Original Article

Evaluation of predictors for anatomical success in macular hole surgery in Indian population

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Purpose: The aim was to evaluate outcomes and predictors for anatomical success in macular hole (MH) surgery. **Materials and Methods:** This was a prospective cohort study of patients operated for idiopathic MH with stages II, III or IV. Patients underwent pars plana vitrectomy with internal limiting membrane (ILM) peeling, internal gas tamponade, and postoperative face down positioning. The primary outcome measure was anatomical closure of MH, while secondary outcome measure was postoperative external limiting membrane (ELM) continuity. Effect of MH size, duration of MH, size of ILM peel, type of gas tamponade (SF6 vs. C3F8) and macular hole index (MHI) on anatomical MH closure was also evaluated. **Results:** Of the 62 eyes operated, anatomical closure of MH was achieved in 55 eyes (88.7%). The median duration of follow-up was 8 months (range: 6–15 months). Mean BVCA improved from 0.94 ± 0.26 at baseline to 0.40 ± 0.23 logMAR at last follow-up (P = 0.01). There was a statistically significant association between size of ILM peel and anatomical closure of MH (P = 0.04). Duration of symptoms, size of MH, type of gas tamponade, MHI had no effect on anatomical closure (P = 0.22, 0.28, 0.40 respectively, Chi-square test). Postoperative continuity of the ELM was significantly associated with a shorter symptom duration (<6 months) before surgery. **Conclusion:** Acceptable anatomical closure could be attained with the defined technique. Size of ILM peel is a new predictor of anatomical success while symptom duration affects postoperative ELM continuity.

Key words: External limiting membrane, macular hole, predictors

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Idiopathic macular holes (MHs) result from tangential and antero-posterior traction on the fovea by prefoveal cortical vitreous.[1,2] Historically, the initial focus in the management of MH is prevention by separation of the posterior cortical vitreous.[3-7] Kelly and Wendel described role of vitrectomy and posterior hyaloid peeling to relieve macular traction and reported an anatomic MH closure rate of 58%.[8] In the last decade, the success rate of MH closure after primary surgery has increased dramatically. Success rates of up to 70% have been recorded after vitrectomy, SF_6 gas tamponade and selective epiretinal membrane (ERM) peeling.[9] MH closure rates of up to 90% have also been reported after aggressive internal limiting membrane (ILM) peeling, and C_3F_8 gas tamponade.[10-18] Previously, predictors of surgical outcomes have been described, which include size and duration of MH, ILM and ERM peeling, type of gas tamponade used and duration of face-down positioning. In the current study, we assessed the outcomes and predictors of MH surgery in cases of idiopathic MH in our practice.

Materials and Methods

A prospective cohort study was conducted at a tertiary care center, between June 2011 and June 2012. The study was approved by the Institutional review board and written informed consent was taken from all the subjects.

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Consecutive patients with idiopathic full thickness MH (stage II and above), with a baseline best-corrected vision acuity (BCVA) >6/60 were included. Exclusion criteria included age-related macular degeneration, diabetic retinopathy, high myopia (>6D), vitrectomized eyes, glaucoma, previous intraocular surgery (except uncomplicated phacoemulsification surgery), traumatic MHs, patients unable to maintain postoperative prone positioning and any systemic contraindication for surgery.

All surgeries were done by a single surgeon (A.K.). Surgeries were performed under peribulbar block with 5 ml of 2% lignocaine hydrochloride and 125 IU hyaluronidase mixed with 5 ml of 0.5% bupivacaine. Standard 23/25-gauge pars plana vitrectomy was conducted using the Constellation vitrectomy system (Alcon Labs Inc., Fort Worth, TX). Core vitrectomy was performed; triamcinolone (Retilone, Cipla, Mumbai, India) assisted posterior vitreous separation was done using the vitrector. ERM, if present, was visualized using triamcinolone and peeled using ILM forceps (D.O.R.C., Zuidland, Netherlands). Brilliant blue G (0.5%) dye assisted ILM peeling was initiated using intravitreal ILM forceps (Grieshaber, Alcon, USA). The area of ILM peeling was approximately measured using optic disc size as a size reference [Fig. 1]. Peel <2 disc diameter (DD) was referred to as partial peel and >2 DD as complete peel. At the time of ILM peeling, precautions were taken to avoid contact with the base of MH to prevent photoreceptor damage. Peripheral vitrectomy was completed, and fluid-air exchange was performed. Eighteen percentperfluoropropane (C_3F_8) or 25% sulfur hexafluoride (SF_6) gas was used as a postoperative tamponade. The choice of gas used was as per patient preference after explaining the advantages and disadvantages of both. Surgery was completed by removal of the entry site alignment cannulas without suturing the conjunctiva and sclera.

