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Anatomical and Functional Outcome of Epiretinal Membrane Peeling Surgery

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Abstract
Background*: The purpose of this study is to study the anatomical and functional outcome of epiretinal membrane peeling surgery by evaluating the visual outcomes, comparing the pre and post operative macular thickness and functional changes through electroretinogram.*
Methods*: It is a non-randomized, open labelled, prospective study conducted in a tertiary eye care centre. The anatomical and functional outcome of epiretinal membrane peeling surgery was evaluated by comparing the preoperative BCVA, OCT and ERG with post operative results of the same, at 4 & 12 weeks after the surgery in 25 eyes.*
Results: *There was a significant reduction in CFT (p ≤0.05) with marked improvement in vision on follow ups at 4 weeks and 12 weeks after removal of ERM with significant reduction in the macular edema.*
Conclusions:*ERM peeling surgery in selected cases improves visual acuity significantly in majority of the patients. CFT and foveal architecture significantly improves with ERM peeling surgery which also explains the improvement in functional visual acuity. ERG interpretation goes along the improvement in best corrected visual acuity signifying improvement in functioning of macula.*
Keywords*:Retina, Epiretinal membrane(ERM), Optical coherence tomography(OCT), Electroretinogram(ERG), Central Foveal Thickness(CFT).*

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I. Introduction :

An epiretinal membrane (ERM) is a thin sheet of fibrous tissue that can develop on the surface of the macular area of the retina and cause disturbance in vision. An epiretinal membrane can also be called macular pucker, premacular fibrosis, surface wrinkling retinopathy or cellophane maculopathy. Most commonly, macular epiretinal membrane are asymptomatic or causes mild symptoms of metamorphopsia and/or modest decrease in central visual acuity. A minority of these membranes can cause macular distortion or macular edema to induce clinicians to recommend ERM removal via pars plana vitrectomy.

Optical coherence tomography (OCT) has become the most useful, noninvasive ancillary test for the evaluation of epiretinal membranes. OCT may be predictive of visual outcomes with ERM surgery. The hyperreflective line above retinal pigment epithelium (RPE) demonstrates the inner segment/outer segment (IS/OS) junction of photoreceptors. Several studies have demonstrated that an intact continuous IS/OS junction is predictive of better visual outcome at 12 months.[1,2] OCT also helps in distinguishing macular pseudo holes from full thickness macular hole which is an exclusion criterion for this study. [1]The detection of elevated ERM via enface OCT could assist safer grasping of the ERM and indicate the potential for visual outcome improvement after PPV and ERM peeling.[3]

The multifocal electroretinogram (mfERG) represents a cone generated response of localized retinal function in the central macula, which is useful in establishing the presence of macular dysfunction. [4] Multifocal electroretinography (mfERG), is a noninvasive, objective method to detect regional functional changes in the central retina by measuring electrophysiologic responses, has demonstrated macular function changes in eyes with ERM by several reports. [5,6]The biphasic first order response of the mfERG includes an initial negative deflection [N1] followed by a positive peak [P1]. Previous studies have found that abnormalities in the P1 latency disorders might reflect dysfunctions of the inner retinal layers and Müller cells.[7]

The mfERG values might be associated with numerous factors. In another study it was demonstrated that there was a significant correlation between P1 implicit time and CMT. MfERG abnormalities appear to demonstrate subtle macular function changes and correlate with visual acuity and central macular thickness in

eyes with ERM. In first-order mfERG responses, P1 wave changes may be a sensitive functional measurement for ERM patients.

The goal of membrane peeling is to reduce or eliminate the most common mechanisms of visual loss, including macular distortion, traction macular detachment, foveal ectopia, tissue that covers the fovea, retinal vascular leakage with macular edema, and traction induced obstruction of axoplasmic flow. In general, most patients considered for vitrectomy have significant visual impairment.

ERMs are found most frequently over the age of 50 and several large clinical studies have noted a clinical prevalence lying between 7% and 11.8%. **(8,9)** Most of these are asymptomatic, with many being extra foveal in location. There appears to be no significant gender predilection and 20 to 30 % are bilateral. Other eye involvement was reported in the Blue Mountains Eye Study to occur in 13.5% of patients over a 5 years time period. **(10)** The majority of ERMs are globally adherent to the retinal surface, however, some appear to have focal adhesions.**(11)**These focal adhesions are more common in eyes with secondary ERMs.

