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Comparison of visual outcomes after epiretinal membrane surgery

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ABSTRACT

Purpose: To elucidate the anatomical and visual outcomes of patients with idiopathic epiretinal membranes (ERM) who underwent vitrectomy, membrane removal only, or with internal limiting membrane (ILM) peeling under the assistance of different dyes.

Methods: A retrospective chart review of patients with idiopathic ERM who received surgical treatment between January 2004 and December 2009. The patients were grouped according to the usage of staining materials assisting ILM peeling. Group 1 consisted of 61 eyes that underwent conventional vitrectomy and ERM peeling without staining-assisted ILM peeling. Group 2 consisted of 20 eyes with triamcinolone acetonide-assisted ILM peeling following conventional vitrectomy. Group 3 consisted of 23 eyes with indocyanine green-assisted ILM peeling following conventional vitrectomy.

Results: This study included 104 eyes from 104 patients. There was no significant difference in age, sex, preoperative visual acuity, retinal thickness or follow-up duration among the three groups. Overall, the mean best-corrected visual acuity improved significantly from baseline 0.15 to postoperative 0.41 ($p < 0.0001$). Among the three groups, the mean logarithm minimum angle of resolution acuity markedly improved. There was no significant difference in postoperative visual acuity among groups. As measured by ocular coherent tomography, the mean central foveal thickness decreased from 465.21 ± 86.18 to 299.16 ± 70.14 μm . Although there was no difference between groups, postoperative retinal thickness was thicker than that observed in the normal population. The incidence of recurrent ERM was 13.1% in Group 1 and 0% in Groups 2 and 3; this incidence was significantly higher than in the conventional surgery group. Visual outcome was statistically more deteriorated in recurrent cases than in non-recurrent cases ($p = 0.011$).

Conclusions: ERM surgeries with or without dye-assisted ILM peeling showed similar results. Moreover, the incidence of recurrence is lower in the ILM peeling groups and plays a primary role in determining the final postoperative vision outcome.

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1. Introduction

Epiretinal membranes (ERMs) typically affected patients older than 50 years of age and may be idiopathic or secondary to a variety of ocular conditions.^{1,2} Idiopathic ERM have no obvious causes, and patients may experience reduced visual acuity, metamorphopsia, or micropsia as a result of macular edema and retinal traction. The visual acuity may remain good, but most cases have slowly progressive visual loss.³ The removal of epiretinal tissue has

become a standard procedure during vitrectomy when the vision of patients further deteriorates and necessitates surgical intervention. Several reports have been published to describe visual outcomes after the surgery.^{4,5}

During the operation, the removal of ERM may be incomplete, because it is difficult to visualize the extent of the membrane if fibrosis or pigment deposition is not conspicuous. Inadvertent trauma to the retina may therefore occur, in particular during intentional internal limiting membrane (ILM) peeling for inexperienced surgeons.^{6,7} To overcome this challenging maneuver in vitreoretinal surgery, the intraoperative application of materials such as indocyanine green (ICG), trypan blue, and triamcinolone acetonide (TA) to stain the membranes has become popular in vitreoretinal surgery.^{8–10}

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ICG, one of the vital dyes used in ocular surgery, can be used to selectively stain the ERM and represent a contrast stain to assist in membrane removal. Although several reports raised concern about possible toxic effects on the retina in certain conditions,^{11,12} some surgeons find ICG staining of the ERM indispensable. Most surgeons agree that there is a need for a safe and effective dye for staining to facilitate membrane removal.^{13,14}

TA, particularly with white specks and crystal deposits, was introduced to help with membrane peeling under enhanced visibility of both the ERM and ILM during membrane dissection.¹⁵ Although no clinical studies showed that TA was toxic to patients, some experimental reports mentioned that TA might not be as safe as originally used in vitrectomy.¹⁶

The comparison of safety between ICG and TA used in ERM surgery with intentional ILM peeling has not been well discussed in the literature. Its effect on anatomical and visual improvement has not yet been thoroughly evaluated. Therefore, we performed a large, consecutive case series of ERM patients undergoing surgical intervention with the assistance of ICG or TA staining with or without ILM peeling to investigate the factors contributing to final visual outcomes.