Sclerotomy sites were sutured with a single 7–0 vicryl suture after performing a limited peritomy if any leakage was noted. Patients were prescribed strict postoperative face down position for 18 h daily for 3 days. Postoperatively, topical antibiotics, cycloplegics, steroids and oral analgesics were prescribed and gradually tapered.

Duration of MH was assessed on the basis of patient history regarding onset of symptoms and previous records (if any). Preoperative ocular examination included BCVA, lens status evaluation and biomicroscopic examination of fovea and vitreous. Any other anterior or posterior segment abnormalities were noted, and intraocular pressure was recorded. BCVA was measured using a standard wall-mounted Snellen chart with spectacle correction.

Optical coherence tomography (OCT) of the macula (Cirrus HD-OCT, Carl Zeiss Meditec) was done in all eyes to confirm the diagnosis and measure the height and base of the MH. Macular hole index (MHI) was calculated as the ratio of its height and base.[19] The maximum diameter of the ILM peel was noted during each surgery. Patients were followed-up on day 1, day 7, day 14 and monthly thereafter for a minimum duration of 6 months. BCVA, lens status, status of MH and the intraocular pressure were assessed at each follow-up. OCT was repeated after the gas bubble receded from the posterior pole in order to document hole closure and to assess the continuity of the external limiting membrane (ELM).

The primary outcome measure was anatomical closure of the MH. Secondary outcome measure was ELM continuity postoperatively. Predictors for anatomical closure and ELM continuity that were studied included size of the hole (≤400 μm vs. >400 μm); duration of hole (≤6 months vs. >6 months); size of ILM peel (≤2 DD, partial peel vs. >2 DD, complete peel); stage of MH and postoperative gas tamponade used (25% SF_6 vs. 18% C_3F_8). Anatomical closure and ELM continuity were also correlated with functional success (two-line improvements of vision).

Statistical analysis was performed using SPSS advanced statistical software version 17.0 (SPSS Inc., Chicago, IL) for Windows. BCVA was converted to logMAR units for analysis. Qualitative data was expressed as a percentage and quantitative data as mean ± standard deviation. The Student's *t*-test and Fischer's exact test were used to analyze quantitative and categorical data respectively. Odds ratio (OR) with 95% confidence interval (CI) were calculated for each variable. $P \leq 0.05$ was considered as significant.

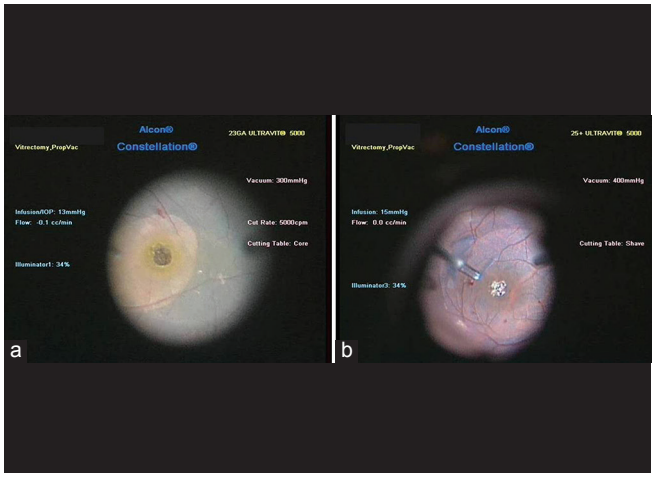

Figure 1: Intraoperative photographs of patient during macular hole surgery with partial (<2 disc diameter [DD]) internal limiting membrane peel (a) and complete (>2 DD) peel (b) Please note that partial peel is eccentric (A) in this case

Results

Sixty-two eyes of 62 patients meeting the inclusion and exclusion criteria were recruited and followed-up for a median duration of 8 months (range: 6–15 months). Mean age of patients was 64.37 ± 8.75 years; 32 eyes (56.6%) were pseudophakic and 30 eyes (48.39%) were phakic. Sixteen eyes (25.8%) had stage II MH, 29 had (46.77%) stage III MH and 17 eyes (27.42%) had stage IV MH.

Anatomical closure of the MH was achieved in 55 eyes (88.7%) after surgery. In these eyes, BVCA improved from 0.94 ± 0.26 logMAR preoperatively to 0.40 ± 0.23 logMAR at last follow-up ($P = 0.01$). None of the patients developed retinal tear or detachment; two patients developed raised intraocular pressure on follow-up, which was managed with a topical antiglaucoma therapy. Twelve phakic eyes (40%) developed cataract or showed progression in nuclear sclerosis during this time, thus eventually required cataract surgery.