The incidence of symptomatic ERM formation is 4-8% after repair of rhegmatogenous retinal detachment, **(12,13)**and 1-2 % after prophylactic treatment of peripheral retinal breaks.**(14)**

The electroretinography (ERG) is a diagnostic test that measures the electrical activity generated by neural and non-neuronal cells in the retina in response to a light stimulus. The electrical response is a result of a retinal potential generated by light-induced changes in the flux of transretinal ions, primarily sodium and potassium. Most often, ERGs are obtained using electrodes embedded in a corneal contact lens, which measure a summation of retinal electrical activity at the corneal surface. The International Society for Clinical Electrophysiology of Vision (ISCEV) introduced minimum standards for the ERG in 1989. The ERG can provide important diagnostic information on a variety of retinal disorders. Moreover, an ERG can also be used to monitor disease progression.

II. LITERATURE SURVEY

Epiretinal membrane is a commonly occurring condition affecting the posterior pole of the retina over the macula. It appears as a greyish semi-translucent avascular membrane over the internal limiting membrane (ILM) on the surface of the retina. Etiology is unknown and can be seen as an idiopathic (IERM) condition or secondary to trauma, post intraocular surgery, chronic ocular diseases, etc. It progressively affects the central vision and causes metamorphopsia**.**

Etiology is unknown, and the most common cause of the epiretinal membrane (ERM) is idiopathic (IERM). Secondary epiretinal membranes are seen in trauma, intraocular surgery, post-macular lasers, diabetic retinopathy, retinal vein occlusion, chronic macular edema, chronic intraocular inflammation, retinal detachment, and intraocular tumors. Increasing age, ERM in the other eye, and posterior vitreous detachment (PVD) are other risk factors.

The most common type of epiretinal membranes is idiopathic and is common in patients over the age of 50. Approximately 20% of patients over the age of 75 have an epiretinal membrane with both sexes equally affected. Some reports show a slightly higher incidence in females.

In a multi-ethnic study of the United States population done in 2011 involving 5960 participants aged 45 to 84 years, it was shown that Chinese(39%) show significantly higher prevalence compared to Hispanics (29.3%), Whites (27.5%) and Blacks (26.2%).[2] Increasing age, diabetes, and hypercholesteremia were found to be risk factors for the epiretinal membrane.

In a multicentric meta-analysis of population-based studies involving 40,000 participants, it was shown that 9% had some form of ERM. Epiretinal membranes are classified into two groups: one with retinal folds called preretinal macular fibrosis (PMF) and second without retinal folds called cellophane macula reflex (CMR). Of the ERM patients, 6.5% had CMR, and 2.6% had an advanced form of PMF. Older and female participants showed a higher risk

The Blue Mountains study was done over five years to study the incidence and progression of epiretinal membranes in the older Australian population.[3] Three thousand six hundred fifty-four persons, 49 years or older, living in the Blue Mountains area, west of Sydney, Australia, participated in the study from 1992 to 1994. The mean age was 65 years. The incidence of ERM's in the first eye was 5.3%, and the progression of early ERM to an advanced stage of ERM of 9.3%. Five-year cumulative incidence rates of PMF and CMR were 1.5% and 3.8 %, respectively. Of these, 13.9% developed ERM in their second eye after five years.

Optical coherence tomography (OCT) is a highly sensitive routinely done investigation for retinal disorders and is the investigation of choice to diagnose epiretinal membrane and vitreomacular traction (VMT).

Stage 1: ERMs were mild and thin. Foveal depression is present.
Stage 2: ERMs with a widening of the outer nuclear layer and loss of the foveal depression.
Stage 3: ERMs with continuous ectopic inner foveal layers crossing the entire foveal area
Stage 4: ERMs were thick with continuous ectopic inner foveal layers and disrupted retinal layers.

Most patients with epiretinal membrane (ERM) do not require treatment if it doesn't affect vision or cause significant metamorphopsia. Blue Mountains study [3] involving 3654 subjects showed that only 20% of epiretinal membranes progressed over five years, 26% regressed, and 39% remained the same. Only 20% of eyes with cellophane maculopathy progressed over a while. The primary treatment for ERM apart from observation is surgical. Surgery for ERM has a reasonable success rate, and most patients show improvement in visual acuity and a decrease in metamorphopsia. Hence the aim of treatment for ERM should be to preserve or improve vision, minimize symptoms like metamorphopsia, diplopia, etc. and enhance the quality of life. Factors that affect the visual outcome include the duration of the condition, the degree of vitreomacular traction, and the cause for ERM. Idiopathic ERM has a better prognosis than ERM secondary to ocular pathology.

Non-surgical management includes the use of vitreopharmacolysis with ocriplasmin. Ocriplasmin is a recombinant proteolytic enzyme approved by the FDA for intravitreal injection for the treatment of symptomatic VMT. Ocriplasmin can relieve the VMT associated with ERM, which might provide relief from the associated metamorphopsia. It does not affect ERM. Its use in patients with both ERM and VMT is controversial. In patients unfit for lengthy retinal surgical procedures, intravitreal ocriplasmin can treat visual disturbances induced by VTM.