2. Materials and methods

A retrospective study was conducted by a chart review of all patients with idiopathic ERM who underwent pars plana vitrectomy and membrane peeling at Chang Gung Memorial Hospital, Linkuo, Taoyuan between January 2004 and December 2009. The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital in Taiwan. Eyes with idiopathic ERM with vision deterioration that had undergone vitrectomy with ERM removal were included. Due to the possibility of vision deterioration, eyes with a history of previous retinal surgery, retinal detachment, diabetic retinopathy, retinal vascular occlusion, uveitis, vitreous hemorrhage, trauma, ocular tumors, glaucoma, optic atrophy, and corneal opacity were excluded. Patients with late complications, such as retinal detachment, that would affect visual acuity and require surgical intervention were also excluded.

Both inpatient and outpatient records were reviewed in detail. The demographic data collected included the patient's age, sex, previous ocular history, and initial best-corrected visual acuity (BCVA). Clinical manifestations, late complications, and final BCVA were also recorded. For statistical analysis, BCVA was converted to the logarithm of the minimum angle of resolution (logMAR) for calculation. Visual acuities of counting fingers, hand motion, light perception, and no light perception were assigned values of 1/200, 1/400, 1/800, and 1/1600, respectively.¹⁷ A thorough chart review was performed to screen for patients with a minimum of 3 months of follow-up.

Regarding the surgical procedure, a standard three-port pars plana vitrectomy was performed in all patients using retrobulbar anesthesia. Following core vitrectomy, an ERM within the vascular arcade was then dissected from the retina. In some cases, the ERM was removed without staining-assisted ILM peeling, and some cases underwent ERM removal, followed by ILM peeling assisted by ICG or TA staining. After the surgery, the retina was then inspected (360°) to determine if any tears had been intraoperatively created. Laser photocoagulation was applied to the tears or lattice if necessary. Intravitreal tamponade was not applied in these cases.

Overall, ocular findings of ERM include extending retinal folds, distortion of the retinal vessels, and retinal edema. In this study, the patients were grouped according to the staining materials used. Group 1 comprised patients undergoing vitrectomy with ERM removal alone and without staining-assisted ILM peeling. In Group 2, ICG was applied for staining before the membrane peeling. The

ICG staining technique used was similar to that in previous publications. Briefly, the membrane was stained in an air-filled vitreous cavity, and ICG was applied in 0.5 mg/ml for one minute. In Group 3, TA was utilized to assist in the visualization of ERM and ILM peeling during the procedure. In our study, the TA preservative was washed out, and the membrane was stained with preservative-free TA (a concentration of 20 mg/cc) in the fluid-filled vitreous cavity.

To assay the morphology, retinal thickness were measured using the Stratus OCT3 system (Stratus; Carl Zeiss Meditec, Dublin, CA). A macular thickness map analysis program was used for the measurements. In all measurements, retinal thickness and volumetric analyses were performed in a circle with a 1-mm diameter in the central macula. All the OCT maps were checked for artifacts, and the measurements were repeated until high-quality measurements could be achieved. According to Chan and colleagues,¹⁸ central foveal thickness (CFT) is $182 \pm 23 \mu\text{m}$ in healthy eyes. CFT and ERM recurrence were also observed during the follow-up period.

For analysis, abstracted data were entered into a Microsoft Excel (Microsoft Corp., Redmond, WA, USA) spreadsheet and analyzed using SPSS software (SPSS Inc., Chicago, IL, USA). Means, medians, and standard deviations were then calculated as usual. We conducted descriptive analysis and compared variables between groups with and without staining using the analysis of variance method. Visual outcomes and changes in macular thickness after surgery were analyzed by using a paired t test. Furthermore, we evaluated the differences between recurrent and non-recurrent participants. A $p < 0.05$ was considered to be statistically significant.

3. Results

A total of 104 consecutive patients (104 eyes) with idiopathic ERM undergoing surgical treatment were retrospectively identified. The mean age of all patients was 67 ± 10.06 (mean \pm standard deviation) years, and the follow-up period was 20.74 ± 9.8 months. In Group 1, 61 eyes underwent conventional vitrectomy with ERM removal alone without ICG- or TA-assisted ILM peeling. In 20 eyes from Group 2, TA without preservative was employed to assist in the surgical procedures. In 23 eyes from Group 3, ICG (0.5 mg/ml) was applied during surgery. Demographic characteristics for each of these three groups are presented in Table 1. As can be seen, there is no significant difference in gender, age, baseline BCVA or CFT among the participants.