Size of peeled ILM was found to be significantly associated with anatomical closure of MH [Table 1]. In 38 eyes (61.30%), ILM peeling of more than 2 DD was achieved during surgery and in the remaining 24 eyes (38.70%), it was partial. Anatomical hole closure was found to be significantly associated with large ILM peel (OR: 6.00,

Table 1: Study predictors for anatomical closure of macular hole

Predictor	Number of eyes (*n*=62) (%)	Closed holes	Open holes	Odds ratio (CI)	*P**
Duration					
>6 months	23 (37.1)	19	4	0.39 (0.08-1.95)	0.40
≤6 months	39 (62.9)	36	3		
Stage					
II	16 (25.8)	15	1	NA	0.38
III	29 (46.77)	24	5		
IV	17 (27.42)	16	1		
Size of hole					
>400 μm	17 (27.42)	16	1	2.46 (0.27-22.13)	0.66
≤400 μm	45 (72.58)	39	6		
MHI					
>0.5	42 (67.74)	38	4	1.67 (0.33-8.32)	0.67
≤0.5	20 (32.26)	17	3		
Size of ILM peel					
>2DD	38 (61.3)	36	2	6.00 (1.09-32.77)	0.04
≤2DD	24 (38.7)	19	5		
Gas tamponade					
18% C3F8	42 (67.7)	38	4	0.33-8.32	0.67
25% SF6	20 (32.3)	17	3		

*P: Fischer exact test. ILM: Internal limiting membrane, CI: Confidence interval, DD: Disk diameter, NA: Not applicable

CI-1.09–32.77, $P = 0.04$). All other evaluated parameters such as duration of MH, size, stage, MHI and type of gas used were not significantly associated with anatomical closure [Table 1].

Continuity of ELM postoperatively was significantly associated with duration of MH [Table 2]. Duration of MH of more than 6 months (23 eyes, 37.1%) had a less chance of ELM continuity than duration < 6 months (39 eyes, 62.9%) (OR: 0.27, CI-0.08–0.88, $P = 0.03$). Other predictors like stage of MH, size, MHI, size of ILM peel and type of gas tamponade had no effect on postoperative ELM continuity [Table 2].

Functional success defined as two-line improvement in Snellen's visual acuity was achieved in all patients in whom anatomical closure was documented. Vision improvement was not seen in eyes where the hole failed to close. In eyes with preexisting ELM continuity, vision gradually improved till 6 months compared with those who had a noncontinuous ELM postoperatively [Fig. 2].

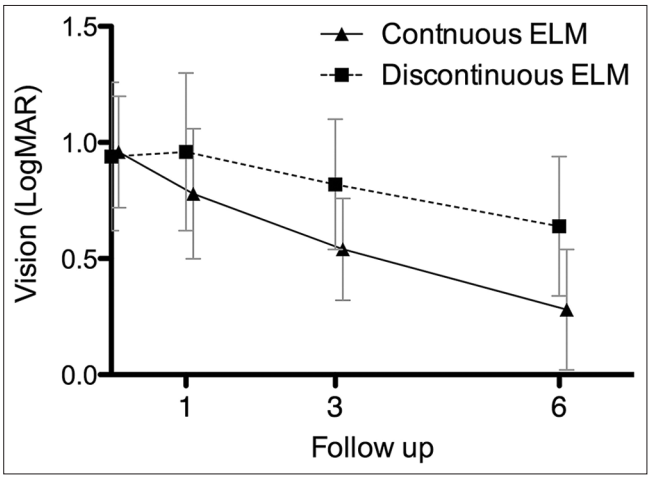

Figure 2: Correlation between postoperative external limiting membrane status and best corrected visual acuity over 6 months of follow-up

Discussion

Modern day MH surgery is associated with good anatomical success with few complications. Previous studies have evaluated predictors for MH closure such as duration and size of MH, MHI, ILM peeling and gas tamponade.[17-20] In this study, we evaluated all known predictors of anatomical hole closure along with ELM continuity in a strictly North Indian population.

We achieved an overall anatomical hole closure in 88.7% of our cases that is comparable to past reports.[10,14,15,17,18] During the last decade, there has been increasing focus towards ILM peeling during surgery for MH. ILM is a basement membrane supporting cellular proliferation of Muller cells. Contraction of the ILM has been the implication in traction, which might act as a contributing factor in the pathogenesis of MH. ILM peeling has been postulated to relieve this traction and aid in the surgical success. Some investigators have also suggested that ILM peeling by virtue of relieving tangential traction may decrease the need for prolonged prone positioning.[20,21] We demonstrated a significant association between anatomic hole closure and the size of ILM peel (>2 DD) in our study. This is a novel observation as the size of ILM peeling as a factor for MH closure has never been described. This result adds to the previous knowledge that greater size of peeled ILM helps relieve tangential traction, helps attain anatomical closure of MH without prolonged postoperative positioning.[20,21]