Surgical management involves pars-plana vitrectomy (PPV) with ERM and ILM peeling. PPV with membrane peeling has been used successfully for many decades, with an excellent visual outcome and a reduced recurrence rate. ILM is thought to provide a platform for the proliferation of fibroblasts, glial cells, and astrocytes for the retina to form ERM.[11] ILM peeling along with membrane peeling has become a standard procedure following the advent of staining dyes like trypan blue, indocyanine green (ICG), and brilliant blue G (BBG).[12] Triamcinolone is used to stain the vitreous and the membrane. Triamcinolone staining helps to induce posterior vitreous detachment and to ensure an excellent subtotal vitrectomy. Accelerated nuclear sclerosis or a worsening of cataract is the most common complication of vitrectomy. If a cataract is present, the procedure should be combined with a cataract removal to ensure better visualization of the surgical procedure and also to prevent a subsequent second surgery.

III. Materials and Methods:

This is a non randomized, open labelled, prospective study conducted in a tertiary eye care centre. In this study 25 eyes are included as per the inclusion and exclusion criteria mentioned below.

In this study a detailed history and clinical examination were performed with necessary investigations as and when required. Pre-operatively patients were evaluated for Best Corrected Visual Acuity (BCVA), metamorphopsia, fundus examination with indirect ophthalmoscopy and slit lamp biomicroscopy, fundus photographs were taken of all patients. Optical Coherence Tomography (OCT) was performed preoperatively to assess the macular anatomy and to measure Central Foveal Thickness (CFT). Multifocal Electroretinogram (mfERG) was performed in all patients for preoperative evaluation of electrophysioloigc response of central retina. Patients in this study then underwent pars plana vitrectomy with epiretinal membrane peeling. BCVA was assessed at post-operative day 1 and post operative 1 week, 4 weeks and 12 weeks with focus also on improvement in the quality of the vision and reduction in metamorphopsia. OCT was performed at 4weeks and 12 weeks to evaluate the change in macular anatomy and central foveal thickness after epiretinal membrane peeling surgery. ERG was performed in all patients 12 weeks after surgery to evaluate the electrophysiologic response of central retina post surgery. Thus in this study anatomical and functional outcome of epiretinal membrane peeling surgery was evaluated by comparing the preoperative BCVA, OCT and ERG with post operative results of the same, 12 weeks after the surgery.
The Ethical approval for the study was taken from the local Institutional Ethical Committee.

Inclusion criteria:

- Patients between the ages of 20 to 80 years.
- Intraocular pressure < 21mmHg.
- Fundoscopy showing physiological cupping.
- Slit Lamp Examination showing: clear cornea, normal anterior chamber depth.
- Normal pupillary shape, size and reaction.
- Preoperative OCT presence of ERM on macular area covering central fovea with or without macular edema.
- Clearance of media for preoperative mfERG and OCT.
- Visual acuity - BCVA (Best Corrected Visual Acuity) </= 6/12.

Exclusion criteria:

- Patient's age < 20 years or > 80 years.
- Higher Intraocular pressure > 21mmHg.
- Poor fixation for OCT examination.
- Cataract, which precludes OCT.
- Patients with pre-existing macular hole, optic atrophy, vitreomacular traction, choroidal neovascular membrane, macular ischemia from previous retinal vascular occlusion or any other pre existing macular disorder.
- Patients with rubeosis iridis or glaucoma.
- Only eyed patient.
- Uncontrolled diabetes.

History

Detailed clinical history of the patients were taken according to the proforma as mentioned below.
Clinical examination:
1.Vision with or without glasses
2.Torch light & Slit lamp examination
3.IOP by Applanation tonometer
4.Fundoscopy by Slit lamp biomicroscopy using 90 D, Direct & and Indirect Ophthalmoscopy
5.Optical coherence tomography (OCT)
6.Electroretinogram

Based on this, patients having epiretinal membrane were diagnosed and operated. Patients were followed up at day-1, 1 week, 4 weeks and 12 weeks and were assessed for best corrected visual acuity, evaluation of metamorphopsia, fundus examination, OCT and mfERG (pre-operative and post-operative at 12 weeks).

DATA ANALYSIS (RESULTS)

A Non randomized, open labelled prospective study of 25 eyes of patients with epiretinal membrane of idiopathic origin as well as other causes were carried out at M and J Institute of Ophthalmology, Civil Hospital, Ahmedabad.

DEMOGRAPHIC & BASELINE RESULTS

1. AGE

Of 25 patients, 1 patient was of 40 years of age, 2 were in 40-50 age group, 7 in 50-60 age group, 14 were in 60-70 age group, and 1 was above 70years of age.

