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# Inverted Internal Limiting Membrane Flap For Large Traumatic Macular Holes

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**Abstract:** The aim of the study was to assess the role of inverted internal limiting membrane flap as a treatment option for large traumatic macular holes.

This is a prospective noncomparative study in which 12 eyes with large traumatic macular holes (basal diameter of  $1300-2800 \ \mu m$ ) since 3 to 6 months were subjected to standard 23-gauge vitrectomy with removal of the posterior hyaloid, brilliant blue G (BBG)-assisted internal limiting membrane peeling in a circular fashion keeping it attached to the edge of the hole to create a flap. At the end of the surgery, air fluid exchange was done with inversion of the internal limiting membrane flap inside the macular hole using the soft tipped cannula and sulfur hexafluoride 20% as tamponade. The main follow-up measures are the best corrected visual acuity and the optical coherence tomography for 6 to 9 months.

All the included eyes had a closed hole from the first week postoperative and along the follow-up period (6-9 months). The best corrected visual acuity improved from 20/2000 to 20/200 with a median of 20/400 preoperatively to 20/400 to 20/50 with a median of 20/100 at the end of follow-up period.

Inverted internal limiting membrane flap is a good adjuvant to standard vitrectomy in the management of large traumatic macular holes that led to the 100% closure rate and improvement of best corrected visual acuity.

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**Abbreviations:** BBG = brilliant blue G, BCVA = best corrected visual acuity, BD = basal diameter, ILM = internal limiting membrane, MH = macular hole, MLD = minimum linear dimension, RD = retinal detachment, SD-OCT = spectral domain optical coherence tomography.

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Summary: The study included 12 eyes with large traumatic macular holes (basal diameter of 1300–2800  $\mu$ m). The included eyes were subjected to standard 23-gauge vitrectomy with removal of posterior hyaloid, and internal limiting membrane peel in a way keeping it attached to the edge of the hole to create a flap that was inverted inside the hole upon air–fluid exchange. Followup at 1 week, 1, 3, 6, and 9 months revealed hole closure in 100% of the cases and improvement in the best corrected visual acuity.

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#### INTRODUCTION

T rauma is the second most common cause of macular hole (MH). In traumatic MH, vitreoretinal traction is claimed to cause antero-posterior compression and equatorial expansion of the globe that may cause immediate stress at those points of the retina at which vitreo-retinal adherence is relatively strong. Sudden traction on the thin perifoveal area can lead to a macular cyst or an immediate MH.<sup>1</sup> Similarly, countercoup forces can lead to immediate MH formation or to a cyst that progresses to a full-thickness hole.<sup>2</sup>

Vitrectomy surgery for traumatic MH has been shown to improve vision in some eyes. Current techniques include removal of the posterior hyaloid, epiretinal membranes, with or without internal limiting membrane (ILM) peeling, and postoperative gas or silicone oil tamponade.<sup>3–16</sup> Complete removal of the posterior hyaloid is a crucial step for the success of vitrectomy surgery for macular hole.<sup>17</sup>

Reports for traumatic MH closure after vitrectomy were variable. Garcia-Arumi et al reported successful anatomic MH closure in 13 (92.86%) of the 14 eyes included in their study.<sup>15</sup> Robert Johnson et al combined the previous reports of traumatic macular holes, 81 eyes have been reported, of which successful closure of the hole after 1 vitrectomy surgery occurred in 67 cases (83%).<sup>4</sup>

In 2010, Jerzy Nawrocki et al conducted a study for the inverted ILM flap technique for large idiopathic macular holes. They concluded that the inverted ILM flap technique prevents the postoperative flat-open appearance of a macular hole and improves both the functional and anatomic outcomes of vitrectomy for macular holes with a diameter >400  $\mu$ m. In their study, spectral domain optical coherence tomography (SD-OCT) after vitrectomy with the inverted ILM flap technique suggested improved foveal anatomy compared with the standard surgery.<sup>18</sup>

In 2014, another study by Nawrocki et al proved the value of inverted ILM flap technique for myopic macular holes. They concluded that vitrectomy with the inverted ILM flap technique may be an effective addition to the surgical options for treating myopic macular holes. SD-OCT images confirmed that the process of foveal architectural repair after this surgery continues over at least a 12-month period.<sup>19</sup>

Depending on the last mentioned 2 studies, and when comparing their rate of closure of idiopathic and myopic MH with that of traumatic MH in previous studies, it was hypothesized that the inverted ILM flap technique for large traumatic MH may be of value regarding improving the rate of closure, the foveal architecture, and the visual improvement.

