

Pars Plana Vitrectomy and Internal Limiting Membrane Peeling for Macular Oedema Secondary to Retinal Vein Occlusion: a Pilot Study

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Abstract

Introduction: Macular oedema is the main cause of visual impairment following retinal vein occlusion. The purpose of this study was to evaluate the anatomical and functional outcome of pars plana vitrectomy and internal limited membrane (ILM) peeling for macular oedema secondary to retinal vein occlusion. **Clinical Picture:** This pilot study is a prospective non-randomised series of 11 eyes of 11 patients with macular oedema secondary to retinal vein occlusion. The best-corrected visual acuity (BCVA), foveal thickness on optical coherence tomography, fundus fluorescein angiography (FFA) and multifocal electroretinography were evaluated. **Treatment and Outcome:** All 11 patients underwent pars plana vitrectomy with ILM peeling. The mean postoperative follow-up was 13.5 months (range, 1.5 to 24). The mean thickness at the foveal centre decreased from $794 \pm 276 \mu\text{m}$ preoperatively to $373 \pm 150 \mu\text{m}$, $302 \pm 119 \mu\text{m}$, $249 \pm 203 \mu\text{m}$ and $185 \pm 66 \mu\text{m}$ at 1 week, 1 month, 3 months and the final visit postoperatively, respectively (all $P < 0.001$, paired t -test, compared to preoperative thickness). Postoperative FFA demonstrated markedly reduced leakage in the macular region. At the final visit, BCVA improved 2 lines or more in 72.7% (8/11) of patients and was unchanged in 27.3% (3/11) patients. Complications included cataract in 7 patients and vitreous haemorrhage, recurrence of macular oedema and visual field defect in 1 case each. **Conclusion:** Pars plana vitrectomy and ILM peeling rapidly reduced the macular oedema caused by retinal vein occlusion, with improvement in BCVA.

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Key words: Foveal thickness, Internal limiting membrane peeling, Macular oedema, Retinal vein occlusion, Visual acuity

Introduction

Macular oedema is a major cause of visual impairment in a number of ocular conditions such as diabetic retinopathy, retinal vein occlusion, Irvine-Gass syndrome and uveitis.¹ In one study, cystoid macular oedema contributed to 37.9% of low vision in patients with retinal vein occlusion.² Persistent macular oedema may lead to the irreversible loss of photoreceptors and vision.³ The pathogenesis of macular oedema is diverse. Breakdown of the blood-retinal barrier and traction at the vitreomacular interface have been suggested to be important factors in several studies.⁴⁻⁹

The treatment of macular oedema remains difficult and controversial. Carbonic anhydrase inhibitors are limited by

systemic complications such as disturbance of the water-electrolyte balance.¹⁰ Non-steroidal anti-inflammatory drugs (NSAIDs) fail to reduce macular oedema caused by retinal vascular disorders.¹¹ Although intravitreal injection of corticosteroid may reduce diabetic macular oedema and improve visual acuity, its use is associated with complications such as glaucoma, endophthalmitis and recurrence of the macular oedema.¹² Laser photocoagulation has been shown to be of little benefit in improving visual acuity in cystoid macular oedema.¹³

Several studies have demonstrated the regression of macular oedema and improvement in visual acuity after pars plana vitrectomy for diabetic retinopathy, retinal vein

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occlusion, uveitis and Irvine-Gass syndrome.¹⁴⁻¹⁷ One study showed that additional internal limiting membrane (ILM) peeling yielded better anatomical and functional outcome than pars plana vitrectomy alone for diabetic macular oedema.⁴ The purpose of this pilot study was to prospectively evaluate the anatomical and functional outcome of pars plana vitrectomy and ILM peeling for macular oedema in patients with retinal vein occlusion.

Case Reports

Patients

This study was a prospective non-randomised clinical series involving 11 eyes of 11 patients. Patients with diffuse or cystoid macular oedema secondary to retinal vein occlusion and with best-corrected visual acuity (BCVA) worse than 20/50 were invited to participate in the study. Patients with concurrent ocular pathology that may cause visual impairment such as severe cataract, vitreous haemorrhage, tractional retinal detachment or neovascular glaucoma were excluded. The research followed the tenets of the Declaration of Helsinki. The institutional review board approved the study and all patients gave written informed consent for the study.