Comparing the final visual outcome of all three groups revealed no statistically significant difference in postoperative BCVA (Table 1). In addition, for all 104 ERM patients, vision improved from 0.15 to 0.41 (Snellen equivalent) after vitrectomy with ERM removal ($p < 0.0001$). These results are shown in Table 2. In other

Table 1
Demographic characteristics and comparison of variables among participants.

Variables	Total (n = 104)			p value Analysis of variance
	NA (n = 61)	TA (n = 20)	ICG (n = 23)	
Sex				
Man	25 (41.0%)	8 (40.0%)	10 (43.5%)	0.971
Woman	36 (59.0%)	12 (60.0%)	13 (56.5%)	
Mean \pm SD				
Age (y)	62.08 \pm 10.52	63.80 \pm 9.63	63.26 \pm 9.72	0.769
Follow-up (mo)	21.97 \pm 11.08	17.55 \pm 4.19	20.26 \pm 9.51	0.214
Pre-OP VA	0.14 \pm 0.11	0.21 \pm 0.18	0.14 \pm 0.10	0.113
Post-OP VA	0.39 \pm 0.28	0.41 \pm 0.27	0.49 \pm 0.35	0.383
Pre-OP CFT (μm)	462.70 \pm 83.90	470.30 \pm 87.34	467.43 \pm 94.56	0.935
Post-OP CFT (μm)	299.44 \pm 63.57	295.35 \pm 86.82	301.74 \pm 74.04	0.956

CFT = central foveal thickness; ICG = indocyanine green; NA = no staining applied; OP = operation; SD = standard deviation; TA = triamcinolone acetonide; VA = visual acuity (Snellen equivalent).

Table 2
Postoperation visual improvement and macular edema resolution.

	Preoperation VA	Postoperation VA	p value (paired t test)
Total	0.15 ± 0.13	0.41 ± 0.29	<0.0001*
NA (n = 61)	0.14 ± 0.11	0.39 ± 0.28	<0.0001*
TA (n = 20)	0.21 ± 0.18	0.41 ± 0.28	0.001*
ICG (n = 23)	0.14 ± 0.10	0.49 ± 0.35	<0.0001*
	Preoperation CFT	Postoperation CFT	
Total	465.21 ± 86.18	299.16 ± 70.14	<0.0001*
NA (n = 61)	462.70 ± 83.90	299.44 ± 63.57	<0.0001*
TA (n = 20)	470.30 ± 87.34	295.35 ± 86.82	<0.0001*
ICG (n = 23)	467.43 ± 94.56	301.70 ± 74.04	<0.0001*

CFT = central foveal thickness; ICG = indocyanine green; NA = no staining applied; TA = triamcinolone acetonide; VA = visual acuity.

*p value ≤ 0.001.

words, our findings revealed significant improvement in vision ($p < 0.05$) after surgical intervention and comparable final visual outcomes of ERM surgery performed with or without staining-assisted ILM peeling.

As for anatomic evaluation, the CFT was measured before and after ERM surgery. The results are listed in Table 1. In general, the thickness decreased from 465.21 ± 86.18 to 299.16 ± 70.14 μm after the surgery. There was no difference between pre- and postoperative CFT in each group. Furthermore, the mean postoperative retinal thickness of all eyes was still thicker than that of the normal population (Table 2).

Overall, recurrent ERM was documented in eight out of 104 cases (7.7%) in our study. Among the three groups, the incidence of recurrence was significantly higher in Group 1, and there was no recurrence in Group 2 or 3. Further analysis also showed that the recurrent cases had significantly poorer postoperative vision than the nonrecurrent cases [logMAR (Snellen equivalent) 0.87 ± 0.34 (0.18 ± 0.13) vs. 0.50 ± 0.39 (0.43 ± 0.30), $p = 0.011$]. These results are shown in Table 3.

4. Discussion

For macular ERM, vitrectomy with ERM peeling can effectively relieve traction to the retina, thus improving vision and decreasing metamorphopsia.^{4,5,19} To facilitate visualization of the epiretinal membrane and ILM peeling, we used staining materials including ICG and TA to assist in peeling the membranes and prevent potential damage to the retina. To our knowledge, ICG had been widely employed to enhance the visualization of ILM during macular pucker and macular hole surgery.^{20,21} Nevertheless, the toxic effects of ICG on retinal pigment epithelium and retinal ganglion cell were shown to be time- and dose-dependent in cell culture studies.^{11,12} Particularly in macular pucker cases, Haritoglou

Table 3
Comparison of differences between recurrent and nonrecurrent cases.