#### AIM OF THE WORK

The aim of this study was to assess the role of inverted internal limiting membrane flap as a treatment option for large traumatic macular holes.

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#### PATIENTS AND METHODS

The study included 12 eyes of 12 patients with traumatic MH. The included eyes were subjected to:

- (1) Full history taking.
- (2) Refraction and best corrected visual acuity (BCVA) using tumbling E chart.
- (3) Anterior segment slit lamp examination.
- (4) Intra-ocular pressure using applanation tonometry.
- (5) Fundus biomicroscopy using noncontact +78 diopter lens.
- (6) Peripheral retinal examination using Goldman 3-mirror lens.
- (7) Fundus color photography
- (8) SD-OCT macular scanning using macular cube (512 by 128 A scans) and high definition 5 line raster of Cirrus HD-OCT, software version 6.0; Carl Ziess Meditec, Inc.

The basal diameter (BD) and the minimum linear dimension (MLD) were manually calculated for the included eyes (Figure 1).

#### **Ethical Consideration**

The study was approved from the ethical committee of Alexandria University. Full explanation of the procedure was done for patients, their parents, and informed consent was signed by the patient or his parents.

#### **Operative Procedure**

The included eyes were operated between November 2014 and February 2015 and followed up for 6 to 9 months. Under general anesthesia, standard 23-gauge pars-plana vitrectomy was done, triamcinolone assisted removal of the posterior hyaloid, brilliant blue G (BBG) staining of ILM, ILM peel in circular fashion keeping it attached to MH edge, air fluid exchange, using soft tipped cannula to direct the ILM flap into the MH, and sulfur hexa-fluoride 20% as a tamponade.

## **Postoperative**

Treatment with antibiotic-steroid combination and cycloplegic eye drops, face down position for 2 weeks.

## **Follow-Up Visits**

Patients were examined first postoperative day, 1 week, 1, 3, 6, and 9 months.

In every visit, full ophthalmic examination, including BCVA, slit lamp anterior segment, and posterior segment examination using noncontact +87 lens biomicroscopy, was performed.

Postoperative SD-OCT examinations were performed at 1 week, 1, 3, 6, and 9 months.

#### **Statistical Methods**

Clinical findings were statistically evaluated using Excel 2007 (Microsoft Corp.) and SPSS software version 15.0 (SPSS Inc, Chicago, IL). Means and standard deviations were calculated.

#### RESULTS

The study included 12 eyes (7 left and 5 right) of 12 patients (8 men and 4 women) with traumatic MH. The age of the included patients ranged from 5 to 50 years with a mean of  $23.25\pm14.11$  years. The included eyes developed macular holes after blunt, nonpenetrating trauma. Time elapsed from the insult of trauma till the surgical intervention ranged from 3 to 6 months with a mean of  $3.75 \pm 1.06$  months. The nature of trauma varied from football or tennis ball trauma (4 eyes), trauma by stone (3 eyes), road traffic accident (2 eyes), animal trauma, fist trauma, and wooden stick (1 eye for each). The preoperative visual acuity in the affected eye ranged from 20/ 2000 to 20/200 with a median of 20/400. The slit-lamp anterior segment examination of the included eyes was unremarkable. Base diameter (BD) of macular holes in the included eyes ranged from 1300 to 2800  $\mu$ m with a mean of 1800  $\pm$  473 µm. Minimum linear dimension (MLD) of macular holes in the included eyes ranged from 250 to 1500 µm with a mean of  $696 \pm 445 \ \mu m.$ 