AGEGROUP	Frequency	Percent	Cum. Percent
>30 - 40	1	4.00%	4.00%
>40 - 50	2	8.00%	12.00%
>50 - 60	7	28.00%	40.00%
>60 - 70	14	56.00%	96.00%
>70 - 80	1	4.00%	100.00%
Total	25	100.00%	100.00%

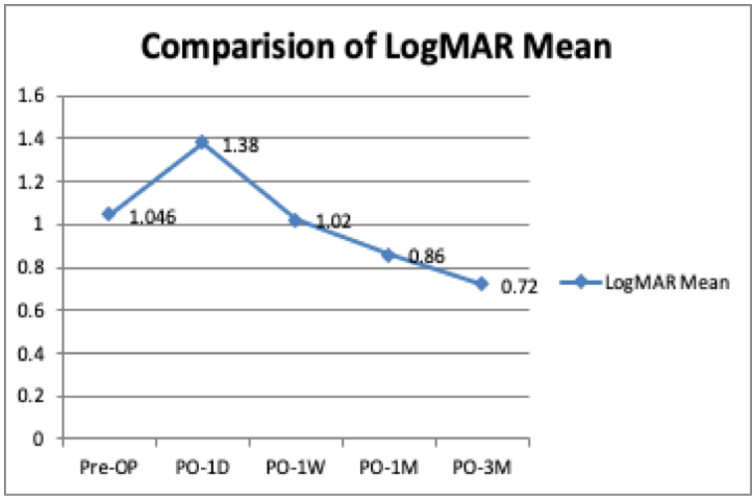
2. SEX

In this study, 13 patients (52%) were female & 12 patients (48%) were male.

3.BEST CORRECTED VISUAL ACUITY

SR.NO	PRE-OP	POD-1	POST-OP 1 WEEK	POST-OP 4WEEKS	POST-OP 12 WEEKS
1	1.3	1.48	1.08	1	0.3
2	0.48	1.78	0.6	0.18	0
3	0.6	1.18	1	0.6	0.3
4	0.3	1.08	0.6	0.3	0.3
5	1.78	1.78	1	0.78	0.6
6	0.3	1	0.78	0.48	0.18
7	0.6	1.18	0.78	0.6	0.3
8	1.48	1.78	1.3	1.48	1.08
9	1.48	1.78	1.78	1.48	1.48
10	1.78	1.78	1.3	1.08	1.08
11	0.3	1	0.6	0.3	0.3
12	2.48	1.78	1.78	1.78	1.78
13	1.08	1.18	1	0.78	0.6
14	1.18	2.48	1.18	1.08	2.48
15	1.08	1.48	1.08	1	1
16	1.08	1.18	0.78	0.78	0.48
17	1.08	1.08	1	1	0.6
18	1.48	1.3	1.18	1.18	1.18
19	0.78	1.08	0.78	0.78	0.6
20	1.18	1.18	1.08	1	1
21	1	1.18	1	0.78	0.78
22	0.78	1.08	1	0.6	0.6
23	1.18	1.78	1.3	1.3	1.3
24	0.78	1	0.78	0.78	0.6
25	0.6	1	0.78	0.6	0.48

In our study, post operative day 1 mean visual acuity improved from 1.04 (+0.52) to 1.38 (+0.38) which was statistically significant (p=0.01), after 1 week mean VA was 1.02 (+0.31), which was statistically not significant (p=0.87). After 4 weeks mean VA was 0.86 (+0.38), which was statistically significant (p=0.001). After 12 weeks mean VA was 0.72 (+0.45), which was statistically significant (p=0.001).

