- and 12-month measurements present a similar finding. Correlation coefficient for BCVA fell in excellent ranges ($r>0.8$) for ERM stage-II and III, while it fell in moderate range for stage-IV, ($r=0.6$). On the other hand, adjusted correlation for CST fell in moderate ranges ($r>0.3$) for ERM stage II-IV. Govetto *et al*[15] presented outcomes of their own patients at 12mo follow up and reported a significant improvement in BCVA in stages II, III and IV. They remarked that the biggest change was seen in stage IV up to 6mo post-operatively, whereas vision continued to improve in the other stages till 12mo. They also concluded that the thickness of the inner foveal layers had a negative relation with both pre and post-operative visual acuities.

Govetto *et al*[13,15] classification has been studied by several recent studies in their respective populations. They have looked at various parameters and reached differing conclusions in terms of post-surgical outcomes. González-Saldivar *et al*[16] at University of Toronto reported improvement in final visual acuity in Govetto *et al*[13,15] stages II through IV. Similar to our study population, they found that earlier stages had a better visual outcome as compared to later stages. They did not include any patients with stage I in their analysis as they mentioned that no stage I patients were operated in their setting. Even from our limited data for stage I, we cannot see the benefit of surgical intervention as no significant improvement was seen in post-operative outcomes. Terashima *et al*[17] used a slightly different approach in using the Govetto *et al*[13,15] classification system. They grouped stages I, II and III into group A and stage IV and pseudo-macular hole (PMH) into group B on the basis of presence of disruption of inner retinal layer. They found out that a better visual outcome after 12mo was seen in group A as compared to group B, however improvement was noted in both groups. Since they did not report and compare findings of each stage individually, it would be difficult to ascertain which stages benefit most from surgery in terms of functional outcome.

Karasu and Celebi[18] reported findings of 138 eyes who underwent pars plana vitrectomy with ERM peeling at a tertiary care centre in Turkey. They concluded that the higher the ERM stage, poorer the postoperative anatomical and visual outcomes and suggested that operating in either stage I and II should be favoured as compared to operating in later stages. In contrast to our study, they had a good sample size of patients with stage I (n=26) and BCVA (logMAR) in this group showed a significant improvement from a baseline value of 0.46±0.22 to 0.11±0.12. This was the best improvement in visual acuity in all 4 groups of their study and is different to both our and González-Saldivar *et al*[16] findings for stage I. In another study from Turkey, Mavi Yildiz *et al*[19] reported significant improvement in BCVA from baseline, in all four ERM stages (P<0.05). However, they noted an insignificant relation between the central foveal thickness and visual outcomes and concluded that limited beneficial improvement was seen in stages III and IV. Whereas, in our findings, even though the final visual acuity was poorer in higher stages III and IV, the gain in visual acuity was comparable to stage II.

In conclusion, we can say that the decision of operating in stages II to IV had a beneficial outcome for our patient population and these findings can be useful in decision making in our practice. Even though we have a limited sample size for stage I, it can be said that it is better to have a more guarded approach while operating stage I ERMs. However, for all other stages, earlier the stage better the post-operative gains and prognosis. Our study helped assess post-operative visual outcomes in patients presenting with ERM for better management decisions. The weaknesses of our study include a small sample size and it's retrospective design. The strengths include independent masked staging by experienced surgeons, identical surgical technique and at least one year follow-up.

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