Early surgery preserves more vision for patients with Epiretinal Membranes

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ABSTRACT

Purpose: To establish whether early vitrectomy for epiretinal membrane (ERM) is preferable to delayed surgery.

Methods: We carried out a retrospective study of 120 eyes from 120 patients with pre-operative visual acuity (VA) of 6/60 or better. Pre-operative logMAR score was considered to act as an appropriate proxy measure for time of surgical procedure, with scores of 0.3 or less considered to represent *Early* surgery, scores of 0.4 or 0.5 considered to represent *Medium* surgery; and scores of 0.6 or more considered to represent *Late* surgery for ERM. Patients were either pseudophakic at the time of vitrectomy or underwent combined phaco-vitrectomy for symptomatic ERM.

Results: Evaluation of parameter coefficients indicated that controlling for other factors, a delay of the surgical procedure from a state of *Early* to *Medium* corresponded to an increase (i.e. disbenefit) of 0.074 units in post-operative logMAR score (95% confidence interval -0.001 – 0.15). A delay of the surgical procedure from a state of *Early* to *Late* corresponded to an increase (i.e. disbenefit) of 0.21 units in post-operative logMAR score (95% confidence interval 0.13 – 0.29). Mean post-operative visual acuity for *Early* surgery was 0.16, out of which 36.2% of patients had a LogMAR score of 0.1 or better. This is in comparison to 17.2% in *Late* ERM (those with a pre-operative logMAR score of 0.6 or more).

Conclusion: We conclude that early surgery is associated with lower (i.e. better) post-operative logMAR score. Vitrectomy for early symptomatic ERM, in carefully selected patients, is beneficial in preserving excellent vision and allows quicker visual rehabilitation.

INTRODUCTION

Epiretinal membrane (ERM) can be defined as a fibrocellular growth on the surface of the retina causing tangential forces, leading to deformation of retinal architecture. Patients experience distortion, blurring of vision or loss of binocularity. In the early stages some patients may have impaired central visual function which cannot be detected by their near normal vision on conventional visual acuity (VA) testing. Surgery is typically offered only to those with marked retinal distortion and substantial visual impairment.

Surgery for ERM aims to improve or stabilise VA, decrease metamorphopsia and restore macular anatomy. Irreversible photoreceptor disruption detected by optical coherence tomography (OCT) is a predictor of poor visual outcome in eyes with ERM[1,2]. A previous study has shown that vitrectomy for ERMs in patients with relatively good pre-operative vision is beneficial[3]. This could prevent further progression of photoreceptor damage and preserve excellent vision. However, accelerated development of post-vitrectomy cataract in phakic eyes impairs accurate assessment of postoperative visual improvement after surgery. Hence combined phakovitrectomy is essential in phakic eyes with ERM to achieve long-term improvement in VA. To our knowledge this is the first study assessing visual outcomes for ERMs in patients where this confounding factor has been eliminated by performing combined surgery.

METHODS

This study was a retrospective review of 23G transconjunctival sutureless (TSV) vitrectomy in 120 consecutive patients with idiopathic epiretinal membranes. Demographic data (age and sex) was recorded on all patients. Pre and postoperative VA were measured and best-corrected visual acuity (BCVA) was converted to the logMAR scale for statistical purposes.

Inclusion criterion was symptomatic patients with pre-operative VA of 6/60 (logMAR 1.0) or better. Symptoms secondary to ERM included central blurring, distortion, monocular diplopia, interfering with binocular vision. An objective test for measuring distortion was not available and was therefore not performed. Eyes with ERMs associated with proliferative diabetic retinopathy, posterior uveitis, vitreomacular traction (VMT), previous macular surgery, full thickness macular holes and prior retinal detachment were excluded from this study. Surgery was performed between January 2007 and January 2011. Patients with visually significant cataracts were excluded from the study to avoid improvement in VA that could be partially accounted for removal of co-existing lens opacity.

Informed consent was obtained and OCT examinations were performed using the spectral domain SD-OCT (Optovue RTVue-100 with Version 4.0 software; Freemont, CA, USA). Twelve radial 6mm OCT images (MM6/Radial slice 0.27 sec) through the centre of the macula were obtained by skilled operators in all patients. All operations were performed by the same surgeon (RR). Co-morbidities included primary open angle glaucoma, diabetes without retinopathy and myopia.