We are at odds to explain the relation between the size of the ILM peel and a higher MH closure rate. A large ILM peel may prevent reopening of MH since the ILM acts a scaffold for

Table 2: Study predictors for ELM continuity

Study predictor	Number of eyes (*n*=62) (%)	Continuous ELM	Discontinuous ELM	Odds ratio (CI)	*P**
Duration					
>6 months	23 (37.1)	14	9	0.27 (0.08-0.88)	0.03
≤6 months	39 (62.9)	33	6		
Stage					
II	16 (25.8)	14	2	NA	0.13
III	29 (46.77)	23	6		
IV	17 (27.42)	10	7		
Size of hole					
>400 µm	17 (27.42)	10	7	0.30 (0.09-1.05)	0.09
≤400 µm	45 (72.58)	37	8		
MHI					
>0.5	42 (67.74)	35	7	3.33 (0.99-11.16)	0.06
≤0.5	20 (32.26)	12	8		
Size of ILM peel					
>2DD	38 (61.3)	30	8	2.14 (0.65-6.99)	0.23
≤2DD	24 (38.7)	17	7		
Gas tamponade					
18% C3F8	42 (67.7)	31	11	0.70 (0.19-2.57)	0.75
25% SF6	20 (32.3)	16	4		

**P*: Fischer exact test. ILM: Internal limiting membrane, ELM: External limiting membrane, CI: Confidence interval, DD: Disk diameter, NA: Not applicable

the formation of ERM, the contraction of which is implicated in MH formation. However, ERM formation or re-opening of a closed hole was not observed in eyes where partial ILM peeling was performed.

Preoperative documentation of the size of the MH size using OCT provides a prognostic factor for postoperative visual outcome and anatomical success rate of MH surgery. MHI > 0.5 which is a reflection of smaller basal diameter as compared to the vertical height and may be used to predict better anatomical and surgical outcomes after surgery.[19] In our series, however, MHI was not a significant predictor anatomical hole closure.

Intraocular gas tamponade is used for MH surgery as high surface tension and buoyancy of gas aid in hole closure. Intra-ocular gas and postoperative prone positioning between 3 and 7 days is advocated by most authors. A recent study shows that the MH surgery with SF_6 gas achieves similar results with C_2F_6 for MH tamponade and is absorbed faster, thus allowing quicker visual rehabilitation for the patient.[22] Rahman *et al*. also described surgical success in MH without any postoperative positioning.[22] We also found that the type of gas tamponade in our series did not affect the anatomical outcomes; however, we advised postoperative prone positioning even in cases where C_3F_8 tamponade was used.

Newer generation high resolution OCT machines have substantially improved the visualization of foveal microstructure. Recent reports have demonstrated that the postoperative status of the inner segment – outer segment (IS – OS) junction significantly correlates with the visual outcome after MH surgery; any disruption in this layer may be associated with poorer visual outcomes. The ELM appears as another hyper-reflective landmark in the outer retina. Although less prominent, the ELM line is distinctive, located just above the IS – OS junction hyper-reflective line. Photoreceptor cell bodies containing the nuclei and the apical processes of Muller cells are connected by a row of zonular adherents that collectively form the ELM. The integrity of the ELM appears to have a critical role in the restoration of the photoreceptor microstructures.

Several clinicopathological studies of MH repair have suggested that anatomical repair of full-thickness MH requires the proliferation of glial cells, believed to be originated from Muller cells.[23-25] Madreperla *et al*. demonstrated the sealing of a break in the ELM by Muller cell processes in the eye with stage III MH.[26] We postulate that successful reformation of zonular adherents between photoreceptors' ISs and Muller cells, as evidenced by a continuous ELM line on OCT, is critical for the restoration of the photoreceptor layer as well as for a better visual outcome following MH repair. We found significant visual improvement in cases that achieved continuous ELM postoperatively. Though duration and size of MH did not significantly affect anatomical outcome, these had a positive association with postoperative continuity of ELM and thus may indirectly affect visual outcomes in these patients.

Conclusion

Size of ILM peeling modulated anatomical closure of MH, which is a hitherto unknown finding. ELM continuity was found to be good prognostic predictor for final visual outcome. ELM continuity also had an inverse association with duration of visual complaints. Some of the limitations of the study include the inability to monitor the size of peeled internal membrane using OCT. Exact relationship between the size of the peeled membrane and MH closure could be elicited if size documentation is attempted in future. Nevertheless, this series helps justify larger amounts of ILM peeling for the closure of MH as well as advocates earlier surgery for such cases to help preserve continuity of ELM.

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