All the included eyes were subjected to standard 23-gauge pars plana vitrectomy with successful triamcinolone assisted removal of the posterior hyaloid (that was attached in all cases), no epiretinal membranes were reported in the included eyes, under fluid BBG ILM staining, ILM peel in circular fashion keeping it attached to MH edge, air fluid exchange, using soft tipped cannula to direct the ILM flap into the MH, and sulfur



**FIGURE 1.** Optical coherence tomography scan measurements in macular hole: (a) base diameter, (b) minimum linear dimension, (c) and (d) arms for measuring hole form factor, (e) hole height, (f) macular hole inner opening. Hole form factor.  $(c \pm d)/a =$  macular hole index, e/a = tractional hole index e/b.<sup>20</sup>.



**FIGURE 2.** Pre- and postoperative BCVA of the included eyes. BCVA = best corrected visual acuity.

hexa-fluoride 20% as a tamponade in all eyes (see Videos 1, http://links.lww.com/MD/A636 and 2, http://links.lww.com/MD/A637, Supplemental Video, which demonstrates the surgical technique). The intraoperative examination of the retinal periphery did not reveal peripheral retinal breaks in any of the included eyes. No intraoperative complications were recorded. The follow-up duration ranged from 6 to 9 months with a mean of 7.75 months.

One-week post-operative, the BCVA ranged from 20/600 to 20/200. The crystalline lens was clear in all eyes, gas bubble could be seen in upper fundus, and the retina was attached in all eyes. SD-OCT revealed hole closure in all 12 eyes (100%). Macular holes in the included eyes remained closed during the whole follow-up period (6 to 9 months).

One month and 3 months postoperative, the BCVA improved to be 20/400 to 20/125, and 20/400 to 20/100, respectively. Visual acuity at the end of follow-up duration

ranged from 20/400 to 20/50 with a median of 20/100 (Figure 2). Final BCVA was 20/200 or better in 11 eyes (91.7%), 20/100 or better in 9 eyes (75%), 20/60 or better in 5 eyes (41.6%). Table 1 illustrates the clinical data of the included eyes.

The crystalline lens was clear in all follow-up visits (1, 3, 6, 9 months). Follow-up SD-OCT of the included eyes revealed MH closure along the follow-up visits with restoration of the foveal contour and the structure of the outer retinal layers specially the external limiting membrane (Figures 3 and 4). During the follow-up period (6–9 months), no eyes required second intervention.

#### DISCUSSION

Traumatic macular holes occur in ~1.4% among closed globe injury cases and to a less extent (0.15%) among open globe injury cases.<sup>21</sup> The exact mechanism of traumatic macular hole is not well settled; however, the sudden antero-posterior compression accompanied by the equatorial expansion is highly claimed. The equatorial expansion is accompanied by increased vitreo-macular traction.<sup>4</sup>

Spontaneous closure of traumatic macular holes was documented in many case reports.<sup>22,23</sup> Yanagiya and coworkers observed that most of the traumatic macular hole cases in their series were elliptical and not round. This is why they theorized that the force applied to the front of the eye is transmitted posteriorly and can cause rupture to the fovea.<sup>24</sup>

In opposition to the previous theory, Delori and coworkers in their high-speed photography analysis of ocular trauma observed that no shock waves transmitted to the back of the eye.<sup>25</sup>

Yokotsuka and coworkers theorized that the sudden vitreous separation is the cause of traumatic MH.<sup>26</sup> In opposition of this theory, all eyes included in the present study had attached posterior hyaloid that was detached intraoperatively. In support to our finding, Johnson and coworkers reported that 84% of eyes in their series of traumatic MH had attached posterior hyaloid that was detached intraoperative.<sup>4</sup>

Only few case series documented the spontaneous closure of traumatic macular holes in a rate of 10.7% up to 44.4%. However, spontaneous closure in these cases occurred more in