All patients underwent 23G transconjunctival sutureless vitrectomy. Combined phakovitrectomy procedure was performed in all phakic patients to prevent any interference from postvitrectomy cataract in estimation of final vision. Both ERM and ILM (internal limiting membrane) were removed by end-gripping intraocular forceps. Brilliant peel (Fluoron, Geuder, Germany) allowed staining of the ILM in exposed areas not covered by ERM, which was peeled with the overlying ERM at the same time. In more advanced membranes, the ERM was peeled unaided, and brilliant peel was then used to check for residual ILM after ERM removal. All patients had air tamponade and SF_6 gas only when a lamellar hole coexisted with an ERM.

All patients were seen at 1 day, 2 weeks, 6 weeks and at variable times thereafter until their vision stabilised. Pre- and postoperative OCT scans were assessed to evaluate the status of the inner and outer segment photoreceptor (IS/OS) junction. The state of the IS/OS junction was classified into intact versus disrupted and recorded.

The ERM were classified by their morphological appearance on OCT as M1 (diffuse type), M2 (ERM associated with lamellar hole) and M3 (ERM associated with cystoid intraretinal edema). We did not include ERMs associated with VMT in this study.

Statistical analysis:

Pre-operative vision and post-operative vision (measured on Snellens chart and converted to the logMAR scale) was analysed using analysis of covariance (ANCOVA) in order to account for possible effects of regression to the mean arising from imbalances in patient pre-operative scores. Age, sex and follow-up time were also considered for inclusion in the ANCOVA model. ERM morphology and IS/OS junction status were not included in the ANCOVA model, as a large proportion of cases did not have their ERM morphology classified or an IS/OS assessment, and hence these variables would be missing for these cases. However, supplementary analyses were undertaken on cases with ERM classification to assess the relationship of morphology and IS/OS junction status with vision improvement and final vision. A backward elimination strategy was utilised to obtain a parsimonious regression model.

Post-operative VA was also compared with different levels of pre-operative VA. Pre-operative logMAR score was considered to act as an appropriate proxy measure for time of surgical procedure, with scores of 0.3 or less considered to represent *Early* surgery, scores of 0.4 or 0.5 considered to represent *Medium* surgery; and scores of 0.6 or more considered to represent *Late* surgery for ERM. A second regression model, based on the model outlined above, was derived, with pre-operative VA replaced by proxy variables modelling time of surgical procedure; using indicator variables corresponding to *Medium* or *Late* surgery, with *Early* considered to be a reference category. All other variables were as in the original regression model, with a backward elimination modelling strategy conducted to obtain a parsimonious model, also as in the original model.

RESULTS

All data was analysed using SPSS (Version 18.0). Data was collected on 120 individuals, comprising 43 males (35.8%) and 77 females (64.2%). Patient ages at surgery ranged from 50.0 to 88.5 years. The mean age of all patients was 71.6 years (SD 7.65). Mean follow-up of patients was 6.5 months (range 3 to 13 months).

Forty eight patients (40.0%) were recorded as having OCT type M1; 23 patients (19.2%) were recorded as having OCT type M2; 6 patients (5.0%) were recorded as having OCT type M3. Seventy-three patients did not have ERM classification. Of the 77 patients whose ERM morphology was classified, 57 (74.0%) were recorded as IS/OS junction intact and 20 (26.0%) were recorded as IS/OS junction disrupted.

Pre-operative VA measured on the logMAR scale ranged from 0.0 to 1.0, with a mean value of 0.44 (SD 0.22). Post-operative VA measured on the logMAR scale ranged from -0.10 to 0.80, with a mean value of 0.23 (SD 0.19). Change in logMAR score following surgery ranged from -0.80 to +0.50, with a mean change score of -0.21 (SD 0.21). The negative mean change score indicates an improvement in visual acuity following surgery. Pre-operative and post-operative scores exhibited statistically significant moderately strong positive correlation (r=0.516; p<0.001); suggesting that the ANCOVA model was appropriate for maximising statistical power to show a treatment effect.

The ANCOVA model determined pre-operative logMAR score (p<0.001) to be a significant predictor of the outcome measure of post-operative logMAR score; with the backward elimination strategy excluding follow-up time and age from the final model. Sex was not found to be statistically associated with the outcome measure at the 5% significance level, but did show some substantive significance (p=0.063).

Evaluation of parameter coefficients indicated that controlling for other factors, each unit change in pre-operative logMAR score corresponded to a change of 0.44 units in post-operative logMAR score (95% confidence interval 0.31-0.58). Hence lower pre-operative logMAR score (indicative of early surgery) is associated with lower (i.e. better) post-operative logMAR score. With an adjusted R^2 statistic of 0.264, a model including pre-operative logMAR score and sex had moderate predictive capability.

