Research Article

Current Trends in Ophthalmology

Inverted Internal Limiting Membrane Flap Technique for Extra Large Macular Holes

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Abstract

Aim: To investigate the outcome of the inverted Internal Limiting Membrane (ILM) flap technique for extra large idiopathic macular holes (MHs).

Methods: A retrospective non-comparative surgical case series of seven eyes of 7 patients with MHs (base diameter of at least 1000 μ m) was conducted. All the MHs were treated using pars plana vitrectomy and brilliant blue G (BBG)-assisted inverted ILM flap technique. Spectral Domain- Optical Coherence Tomography (SD-OCT) images were used to assess the anatomical outcomes of surgery including the macular microstructure, while Best Corrected Snellen Visual Acuity (BCSVA) was used to evaluate the functional outcomes.

Results: The average MH size was 1241 microns and average symptom duration was nineteen months. All eyes achieved successful anatomical closure and there was no occurrence of a flat open type closure. SD-OCT microstructural study revealed a reconstruction of the Ellipsoid Zone (EZ) and External Limiting Membrane (ELM), in only 3 eyes. There was an improvement in visual acuity in 5 eyes, while 2 eyes maintained the same as pre operative vision. The largest increase in post operative visual acuity gain was a 4-line improvement in Best Corrected Snellen Visual Acuity (BCSVA) noted in one of the 3 eyes with reconstructed EZ and ELM. The 3 months symptom duration in this patient was the shortest in this series.

Conclusion: Inverted ILM flap technique is a safe and effective approach for the management of extra large chronic idiopathic MHs with demonstrably good anatomical and limited functional results in a majority of cases. Postoperative reconstruction of the microstructure is however seen only in a minority of eyes. Despite an absence of the outer retina (EZ and ELM), some eyes still experience an improvement in vision. The symptom duration may play a vital role in functional outcome in this subset of extra large chronic MHs.

Keywords: Macular hole; Vitrectomy surgery; Internal limiting membrane; Optical coherence tomography.

Introduction

Significant advances have been made in surgery for idiopathic MHs with anatomical success reported to be above 90% by several studies. The introductions of ILM peel and then dye assisted ILM peel have been some of these advances [1,2]. However the anatomical closure rate for large MHs was still less than anticipated. The anatomical closure rate following conventional ILM peel

technique for the more difficult large MHs greater than 400 microns and for myopic MHs has been reported to be about 83%[3], also the incidence of the flat open MH closure configuration (in which there was bare, exposed retinal pigment epithelium (RPE)), was unacceptably common. The flat open MH closure configuration is associated with poorer visual outcome.

This resulted in the introduction by Michalewska et

al. in 2010 of the inverted ILM flap technique [4]. This inverted ILM flap technique has been popularized by its success in large MHs. In this procedure, the ILM around the MH after peeling is left attached to the surrounding edge of the MH. This peri-MH ILM is then inverted upside down and manipulated to cover the MH. An air fluid exchange then concludes the surgery.

This technique has improved the anatomical success to about 100% in surgeries for MH greater than 400microns [4] and also for myopic MHs [5,6] and MH associated retina detachment. One study compared the results of vitrectomy plus complete ILM removal with the results of the inverted ILM flap technique in the treatment of myopic MH without retinal detachment, and noted that the functional and anatomic outcomes reported with the inverted ILM flap technique were superior to those with complete ILM removal for the treatment of myopic MH [7]. Furthermore functional improvement represented by an improved visual acuity in many eyes has been reported.

The question that arises then, is if this approach to MH surgery is equally effective for extra-large, chronic MHs, much greater than 400 microns and if there is any functional benefit of closing such MHs? These extra-large MHs may pose some difficulties achieving success, as the area of tissue defect is obviously wider.

Objective

To determine the outcome of the inverted ILM flap technique for idiopathic MHs with a size of atleast one thousand microns or greater. The size of the MH was taken to be the base diameter of the MH, as case definition and for standardization purposes.