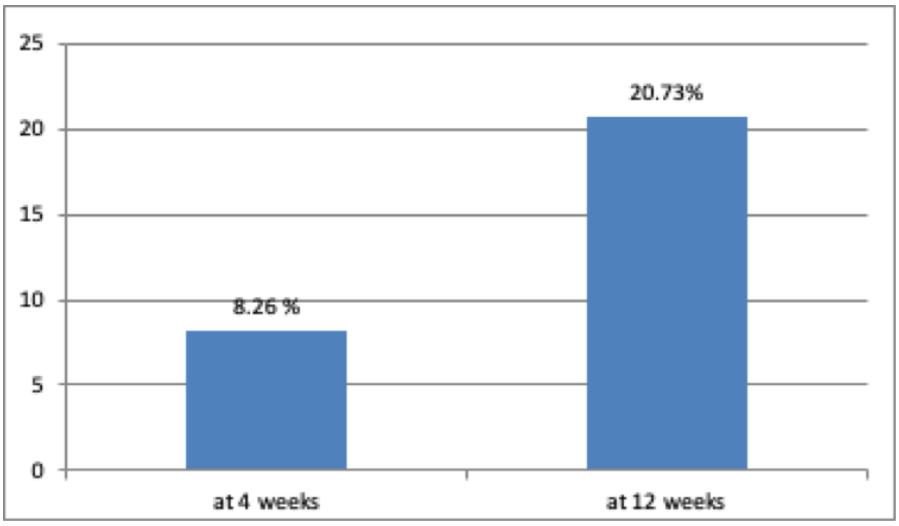


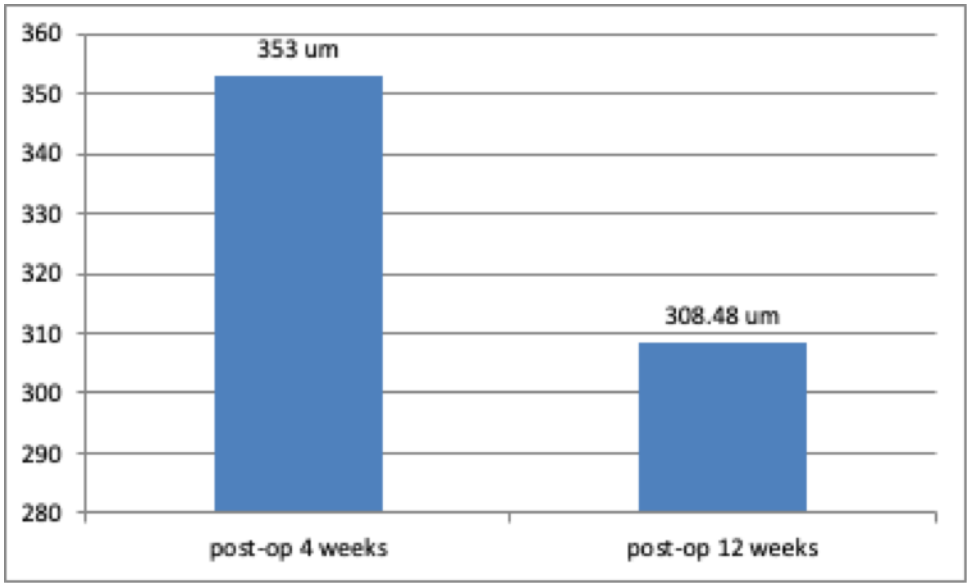
I **CENTRAL FOVEAL THICKNESS.**

SR. NO	PRE-OP	POST-OP 4 WEEKS	DIFFERENCE (IN um)	DIFFERENCE (IN %)	POST-OP 12 WEEKS	DIFFERENCE (IN um)	DIFFERENCE (IN %)
1	245	234	11	4.49	225	20	8.16
2	426	398	28	6.57	310	116	27.23
3	383	345	38	9.2	248	135	35.24
4	305	296	9	2.95	268	37	12.13
5	591	433	158	26.73	290	301	50.93
6	340	325	15	4.41	288	52	15.29
7	375	345	30	8	300	75	20
8	540	500	40	7.4	490	50	9.26
9	308	290	18	5.84	282	26	8.44
10	470	413	57	12.12	362	108	22.98
11	324	288	36	11.11	240	84	25.92
12	320	300	20	6.25	300	20	6.25
13	459	408	51	11.11	300	159	33.98
14	289	275	14	4.84	370	NA	ERR
15	386	350	36	9.33	298	88	22.79
16	373	354	19	5.09	302	71	19.03
17	478	423	55	11.51	288	190	39.74
18	465	438	27	5.8	424	41	8.82
19	389	342	47	12.08	298	91	23.39
20	460	430	30	6.52	356	104	22.61
21	389	355	34	8.74	296	93	23.9
22	280	268	12	4.28	250	30	10.71
23	436	414	22	5.05	398	38	8.71
24	378	348	30	7.93	286	92	24.39
25	295	268	27	9.15	243	52	17.62

In our study above table shows data of 25 patients who were operated & their Central foveal thickness changes in follow ups at 4 weeks and 12 weeks. Overall, there was a significant improvement in CFT statistically ($p=<0.05$).