Ninety-seven procedures (80.8%) led to an improvement in VA; with 23 (19.2%) resulting in stabilisation or deterioration of vision. Of these, only 4 patients had deterioration of vision, necessitating the combination of this category with the larger *Stabilisation* category. Good post-operative VA (defined as achieving a logMAR score of 0.1 or less) was achieved in a total of 30 procedures (25.0%).

Fifty-eight of all procedures (48.3%) were classified as *Early* (using the pre-operative score as a proxy measure); 33 procedures (27.5%) classified as *Medium* and 29 (24.2%) classified as *Late*. Characteristics of patients in each of these three categories are summarised in Table 1 below.

The regression model (including the proxy indicator variables for time of surgical procedure) determined time of surgery to be a significant predictor of the outcome measure of post-operative logMAR score. As in the original analysis, the backward elimination strategy excluded follow-up time and age from the final model. The indicator variable *Medium* exhibited borderline statistical significance at the 5% level (p=0.052). The indicator variable *Late* was significantly associated with the outcome measure at the 5% level (p<0.001). Sex was not found to be statistically associated with the outcome measure at the 5% significance level, but did show some substantive significance (p=0.069).

Evaluation of parameter coefficients indicated that controlling for other factors, a delay of the surgical procedure from a state of *Early* to *Medium* corresponded to an increase (i.e. disbenefit) of 0.074 units in post-operative logMAR score (95% confidence interval -0.001 – 0.15). A delay of the surgical procedure from a state of *Early* to *Late* corresponded to an increase (i.e. disbenefit) of 0.21 units in post-operative logMAR score (95% confidence interval 0.13 – 0.29). Hence the findings of this model are consistent with the findings of the previous regression model: i.e. that early surgery is associated with lower (i.e. better) post-operative logMAR score. With an adjusted R^2 statistic of 0.187, a model including pre-operative logMAR score and sex had moderate predictive capability; but inferior to the original model.

Supplementary analyses conducted on cases for which the ERM morphology type was recorded found that neither morphology type nor IS/OS junction status was significantly associated with either good post-operative VA or improvement in VA.

Visual acuity was noted to deteriorate in 4 patients post surgery. Two of these were patients in the early surgery group with a prop VA of 0.3. One of these was a high myope who developed multiple mid-peripheral breaks during intra-operative posterior vitreous detachment. The second patient developed a small extrafoveal iatrogenic retinal tear during ILM peeling. Both patients required laser treatment to the breaks and experienced a reduction of visual acuity by 2 lines compared to preoperative vision. The maculae in both of these patients showed fine pigmentary disturbance clinically and no residual ERM on post-op OCT. The remaining 2 patients' VA deteriorated from 0.2 to 0.3 Logmar and did not suffer any intraoperative complications. We could not establish an obvious cause for visual deterioration in any of these patients.

Two patients underwent repeat vitrectomy. One of them was treated for a retinal detachment originating from a previously cryo-treated peripheral break, and the other to remove a floater from a free-floating ILM.

One patient had posterior capsule rupture during phacoemulsification and had a sulcus fixated IOL.Ten patients developed postoperative posterior capsular opacification (PCO), which was treated with YAG laser capsulotomy. There were no cases of pupillary capture, erm recurrence or endophthalmitis. However 6 case (5%) developed persistent cystoid edema in the postoperative period. These patient received subtenon's Triamcinolone (40mg) which resulted in complete resolution with corresponding improvement in Visual acuity.

DISCUSSION

Previous studies have shown promising results for early ERM surgery with better visual outcome[3]. Nuclear sclerosis has been shown to decrease VA by 3 to 12 months after vitrectomy surgery, with a decrease of 0.74 Snellen lines per year[3]. Thus progression of nuclear sclerosis in other studies prevented accurate analysis of long-term visual outcome. The result of vitrectomy and combined surgery for ERMs in patients with good VA has not been previously reported.

The predictive capability of both regression models is good, as measured by the adjusted R^2 statistic. The first model is better than the second. Early surgery shows a significant improvement in VA. These patients have very little macular damage, resulting in good recovery of macular function. Using raw post-operative scores as an outcome, pre-operative score is a statistically significant predictor of post-operative score. The finding is the same whether pre-operative score is considered directly as a predictor, or categorised into proxy variables standing for time of surgery.