Case	Age (Years)/ Gender		Type of Trauma	Time Elapsed From Trauma to Surgery (months)	Initial Visual Acuity	Final Visual Acuity	Base Diameter (BD) in μm	Mean Linear Dimension (MLD) in μm	Duration of Follow-Up (months)
		OD/OS							
1	14/M	OS	Stone	3	20/200	20/50	1700	650	9
2	20/F	OD	Tennis ball	6	20/400	20/100	1400	450	6
3	45/F	OS	RTA	4	20/300	20/50	1700	550	9
4	26/M	OD	Football	5	20/200	20/100	2800	1400	9
5	30/M	OS	Wooden stick	3	20/400	20/200	2500	1500	9
6	18/F	OD	Animal trauma	4	20/2000	20/400	2200	1300	6
7	50/M	OD	RTA	3	20/200	20/60	1450	600	6
8	13/M	OS	Fist trauma	3	20/2000	20/50	1480	250	9
9	18/M	OS	Football	3	20/400	20/50	1500	600	6
10	7/M	OD	Stone	3	20/800	20/200	1600	450	9
11	33/F	OS	Tennis ball	3	20/400	20/100	1300	300	6
12	5/M	OS	Stone	5	20/2000	20/100	1970	300	9



FIGURE 3. Case 1, male patient 14 years old with trauma by stone to the left eye since 3 months. Basal diameter =  $1700 \,\mu$ m, mean linear dimension = 650  $\mu$ m. Preoperative best corrected visual acuity = 20/200. Final postoperative best corrected visual acuity 20/50.

small sized holes (0.33 disk diameter) and within the first 3 to 6 months after trauma.  $^{\rm 27-29}$ 

In the present study we included only the large traumatic macular holes (basal diameter of 1300 to 2800  $\mu$ m and minimum linear dimension of 250–1500  $\mu$ m). These holes according to the previously mentioned studies are less amenable for spontaneous closure. Also, the included eyes were operated 3 to 6 months after the claimed trauma to give enough chance for the possibility of spontaneous closure.

Kelly and Wendel in 1991 were the first to report the role of vitreous surgery in idiopathic macular holes with a closure rate of 58% and gain of 2 lines or more of BCVA in 42%.<sup>30</sup> Although the pathogenesis of traumatic MH seems to be different from that of idiopathic MH, vitrectomy seems to have also good results in cases of traumatic MH. Garcia-Arumi et al reported anatomical closure of traumatic macular hole after standard vitrectomy with dissection of posterior hyaloid, sulfur hexafluoride tamponade in 92.86% of the included eyes with a mean of final BCVA of 20/30.<sup>15</sup>

In a similar study, Amari et al reported closure rate of 70% after vitrectomy and a rate of 96% after the second intervention.



FIGURE 4. Case 4, male patient 26 years old with football trauma to the right eye since 5 months. Basal diameter =  $2800 \,\mu$ m, mean linear dimension =  $1400 \,\mu$ m. Preoperative best corrected visual acuity 20/200. Final postoperative best corrected visual acuity 20/100.

The mean of the BCVA changed from 20/160 preoperatively to a mean of 20/60 postoperatively with 61% of the included eyes achieved BCVA of 20/60 or better.<sup>7</sup>

A lot of adjuncts were adopted in addition to standard vitrectomy, removal of posterior hayloid and gas tamponade to improve the rate of traumatic MH closure. These included the use of serum, transforming growth factor B2, plasmin enzymeassisted vitrectomy, and internal limiting membrane peeling.