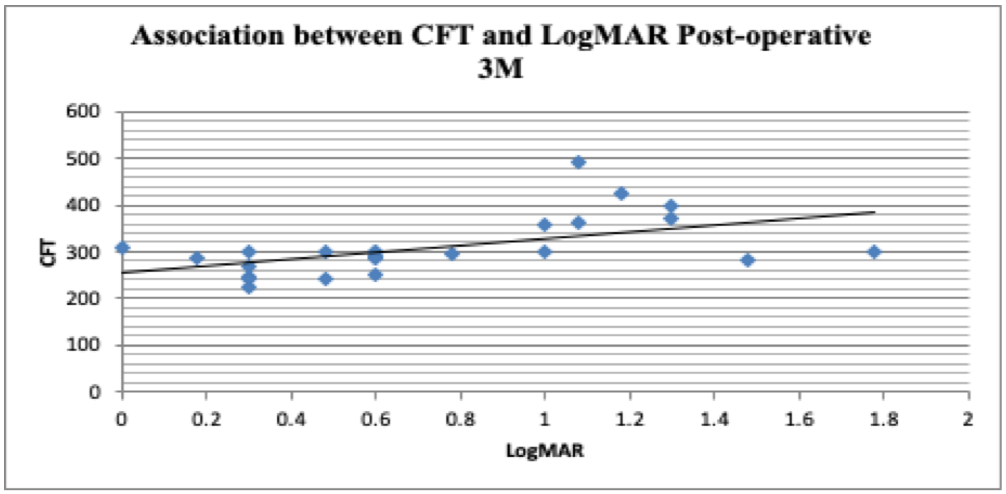
In our study after 4 weeks mean CFT improved from 388mm (+88.16) to 353mm (+67.21) & 8.26 % (35 mm) improvement which was statistically significant also ($p=0.0006$), after 12 weeks mean CFT was 308.48mm (+61.54) & improvement 20.73% (79.52mm) which was statistically significant ($p=0.0006$).

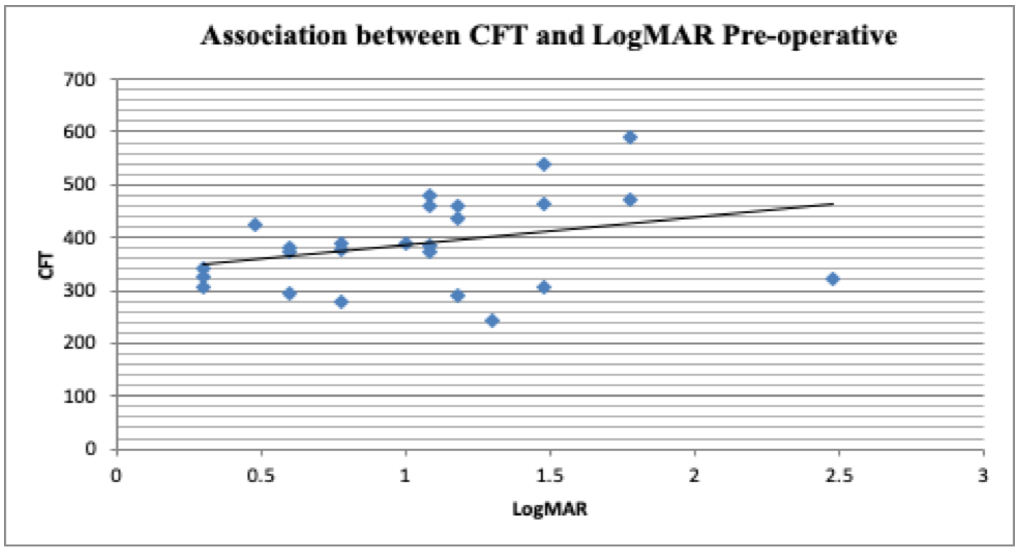


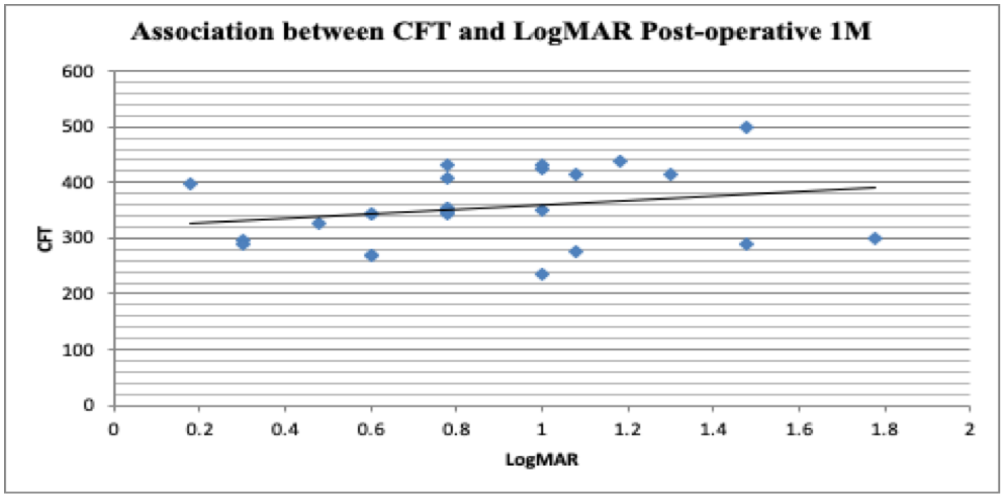


IV. RELATION BETWEEN CFT AND BCVA IN LOG MAR

The below scatter graph shows association between central foveal thickness pre-operative and after removal of ERM at 4 weeks and 12 weeks follow-up. It shows significant relation between BCVA and CFT and also shows marked improvement in vision with reduction in CFT after removal of ERM as the traction at the fovea is released as well as significant reduction in the macular edema.