One consequence of considering pre-operative score to be a proxy for time of surgery is that if the proportions of patients in the *Early*, *Medium* and *Late* categories whose visual acuity improves after surgery are compared, it may be noted that a greater proportion of patients show at least some improvement in vision in the *Medium* group than in the *Early* group, and in turn the proportion of patients showing at least some improvement in vision in the *Later* group is better still (at 100%). This is not necessarily indicative of later surgery leading to better outcomes, but is likely to be an artefact of the lower baseline values of patients undergoing later surgery. If on the other hand post-operative VA in the three groups is compared, it can be seen from Table 1 that outcomes are much better in the early group than in the other 2 groups. Outcomes in the *Late* group appear to be slightly better than in the *Medium* group, but a greater distinction may be observed between the *Early* and *Medium/late* groups. It can be shown that the difference in good outcomes between the groups is statistically significant ($\chi^2_{(2)}=7.74$; $p=0.021$).

Sex shows some substantive significance, with females appearing to show better post-operative scores than males who have similar pre-operative scores. Again, the finding is the same regardless of whether pre-operative raw score, or the categorised proxy-time version is considered as the key predictors.

The majority of patients had either improvement or stabilisation of vision. Only 4 (3.33%) patients had reduced VA after surgery. The risk of decreased VA post-surgery is small. Two of these were patients in the early surgery group with a pre-operative VA of 0.3. One of these was a high myope who developed multiple mid-peripheral breaks during intra-operative posterior vitreous detachment. The second patient developed a small extrafoveal iatrogenic retinal tear during ILM peeling. Both patients experienced a reduction of VA by 2 lines compared to preoperative vision. There was no residual membrane, but fine pigmentary stippling noted at the maculae in both cases. Hence we could not find an obvious cause for visual deterioration. High myopes with attached vitreous should be counselled about the possibility of peripheral breaks formation during intraoperative induction of posterior vitreous detachment.

Bovey et al.[4] have demonstrated better visual outcomes in ERM histological specimens with the presence of ILM. We peeled the ILM in all cases with blue staining to ensure complete separation of

all fibrocellular tissue from the macula. It has been shown that ERM peeling alone leaves residual cells on the ILM allowing for proliferation[5]. Consequently we did not encounter recurrent ERM proliferation in any of our study cases.

We have shown that surgery for early ERM is safe in carefully selected patients preferably those with a PVD and who are symptomatic. There is a small risk of deterioration in vision. A similar incidence of 5% was reported in a previous study of early ERM surgery by Thompson et al.[3] 2 patients out of 40 in this study had deterioration in vision; one due to CMO and other due to unexplained visual loss.

Metamorphopsia occurring in eyes with ERM is one of the most common conditions responsible for deterioration of vision related quality of life[6]. Visual acuity testing alone cannot account for the disabling symptoms associated with early ERMs such as distortion, blurring and micropsia. Snellen's visual acuity does not completely reflect the true predicament these patient regularly experience especially under a low contrast set-up. Hence we should probably institute a questionnaire into our pre-operative workup to assess the whole extent of their visual disability.

Patients with good vision and mild ocular pathology are generally not seen as candidates for vitreo-retinal surgery. This study emphasizes the relatively low risk of substantial visual loss following vitrectomy for ERM in eyes with relatively good pre-operative visual acuity. This does not imply that all patients with 6/9 and 6/12 vision associated with ERM should receive surgery. However given the marked improvement in instrumentation and techniques, this restraining and conservative approach for vitrectomy in patient symptomatic in spite of good Snellen vision has to be readdressed.

There are some limitations to this study. Firstly, Snellen VA was used to measure pre-operative and post-operative vision and then converted to logMAR vision. Secondly, other visual functions such as distortion, contrast sensitivity, visual image disparity were not measured objectively, before and after ERM surgery.

Conclusion:

We conclude that vitrectomy for early symptomatic ERM, in carefully selected patients, is beneficial in preserving excellent vision. People are living and working longer; early ERM can impair visual function and reduce productivity in jobs as well as affect elderly patients in pursuing their hobbies. Best final vision is associated with better pre-operative VA. Combined surgery allows for quicker visual rehabilitation by avoiding the formation of postvitrectomy cataracts. We recommend surgery for patients with ERM-relating symptoms impacting their lifestyles irrespective of Snellen VA where appropriate. Improved objective tests are urgently required to assist in the detailed analysis and grading of subjective symptoms associated with early epiretinal membranes.

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Table 1: Post-operative characteristics of patients receiving early, medium or late treatment

	Patient category		
	Early	Medium	Late
Number (%) achieving vision improvement	39 (67.2%)	29 (87.9%)	29 (100.0%)
Number (%) achieving good post-operative VA	21 (36.2%)	4 (12.1%)	5 (17.2%)
Post-operative vision (Mean (SD))	0.16 (0.17)	0.23 (0.13)	0.36 (0.22)
Follow-up time in months (Mean (SD))	6.83 (3.97)	8.70 (7.62)	8.42 (4.92)