Baseline Data

The preoperative data collected included age, gender, presence of systemic hypertension or other systemic conditions, duration of visual symptoms from the onset to the surgery, treatment history, BCVA and intraocular pressure. Slit-lamp biomicroscopy, optical coherence tomography (OCT), fundus fluorescein angiography (FFA) and multifocal electroretinography (mERG) were also performed.

Eleven eyes from 5 male and 6 female patients were included in the study. Six patients had coexisting systemic hypertension and 1 had hyperlipidaemia (Table 1). None of them had diabetes mellitus. None of the patients had previously received laser or surgical treatment for their retinal vein occlusion.

Eight eyes had central retinal vein occlusion (CRVO) and 3 eyes had branch retinal vein occlusion (BRVO). There was no visually significant cataract, vitreous haemorrhage or neovascular glaucoma in these patients. None of the eyes had posterior vitreous detachment. All cases had diffuse or cystoid macular oedema secondary to the vein occlusion confirmed on FFA. In addition, areas of capillary non-perfusion were also delineated by the FFA. All cases of CRVO were of the ischaemic variety. OCT confirmed the diffuse or cystoid macular oedema in all cases and disclosed additional serous retinal detachment in 5 cases. The mean preoperative foveal thickness was $789 \pm 278 \mu\text{m}$ (range, 482 to 1269). The preoperative BCVA

ranged from counting fingers to 20/50.

Surgical Procedure

All patients underwent a standard 3-port pars plana vitrectomy and ILM peeling under regional anaesthesia by a single surgeon (XL Liang). Separation of the posterior hyaloid was initiated by suction with the vitreous cutter at the posterior pole and continued peripherally. Without air-fluid exchange, 0.2 mL of indocyanine green (2.5 g/L) was injected onto the surface of macula and removed using the vitreous cutter 1 minute later. ILM peeling was performed with fine-end gripping forceps. A roughly circular area of ILM centered on the foveal centre, with an approximate diameter of 3 optic discs was removed. Scatter endophotocoagulation was performed on areas of capillary non-perfusion in the peripheral retina outside the temporal vascular arcade shown on FFA but not on the macula in all cases. Air-fluid exchange was done and the eye was filled with filtered air. After operation, all patients were instructed to assume a facedown positioning until the air was absorbed.

Endpoint Criteria

The mean postoperative follow-up period was 13.5 months (range, 1.5 to 24 months). The follow-up examinations included BCVA, intraocular pressure, slit-lamp biomicroscopy and OCT. FFA and mERG were performed on some cases. Intraoperative and postoperative complications were recorded. Pre- and postoperative foveal thickness were compared using paired *t*-test. The SPSS 12.0 programme (SPSS Inc, Illinois, USA) was used to compute all statistical data.

Results

Anatomical Outcomes

The foveal thickness decreased in all 11 cases and normal or near-normal foveal contour on OCT was restored in 8 patients. The mean retinal thickness at the foveal centre decreased from $794 \pm 276 \mu\text{m}$ preoperatively to $373 \pm 150 \mu\text{m}$, $302 \pm 119 \mu\text{m}$, $249 \pm 203 \mu\text{m}$ and $185 \pm 66 \mu\text{m}$ at 1 week, 1 month, 3 months and the final visit postoperatively, respectively (all $P < 0.001$, paired *t*-test, compared to preoperative thickness) (Figs. 1 and 2).

Postoperative FFA was performed in 5 cases and demonstrated marked reduction of fluorescein leakage in the macular region compared to preoperative FFA. There were also fewer retinal haemorrhages postoperatively compared to preoperatively (Fig. 3).