Materials and Method

A retrospective non comparative study was performed involving seven consecutive eyes of 7 patients who had MH surgery with an inverted ILM flap technique with preoperative MH base diameter measured to be 1000 microns or greater. All patients had idiopathic MHs and no history of trauma was recorded prior to MH formation.

Informed consent was obtained from all seven patients before surgery. The institutional review board waived the ethical approval for this study, as the study was a retrospective one.

The patients underwent pre operative evaluation

including snellen visual acuity assessment, intraocular pressure measurement, binocular non contact funduscopy through a dilated pupil using a 90D (Volk) condensing lens. The diagnosis of the MH was made by clinical examination and with the use of SD OCT (Optovue). The MH based diameter was measured using the measuring calipers on the OCT machine.

The MH repair surgeries were performed by a single surgeon (ONO) between June to December 2016 and post operative follow up ranged from 4 months to 16 months.

The surgical technique involved a standard 23-gauge pars plana vitrectomy with completion of posterior vitreous detachment and trimming of the vitreous base. Then brilliant blue G was used to stain the ILM in the macular area. The ILM peel was initiated and peeled ILM tissue was left attached to the edge of the MH. This piece of ILM tissue was then inverted upside down and manipulated into the MH, to cover it.

Air fluid exchange concluded the surgery, with special attention not to aspirate the ILM flap during the exchange. The tamponade agent used included 16% SF6 in 4 eyes, 10% C3F8 in 2 eyes and air in 1 eye.

The patients were evaluated on the first day post surgery, with in the first month and in a majority of the eyes on the 3rd month, 6th month and subsequent visits.

Postoperative evaluation involved a snellen visual acuity, intraocular pressure measurement, anterior segment examination with a slit lamp bio-microscope, dilated funduscopy and SD OCT imaging of the macular.

Specifically the SD OCT was used in the postoperative evaluation to determine MH closure and presence or absence of the ellipsoid zone (EZ) and external limiting membrane (ELM) in the foveal and perifoveal area.

The main outcome measures were MH closure (anatomical outcome) and best corrected snellen visual acuity (functional outcome). MH closure was defined as the presence of continuous tissue within the previous MH defect.

Results

Seven eyes of 7 consecutive patients that underwent MH repair surgery within the study period using the inverted ILM flap technique and had a MH base diameter of 1000 microns or more were identified.

Figure 1 : Visual acuity (Pre and Post Operative) outcome of seven eyes that had inverted ILM flap technique for extra large MHs

Figure 2 : Post operative SD OCT for patient 1

Figure 3 : Post operative SD OCT for patient 2

Figure 4: Post operative SD OCT for patient 3

The patient demographics, symptom duration, MH size, refractive error and lens status are as shown in Table 1.

Figure 5 : Post operative SD OCT for patient 4

Figure 6 : Post operative SD OCT for patient 5

Figure 7 : Post operative SD OCT for patient 6

Figure 8 : Post operative SD OCT for patient 7

There were more female patients accounting for 71% (5eyes) of the total number and the age of the patients ranged from 59 and 76 years (average 65.7 years). The

average symptom duration was 19 months; individual symptom duration can be seen on table 1. The average MH base diameter was 1241microns. The individual base diameters are as shown also on Table 1. The average follow up duration for all eyes was 10.6 months.

All seven eyes had a closed MH as was seen on SD OCT; a 100% anatomical closure rate.

There was an improvement in postoperative snellen visual acuity from the baseline visual acuity in 5 eyes, while vision remained the same in 2 eyes (one of the two eyes had a significant cataract which possibly could have affected the visual outcome). No eye suffered a decline in post operative visual acuity including the eyes that still had a cataract as at study time. The details of the pre operative versus the postoperative visual outcome for all the patients can be seen in Table 2.

Also the graphic representation shown in Figure 1 demonstrates the general improvement in visual outcome noticed in this series.

The presence of a reconstituted Ellipsoid Zone (EZ) and External Limiting Membrane (ELM) as shown by post operative SD OCT evaluation is also summarized in Table 2. The individual post operative SD OCT outcomes are shown in Figures 2 - 8. Three of the eyes had varying degrees of post operative recovery of EZ and ELM. These were patients 2, 3 and 5.