Rubin et al used transforming growth factor B2 with vitrectomy in 12 eyes with traumatic MH; they reported closure rate of 67% (8 eyes) after the first procedure, and 4 eyes failed to close after the first procedure. Three of these 4 eyes underwent second vitrectomy with reinstallation of transforming growth factor B2; all these 3 eyes had closure of the MH after the second intervention. They reported preoperative BCVA of 20/200 to 20/100 (mean of 20/175) and postoperative BCVA of 20/200 to 20/200.5

Johnson et al reported a series of 25 eyes with traumatic macular holes operated by vitrectomy with posterior hyaloid removal. They added internal limiting membrane peeling in 3 eyes and serum was used as adjunct in 12 eyes (48%). The macular hole closed in all the 12 eyes (100%) in which serum was used as an adjuvant with improvement of the BCVA of 2 or more lines in 11 eyes (92%). On the other hand the MH closed only in 10 of the 13 eyes (77%) in which serum was not used.<sup>4</sup>

In the present study, in spite we included 12 eyes with large traumatic macular holes, the closure rate was 100% at 1 week as seen by SD-OCT. MH remained closed during all the follow-up visits with improvement of the foveal contour and rearrangement of the different retinal layers specially the external limiting membrane (Figures 3 and 4). Visual acuity at the end of follow-up duration (6 to 9 months) ranged from 20/400 to 20/50 with a median of 20/100. Final BCVA was 20/200 or better in 11 eyes (91.7%), 20/100 or better in 9 eyes (75%), 20/60 or better in 5 eyes (41.6%).

Jerzy Nawrocki et al, in a prospective comparative study, compared 2 groups of eyes with large idiopathic macular holes with nearly the same preoperative demographic data and SD-OCT parameters. The first group operated by standard vitrectomy with posterior hyaloid removal and ILM peeling. The second group operated by standard vitrectomy with posterior hyaloid removal and inverted ILM flap. The group in which the inverted flap was successfully left in place, 100% of macular holes closed, and no flat-open macular hole was observed postoperatively. At the end of follow-up (12 months) of this group of eyes the BCVA ranged from 20/1000 to 20/25.<sup>18</sup>

In another prospective interventional study, Jerzy Nawrocki et al investigated the role of inverted ILM flap technique in myopic MH. Their study included 19 myopic MH with mean BD of 801  $\mu$ m that were operated by vitrectomy, posterior hyaloid and epiretinal membrane removal, and inverted ILM flap. They documented 100% closure of MH at the first week proved by OCT with improved mean snellen visual acuity from 0.09 to 0.41.<sup>19</sup>

In a similar study investigating the same technique for myopic MH with (4 eyes) and without (6 eyes) retinal detachment (RD), the closure rate was 80% and the retina was attached in 3 of the 4 eyes with RD after the first surgery. Postoperative best-corrected visual acuity improved by >2 lines in 5 eyes (50%) was unchanged in 4 eyes (40%) and worsened by >2 lines in 1 eye (10%).<sup>31</sup>

The present study included 12 eyes with large traumatic MH, and although the pathogenesis of traumatic MH seems to be different from that of idiopathic and myopic MH, the results of the present study are very comparable to the results of the previously mentioned 3 studies investigating the same technique in idiopathic and myopic macular holes. This could be explained by the histopathologic studies previously proved that stimulation of glial cell proliferation is the key factor for MH closure.<sup>32</sup> This stimulation is initiated by multiple factors such as tissue necrosis growth factor alpha.<sup>33</sup> Peeled ILM contains Muller cell fragments that activate gliosis especially if left at the site of MH. Also the inverted ILM flap may act as a scaffold for cell proliferation.<sup>18</sup>

This may explain the results by Rubin et al who investigated the role of vitrectomy, fluid-gas exchange, and transforming growth factor-beta-2 for the treatment of traumatic macular holes that may initiate or activate the process of gliosis at the site of macular hole.<sup>5</sup>

In spite the encouraging results, the present study has its own limitations such as the small number of the included eyes, the need for longer duration of follow-up, and the need for a control group of eyes subjected to standard vitrectomy with posterior hyaloid removal alone or adding the standard ILM peeling.

In conclusion, standard vitrectomy with posterior hyaloid removal, inverted ILM flap, and sulfur hexafluoride tamponade is a good surgical option for large traumatic macular hole that led to the 100% closure rate with single surgical intervention documented by SD-OCT at the first postoperative week and remained closed throughout 6 to 9 months of follow-up with improvement of the BCVA of all the included eyes approaching 20/200 or better in 91.7% of cases.

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