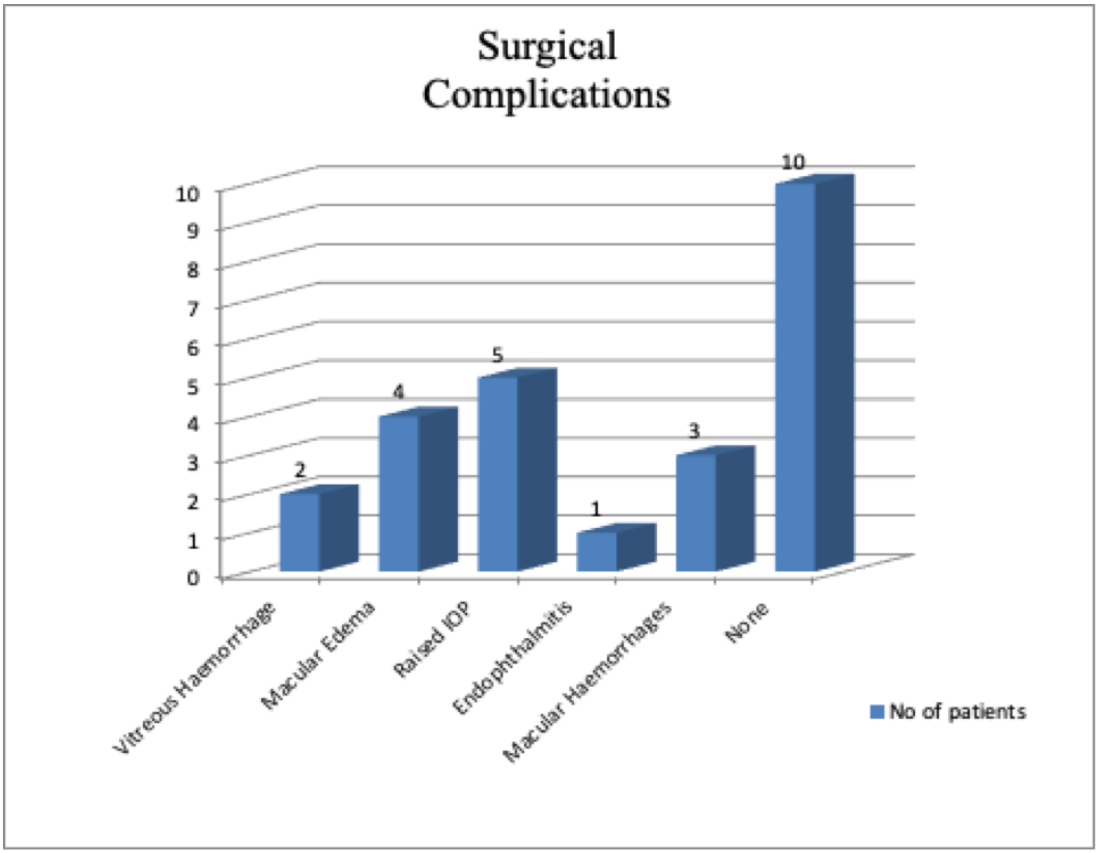
V. ERG INTERPRETATION

In our study 18 (72%) patients showed global improvement in amplitudes and P1 implicit time as compared to their preoperative value while 2 (8%) patients showed global improvement in amplitude but there was still delay in P1 implicit time as similar to their preoperative value and 4 patients (16%) showed no improvement in global amplitude as well as in P1 implicit time.

VI. SURGICAL COMPLICATIONS

Complications	Number of patients
Vitreous Haemorrhage	2
Macular Edema	4
Raised IOP	5
Endophthalmitis	1
Macular Haemorrhages	3
None	10

Out of the 25 patients taken for the study, 2 patients (8%) had vitreous haemorrhage on post operative day 1 which resolved spontaneously with conservative management. 4 patients (16%) had persistent macular edema, 5 patients (20%) had raised intraocular pressure which was managed by topical anti glaucoma drugs. 3 patients (12%) showed haemorrhages at macular area after epiretinal membrane peeling, 10 patients (40%) had uneventful surgery. One of the patients developed post operative endopthalmitis at 12 weeks which was managed with intravitreal as well as systemic antibiotics. This patient later showed signs of pre-phthysical eye as suggested by ultrasonography.