The micro structural changes on OCT are as depicted in the individual patients OCT and show an inner layer irregularity in 5 of the 7eyes. Other findings include presence of intra retinal cysts in one eye, possible ILM tissue filling previous MH defect in three eyes, and one eye with a defective retinal pigment epithelium (RPE), but presence of EZ and ELM, seen in patient five (Figure 6)

All eyes but one had a significant cataract at time of initial surgery, which may have a negative effect on the post operative visual outcome. Till date, three of these eyes [3/6] have undergone an uneventful phacoemulsification with significant improvement in vision noted in 2 of the 3 eyes. The third eye whose vision remained same after the cataract surgery was noted on OCT to have a defective RPE layer. It is likely that the some improvements may be experience by other three eyes following cataract removal.

There was no complication of the initial vitrectomy

surgery or the cataract surgery in these seven eyes.

Discussion:

The inverted ILM flap technique has grown in popularity over a relative short period of time owing to the demonstrable benefit of this technique especially in difficult cases. The anatomical success often is accompanied by some gain in vision. There have been reports of improvement in multifocal ERG (mfERG) following successful MH closure using the inverted ILM flap technique [8]. This promotes the notion that functional improvement follows anatomical success. The micro structural reorganization following this ILM flap technique in which the outer retina comprising of EZ and ELM, is reconstituted is important for visual recovery, and has been reported to continue to occur upto and over a period of 12 months [6]. It is hypothesized that the inverted ILM in the area of the MH functions as a scaffold and encourages tissue proliferation, producing an environment for the photoreceptors to assume new positions in the area of the fovea [4]. The glial tissue in the inverted ILM could play a crucial role in promoting this process of proliferation.

That the inverted ILM flap technique results in MH closure in MHs much greater than 400 microns (which in this study has been characterized as extra large MHs having a base diameter of 1000 microns and above) demonstrates the usefulness of this technique and collaborates the findings of previous reports in which the reported rate of MH closure ranges from 98 to 100% [4,6-8]. These category of MHs would likely suffer a poorer outcome with the use of conventional ILM peel technique as reported rates of surgical success was not comparable to those reported for the inverted ILM flap [9,10]. Considering the larger than usual area of tissue defect in these MHs, the inverted ILM provides alternative tissue to fill the defect caused by the extra large MH. This technique has also been used in MHs associated with retina detachment with good outcome [11].

A similar study to ours considered the use of the inverted ILM flap technique in MHs greater than 700 microns and reported satisfactory outcome in the 5 eyes reported, with all 5 eyes having anatomical closure and improvement of vision [12].

In our study, 5 out of the seven eyes had a demonstrable improvement in functional outcome as evidenced by the improvement in visual acuity, which was the only modality of function assessed. Several of the already mentioned

Table 1: Sample characteristics, including refractive error and lens status.

Patient No	Age	Sex	Eye	MH Size	Symptom Duration in months	Refractive Error.	Lens Status.	Cataract Extraction Done.
Patient 1	62	F	LE	1500	12	Hyperopia	Cataract	Yes
Patient 2	76	F	RE	1300	24	Myopia	Cataract	No
Patient 3	62	M	RE	1140	3	Hyperopia	Cataract	Yes
Patient 4	68	F	RE	1200	24	Emmetropia	Cataract	No
Patient 5	63	F	RE	1000	5	Emmetropia	Cataract	Yes
Patient 6	59	M	RE	1100	6	M y o p i c Astigmatism	Cataract	No
Patient 7	70	F	RE	1450	60	Myopia	PCIOL	--

Table 2 : Visual acuity outcomes, including outer retina (EZ and ELM) presence.