Functional Outcomes

Table 1 includes pre- and postoperative BCVA for all patients. After an average follow-up of 13.5 months, the BCVA improved 2 lines or more in 72.7% (8/11) of patients, and remained unchanged in 27.3% (3/11) of

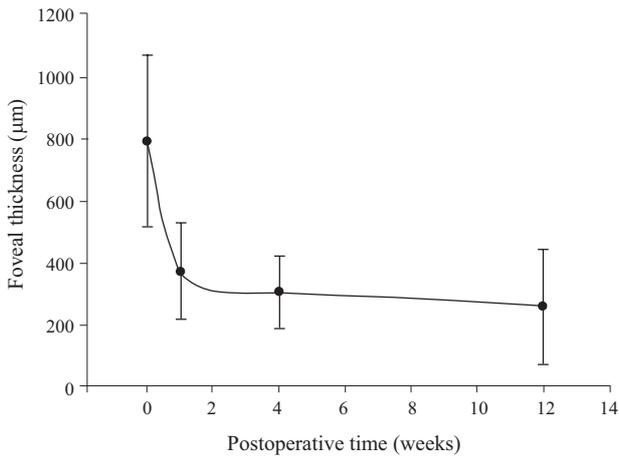


Fig. 1. Changes in foveal thickness over time. The round points refer to mean foveal thickness while the vertical bars refer to standard deviation.

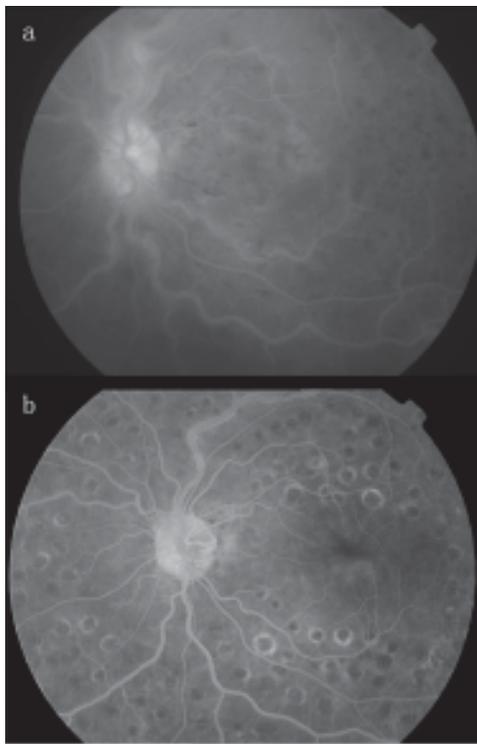


Fig. 3. Fundus fluorescein angiography in an eye with macular oedema before (a) and after (b) pars plana vitrectomy with internal limiting membrane peeling and panretinal photocoagulation (case 1, Table 1). The fluorescein leakage in the macular region seen preoperatively (a) has largely resolved 1 month after the operation (b).

patients. In 8 eyes with CRVO, postoperative BCVA improved 2 lines or more in 75% (6/8) of eyes, and remained unchanged in 25% (2/8) of eyes. In 3 eyes with BRVO, postoperative BCVA improved 2 lines or more in 66.7% (2/3) of eyes, and remained unchanged in 33.3% (1/3) of eyes.

The b-wave amplitude of mERG increased markedly particularly at the macular region after operation (Fig. 4), while the b-wave implicit time did not change.

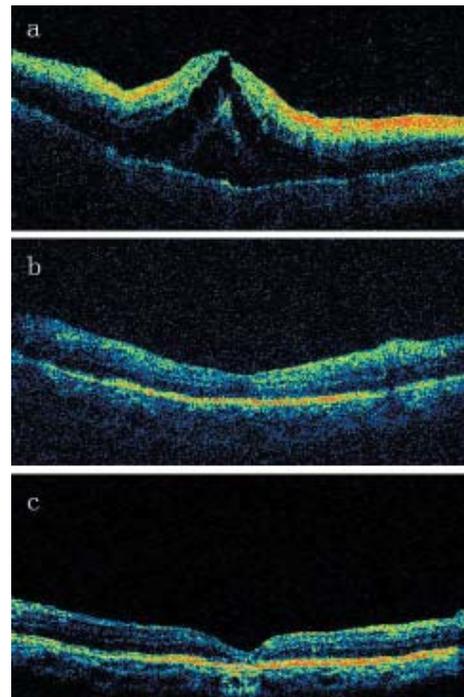


Fig. 2. Optical coherence tomography in an eye with macular oedema before (a) and after (b, c) pars plana vitrectomy with internal limiting membrane peeling (case 4, Table 1). Preoperatively, cystoid changes and serous retinal detachment were present at the fovea and the foveal thickness was 1184 µm (a). One week after the operation, the cystoid cavities have largely disappeared and the foveal thickness decreased to 248 µm (b). Eighteen weeks after the operation, the foveal contour has returned to normal and the foveal thickness was 124 µm (c).