Variables	Recurrent (n = 8)	Nonrecurrent (n = 96)	p value
Staining groups			
Group 1 NA, [No (%)]	8 (100)	53 (55.2)	0.047*
Group 2 TA, [No (%)]	0	20 (20.8)	
Group 3 ICG, [No (%)]	0	23 (24.0)	
Post-OP VA, logMAR (Snellen)	0.87 ± 0.34 (0.18 ± 0.13)	0.50 ± 0.39 (0.43 ± 0.30)	0.011*
Post-OP CFT (μm)	325.13 ± 65.73	290.00 ± 70.39	0.279

Data are shown as mean ± standard deviation. Chi-square test for staining groups, independent sample test for post-OP VA and thickness.

* $p < 0.05$.

CFT = central foveal thickness; ICG = indocyanine green; logMAR = logarithm of the minimum angle of resolution; NA = no staining material applied; OP = operative; TA = triamcinolone acetonide; VA = visual acuity.

and colleagues⁸ revealed possible adverse events of the dye in individuals with more cellular debris on the retina as well as on functional outcomes in patients with large visual field defects after ICG-assisted ILM peeling.

Owing to the concern in recent reports regarding the safety of vital dyes such as ICG and TB, TA was expected to be an alternative to ICG in ILM peeling during macular hole surgery.²² TA had also been employed to enhance visualization and to identify the vitreous cortex during vitrectomy in proliferative vitreoretinopathy.^{23,24} Although there is concern regarding possible toxicity to the retinal vessels,¹⁶ TA is cost effective in clinical use. By contrast to ICG, TA does not possess photosensitizing properties and will not have phototoxic effects on the retina. In addition, TA does not really stain the ILM like other dyes; it only covers the surface of the ILM. This characteristic allows TA to be easily removed after the surgery and reduces the potential toxic effect of long-term retention as is typically observed after the application of ICG. The best way to prevent the potential toxic effect of TA to the retina and RPE is to reduce the accumulation of TA on the retina. However, ILM may not be removed completely after ERM removal due to the difficulty of ILM identification.²⁵

Our results showed that most patients with idiopathic ERM experienced substantial visual improvement after vitrectomy and membrane peeling. The visual recovery result was consistent with that achieved by other conventional ERM surgeries without staining or intentional ILM peeling.^{26,27} Moreover, we found no significant difference in postoperative visual acuity between patients with ICG- or TA-assisted ILM peeling as compared with those undergoing vitrectomy and ERM peeling alone. The higher rate of recurrent pucker observed in Group 1 may have resulted from incomplete removal of the ILM.²⁸ Park and coworkers²⁶ reported 21% recurrent macular pucker or persistent contraction to the ILM without ILM peeling or staining assistance in ERM surgery. In our study, the incidence of recurrence was significantly lower in the staining-assisted groups than in the conventional surgery group without ILM peeling. Furthermore, as the literature on the recurrence rate of conventional surgery without ILM peeling is scarce, our retrospective comparison between ILM peeling with the use of various dyes and conventional ERM surgery demonstrated comparable visual outcome and lower recurrence following ICG- or TA-assisted ILM peeling. As seen in our OCT measurements, retinal thickness decreased significantly after surgery. However, the postoperative retinal thickness was still thicker than that of the normal population. Okamoto and others²⁹ demonstrated a significant correlation between postoperative vision-related quality of life and degree of postoperative metamorphopsia. Indeed, our results showed deterioration in postoperative vision in recurrent ERM. To our knowledge, this is the first study comparing the results of different staining-assisted ERM surgeries. This retrospective study also had several limitations. The number of study patients was small, and the follow-up periods also varied in length. The lens status in each patient differed, and visual acuities were not measured with early treatment of diabetic retinopathy study (ETDRS) charts.

In conclusion, the postoperative vision of idiopathic ERM improved significantly. ERM surgeries with or without dye-assisted ILM peeling showed similar results. The recurrence of ERM played the main role in determining the final visual outcome.

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