Patient No	Pre op Va.	Post op Va.	Ellipsoid Zone (EZ)	External Limiting Membrane (ELM)	Follow up (in Months)
Patient 1	6/36	6/18	Absent	Absent	10
Patient 2	6/36	6/24	Present	Present	4
Patient 3	6/60	6/9	Present	Present	16
Patient 4	CF	6/36	Absent	Absent	13
Patient 5	6/36	6/36	Present	Present	11
Patient 6	6/36	6/36	Absent	Absent	10
Patient 7	6/36-1	6/24	Absent	Absent	10

studies have similarly noted an improvement in visual acuity following ILM flap technique induced closure of the MH. It is expected that the micro structural reorganization of the closed MH would herald improvement in visual acuity. This assertion may not be always so; as there were 2 eyes (patients 1 and 4) with no micro structural reorganization of the outer retina (EZ and ELM) who still had some improvement in acuity (Table 2 and Figure 1). The EZ and ELM may therefore not be always present in these large MHs before an improvement in vision is noticed. This finding has been collaborated by the report of Mahalingam et al in which eyes without outer retina reconstitution still had a gain in vision [12]. Therefore our series collaborates what has been previously reported by the Vitrectomy for Treatment of Macular Hole Study

Group, that showed a clear benefit in closure rates and final visual acuity with surgery versus observation for stage III and IV macular hole [13]. To summarize this point, majority of extra large MH eyes will demonstrate benefit from closure of the MH; even in the absence of micro structural reorganization.

There is a possibility that the presence and removal of cataract could have a confounding effect on the visual outcome. There were 2 eyes in which visual acuity improved despite the pre and post operative presence of cataract. This establishes that the improvement in visual acuity seen despite the presence of cataract in this 2 eyes was likely due to the repair of the large MH in the eye. Vision would be expected to improve further after

cataract removal in these eyes.

Patient 7 had the longest symptom duration of 60 months and also had one of the largest MHs, measuring a base diameter of 1450 microns and was pseudophakic at presentation. Following successful MH repair in this eye and though the outer retina was absent, yet visual acuity did improve, though marginally by about 1 snellen line. This illustrates that chronicity and size may not be limitations to some functional outcome. On the other hand patient 3 who had the largest snellen improvement in post operative vision and regained a 6/9 visual acuity, had the shortest symptom duration of 3 months in this series. Therefore it is reasonable to expect that symptom duration prior to surgery could be an important factor in prognostic outcome. None theless, in our study chronic MHs for upto 60 months duration could still derive some visual benefit if successfully closed; but shorter symptom duration would be associated with a more favorable outcome.

The long duration of follow up of the eyes in this series (average of 10.6months)is strength for this work. The initial report on the inverted retina flap technique by Michalewska et al. [6] reported that the micro structural remodeling that occurs after this technique tends to continue for over and beyond the ensuing 12 months period. In this study all the 4 eyes with absence of EZ and ELM in the foveal and perifoveal region soon after the surgery, never got any further development of this outer layer throughout the follow up period. The 3 eyes in which the EZ and ELM layers was present in the immediate post operative phase continue to have these layers over the follow up period. The eye with defective retina pigment epithelium (RPE), though having presence of ELM and EZ, did not have any improvement in vision (patient 5). A defective RPE, is an important OCT finding. The possible reasons for this occurrence could have been related to a number of factors including iatrogenic trauma, photo toxicity and toxicity from the dye. Indo Cyanine Green (ICG) which has been reported to be phototoxic was not used in any of the eyes [14]. Only BBG was used. But the reason for this finding warrants investigation.

An obvious weakness of this study is the small sample size as patients with such very large MHs are limited in number. A multicenter study on this topic may help to increase sample size. Therefore, care should be taken in extrapolating the findings of this study to other patient groups.

To conclude, this study demonstrates the effectiveness of the inverted ILM flap technique in managing extra large MHs with high rates of anatomical success and some improvement in visual function, which may be affected by degree of MH chronicity. At the moment, there does not appear to be any other surgical technique with comparable or better outcomes for this subset of large chronic MHs. The retina auto graft is a new and evolving technique and will have to show much better outcomes than this if it is to be the preferred surgical technique for these cases.

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