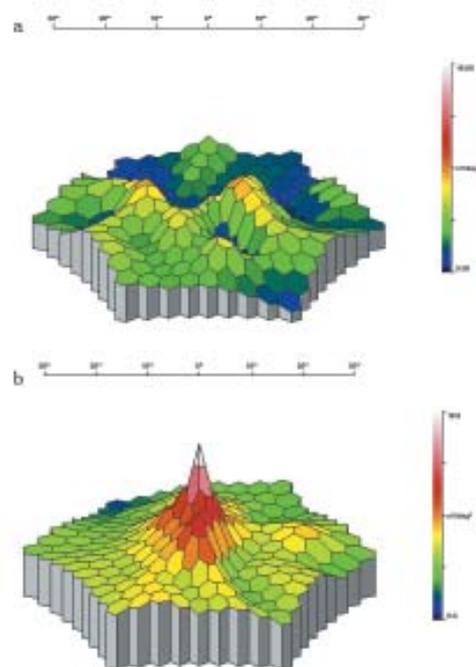


Fig. 4. B-wave amplitudes of mERGs in an eye with macular oedema before (a) and after (b) pars plana vitrectomy with internal limiting membrane peeling (case 11, Table 1). The b-wave amplitudes at the macular region were low preoperatively (a) and increased markedly 1.5 months after the operation (b).

Table 1. Patient Data

Case No.	Sex	Age (y)	Duration of symptoms (mo)	Type	FFA	Follow-up (mo)	Systemic condition	Foveal retinal thickness (μm)					BCVA		Complication
								Preop	1wk	1mo	3mo	Final	Preop	Final	
1	F	57	1	CRVO	Ischaemic	24	-	690		370		149	20/50	20/30	Cataract, visual field defect
2	F	63	6	CRVO	Ischaemic	21	Hypertension	482	232	135	82	91	CF	20/200	Cataract
3	M	36	2	CRVO	Ischaemic	19	Hypertension	1109	614	489	648	123	20/200	20/200	Cataract
4	F	30	2	CRVO	Ischaemic	18	-	1184	248			124	20/500	20/200	Cataract
5	M	60	3	CRVO	Ischaemic	17	Hypertension	1269		341	331	320	20/200	20/70	Cataract
6	M	60	0.3	CRVO	Ischaemic	17	-	514		307		207	20/500	20/50	Cataract
7	F	53	2	CRVO	Ischaemic	4	-	722	481	440	224	224	20/100	20/70	-
8	F	56	12	CRVO	Ischaemic	3	Hypertension	631		240	199	199	20/500	20/200	Vitreous haemorrhage
9	M	68	1	BRVO	Inferior occlusion	20	Hyperlipidaemia	831	381	349	133	248	20/50	20/30	Cataract
10	F	50	2	BRVO	Superior occlusion	4	Hypertension	531		200	207	200	20/100	20/100	-
11	M	53	2	BRVO	Inferotemporal occlusion	1.5	-	773	282	149		149	20/500	20/50	-

BCVA: best-corrected visual acuity; BRVO: branch retinal vein occlusion; CF: counting fingers; CRVO: central retinal vein occlusion; F: female; FFA: fundus fluorescein angiography; M: male; mo: month; Preop: preoperative; wk: week

Complications

There were no intraoperative complications except for small punctate retinal haemorrhages during ILM peeling, which either stopped spontaneously or after elevation of the infusion bottle. Postoperative complications included vitreous haemorrhage in 1 eye and an arcuate scotoma on visual field testing in another eye. The vitreous haemorrhage occurred postoperatively in a hypertensive patient after she stopped using her anti-hypertensive drugs for 2 days. The haemorrhage resolved after 1 month. Macular oedema recurred in 1 eye 4 months postoperatively, but the foveal thickness postoperatively remained lower than the preoperative thickness. Of the 7 eyes with more than 1-year follow-up, cataract either developed or worsened in all eyes after surgery. However, their BCVA had either improved or remained unchanged compared to before the surgery. There was no retinal tear, retinal detachment, epiretinal membrane, secondary glaucoma or endophthalmitis.