VII. DISCUSSION

In the study conducted by James G Wong MMed, Nitin Sachdev PhD, Paul E Beaumont FRANZCO, Andrew A Chang FRANZCO of "Visual outcomes following vitrectomy and peeling of epiretinal membrane"in 125 eyes of 123 patients with visually significant macular epiretinal membranes showed Visual acuity improved by a mean of 0.31 Â± 0.21 logMAR (three lines of vision). [(15)] Whereas our study which showed improvement by mean of 0.72 (+0.45) logMAR. As mentioned in the study, we observed that epiretinal membrane peeling improves vision in the majority of patients with significant symptoms, even if preoperative visual acuity is not substantially reduced. Surgery improves functional vision including metamorphopsia not measurable by visual acuity, and thus assessment of functional vision should be included in surgical case planning.

In a similar study conducted by Ionas Miliatos1 and Gun Lindgren2 of Epiretinal membrane surgery evaluated by subjective outcome in 239 eyes of 231 patients with idiopathic ERM showed that the preoperative visual acuity was mean 0.58 logMAR which improved to post operative visual acuity of mean 0.36 logMAR which was very significant with p value<0.05. [(16)] Where as our study showed improvement in visual acuity from mean 1.04 logMAR pre-operratively to visual acuity of mean 0.72 logMAR which is also significant with p value of 0.001.

In a study conducted by Parisi V, Coppe AM, Gallinaro G, Strip M of "Assessment of macular function by focal electroretinogram and pattern electroretinogram before and after epimacular membrane surgery assessment of macular volume" were evaluated for 22 eyes of 22 patients (mean age +/- SD, 63.20 +/- 10.0 years) with ERM preoperatively (baseline) and 6 months after surgical peeling. Preoperative visual acuity and fERG and pERG amplitudes observed in ERM eyes were compared with those in 15 age-matched control eyes. It was observed that, at the postoperative evaluation, ERM eyes had a correlated significant ($P < 0.01$) increase in visual acuity, fERG amplitude, and pERG amplitude with respect to the preoperative values. All ERM eyes had a significant ($P < 0.01$) reduction in macular volume, and retinal microanatomy was restored to normal conditions. Hence the decrease in visual acuity is related to dysfunction of both preganglionic (abnormal fERG) and ganglionic (abnormal pERG) macular elements. Surgical removal of ERM may induce improvement of the function of both outer and innermost macular retinal layers, leading to a related increase in visual acuity. [(17)] In our study we performed preoperative and post operative multifocal ERGs in 25 eyes of 25 patients which showed improvement in global and P wave amplitudes as well improvement in delay in P1 implicit time post ERM peeling surgery correlated with improvement in visual acuity.

In a study conducted by Liu Z, Ye J, Chen Y, Dong F of "Clinical study of vitrectomy with epiretinal membrane peeling for idiopathic macular membrane" Clinical data of 51 patients (51 eyes) who underwent vitrectomy with ERM peeling were retrospectively investigated. All the patients were examined by visual acuity, slit lamp, fundus under mydriasis, optical coherence tomography (OCT) before and after the surgery. The 3-18 months follow-up were included. There was a negative correlation between visual acuity and mean foveomacular thickness ($r=-0.452$, $P=0.001$), and it was obvious postoperatively ($r=-0.602$, $P=0.000$). The increase of visual acuity was strongly correlated with the decline of mean foveomacular thickness ($r=0.382$, $P=0.006$). It was concluded that Vitrectomy with ERM peeling can improve visual acuity and ease macular edema. And it is a safe and effective therapy to treat patients. [(18)] In our study as mentioned in the scatter graph we observed the significant negative correlation between visual acuity and central foveal thickness both preoperatively and postoperatively at the end of 3 months.

In another study conducted by Soon II Kwon, Sung Jo Ko and In-Won Park of " The Clinical Course of the Idiopathic Epiretinal Membrane After Surgery" in 30 eyes of 30 patients and followed for a period of 7 months after surgery it was observed that there was significant improvement in the visual acuity with upto 2 or more lines of improvement and the mean foveal thickness which was 409.7+/-107.9 micron before surgery was improved to 288.6+/-66.1 micron seven months after surgery. Thus the Foveal thickness and visual acuity improved until seven months after the vitrectomy in patients with idiopathic ERM. Preoperative visual acuity, foveal thickness, and final foveal thickness had a significant correlation with the final visual acuity. [(19)]Whereas in our study the preoperative mean central foveal thickness 388mm (+88.16) was reduced to 308.48mm (+61.54) correlating with the improvement in visual acuity.

VIII. CONCLUSION

1.ERM peeling surgery in selected cases improves visual acuity significantly in majority of the patients.
2.CFT and foveal architecture significantly improves with ERM peeling surgery which also explains the improvement in functional visual acuity .
3.ERG interpretation goes along the improvement in best corrected visual acuity signifying improvement in functioning of macula.

FUTURE SCOPE

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