Discussion

A number of treatment options are available for the management of macular oedema. In some cases, macular oedema may resolve spontaneously. In others, the condition may improve with drugs or laser therapy. However, it often takes several months for the macular oedema to resolve with these treatment modalities. It is known that persistent

macular oedema may lead to apoptosis of the photoreceptors and potentially irreversible visual loss.³ Rapid resolution of macular oedema may therefore be beneficial in preserving visual acuity. In this study, the mean foveal thickness of the 11 eyes with diffuse or cystoid macular oedema treated with pars plana vitrectomy, ILM peeling and scatter laser photocoagulation to areas of capillary drop-out outside the macula decreased by 54% 1 week postoperatively. This rapid regression of macular oedema contrasts with other reports that observed a resolution of macular oedema in 91% of eyes within 15 months of grid photocoagulation¹⁸ and within 4.5 months of simple pars plana vitrectomy.¹⁹

In our series, 72.7% of eyes improved their BCVA by 2 lines or more, and 27.3% of eyes maintained. Furthermore, 75% and 66.7% of eyes with CRVO and BRVO, respectively, significantly improved in visual acuity. This is in contrast with 17% and 27% of eyes with improved visual acuity respectively, following grid photocoagulation¹⁸ and 37% and 60% of eyes respectively after simple pars plana vitrectomy.^{15,20} Our findings of visual improvement following pars plana vitrectomy, ILM peeling and extramacular scatter endolaser photocoagulation for macular oedema secondary to retinal vein occlusion is consistent with the study by Mandelcorn and Nrusimhadevara,²¹ which reported that the vision of 78.6% patients with macular oedema secondary to retinal vein occlusion improved after pars plana vitrectomy with ILM peeling. However, Radetzky

and associates²² reported no visual improvement in 4 patients with CRVO after pars plana vitrectomy and ILM peeling. A larger randomised controlled trial is warranted to study if pars plana vitrectomy and ILM peeling is helpful in the treatment of macular oedema.

The mechanism by which ILM peeling reduces macular oedema is still unclear. A number of possible mechanisms have been suggested. ILM is known to play an important role as a scaffold for proliferating astrocytes and its removal not only completely reduces vitreous-macular interface traction, but also inhibits the proliferation of fibrous astrocytes on the retinal surface. ILM peeling reduces epiretinal membrane formation, which may be associated with a recurrence of macular oedema after simple pars plana vitrectomy.⁴ It is also known that the ILM acts as a diffusion barrier between the retina and the vitreous. ILM peeling removes this barrier and increases the diffusion of large molecules from the retinal tissue into the vitreous cavity and decreases intraretinal osmotic pressure, thereby increasing elimination of water from the retina.²² ILM peeling also increases oxygen diffusion from the ciliary body to the retina and improves the oxygen supply to the retina. Theoretically, the removal of the basal lamina of Müller cells may also lead to changes in the protoplasmic skeleton of the retina and enable a more rapid resolution of macular oedema.⁴ Pars plana vitrectomy may also remove some cytokines and inflammatory mediators within the vitreous, which cause leakage of the retinal vessels, and this may also contribute to the reduction of macular oedema.²³

One patient developed an arcuate scotoma on visual field testing in our series. This defect may have been caused by injury to the retinal nerve fibre layer during ILM peeling. Another case suffered a recurrence of macular oedema 4 months after the operation. To our knowledge, recurrence of macular oedema after ILM peeling has not been previously reported although such recurrence is possible by simple pars plana vitrectomy without ILM peeling.

In conclusion, in a small series of eyes with macular oedema secondary to retinal vein occlusion, pars plana vitrectomy, ILM peeling and extramacular scatter laser photocoagulation resulted in rapid resolution of the macular oedema and improvement in BCVA. A larger randomised controlled trial is warranted to further evaluate the role of this surgery in the management of patients with macular oedema secondary to retinal vein occlusion.

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