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Postoperative microstructural re-modelling and functional outcomes in idiopathic full thickness macular hole

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Purpose: To analyze the effect of various macular hole indices and postoperative microstructural changes of all retinal layers on postoperative functional outcomes in patients with idiopathic full-thickness macular hole (FTMH). **Methods:** In this prospective study, pre and post-operative optical coherence tomography (OCT) scans of 36 eyes with idiopathic FTMH were analyzed. Hole indices and microstructural changes of all retinal layers such as ellipsoid zone (EZ), external limiting membrane (ELM) integrity, outer and inner retinal defects, and cystoid resolution were studied on follow-up visits. **Results:** Out of 36 eyes, type-1 closure was achieved in 23 eyes (65.7%) and type-2 closure in 11 eyes (31.42%), one eye showed persistent hole, and one eye was lost to follow-up. The mean minimum diameter of hole ($P = 0.026$), mean MHI ($P = 0.001$), DHI ($P = 0.158$), THI ($P = 0.001$), and HFF ($P < 0.001$) showed statistical significance with the type of hole closure. Postoperatively, eyes with intact ELM and EZ had better BCVA at the final visit. The BCVA was better by logMAR 0.73 ± 0.38 ($P < 0.001$) in patients with absent outer retinal defects. There was a significant difference in BCVA of 0.52 ± 0.35 at 1 month and 0.64 ± 0.34 at 6 months in eyes without inner retinal defects ($P < 0.001$). At 6 months, cystoid resolution was observed in 28 (80%) eyes. BCVA was significantly better at 1 month ($P < 0.001$) and at 6 months ($P = 0.001$) in eyes with no DONFL. **Conclusion:** Macular hole indices determine the closure type. Postoperative regeneration of outer retinal layers and resolution of retinal defects significantly influence the final visual outcomes. ELM recovery is seen as a prerequisite for EZ regeneration with no new IRD after a period of 3 months.

Key words: Full-thickness macular hole, hole indices, microstructural changes, spectral-domain optical coherence tomography, visual acuity

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Idiopathic full-thickness macular hole (FTMH) is an anatomical defect in the neurosensory retina at the macula or fovea caused by the anteroposterior forces by the vitreous and tangential tractional forces caused by the internal limiting membrane (ILM).[1]

The general prevalence of idiopathic macular hole can vary from 0.2 per 1000[2] to 3.3 per 1000 population (Baltimore eye study). An idiopathic macular hole is usually unilateral. Bilateral involvement varies widely from 2% to 28%, though no definitive systemic association has been reported.[3,4] Females are more commonly involved (F:M = 3:1, range: 1.2:1–7:1) in their sixth or seventh decade of life.[5]

ILM peeling during vitrectomy has become a routine surgical procedure for the treatment of idiopathic FTMH, significantly increasing the closure rate with a reduction in recurrence rate.[6,7] Nowadays, with the evolution of newer diagnostic and surgical techniques, successful hole closure rates have increased to 90%.[8]

The usage of noninvasive imaging techniques, such as optical coherence tomography (OCT), has enhanced the detection of many subtle vitreoretinal interface abnormalities, including macular hole.

Various studies have been published describing the role of macular hole measurements and derived indices preoperatively predicting the anatomic closure and visual gain following MH repair surgery.[9,10] However, very few studies are available on simultaneous microstructural analysis of all retinal layers and their remodeling influencing structural and functional outcomes.[11]

The objective of our prospective study is to analyze the effect of various macular hole indices and postoperative microstructural changes of all retinal layers on postoperative functional outcomes in patients with FTMH.

Methods

This prospective analytical study was conducted at the ophthalmology department of a tertiary hospital on 36 eyes of 36 patients from May 2020 to August 2020.

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Inclusion Criteria: Patients with Idiopathic FTMH presented to ophthalmology OPD who underwent surgery.

Exclusion Criteria: Amblyopia, diabetic retinopathy, panretinal photocoagulation, glaucoma, inflammatory eye diseases, myopia, traumatic hole.

This study adhered to the Helsinki Declaration of 1975. Institutional ethics committee clearance was obtained before the start of the study (IEC/394/20).

Written informed consent was obtained after explaining the procedure and associated risk. All patients underwent comprehensive eye examination, including best-corrected visual acuity (BCVA) (logMAR), applanation tonometry, slit-lamp examination, indirect ophthalmoscopy, spectral-domain optical coherence tomography (SD-OCT), and color fundus photography. SD-OCT was done using Optovue, iVue Scanner Depth resolution (in tissue) - 5 μm, FOV 21º(H) × 21º(V) with external image (live IR) FOV–13 mm × 9 mm. On SD-OCT, the minimum diameter/minimum linear distance (MLD), base diameter (BD), height of hole (HH), and nasal and temporal arm lengths were measured using the caliper software tool. The holes with everted edge configuration were also noted (everted edges: as vertical pillars of tissue projecting into the vitreous cavity).

The derived indices were calculated as follows:

1. Macular Hole Index (MHI) = Height/Maximum basal diameter
2. Tractional Hole Index (THI) = Height/Minimum inner hole diameter
3. Diameter Hole Index (DHI) = Minimum inner hole diameter/ Maximum basal diameter
4. Hole Form Factor (HFF) = Nasal arm length + Temporal arm length/Maximum basal diameter.

The Constellation (Alcon) 23-gauge vitrectomy system was used, and three-port pars plana vitrectomy was done. Based on the size of the hole, three different surgical approaches have been used. Conventional ILM peeling was done for holes size of ≤650 μm, free flap technique for size >650–900 μm, and ILM peeling with the inverted-flap technique for hole size >900 μm. Arcade to arcade ILM peeling was done in all cases. Octafluoropropane (C3F8) (14%) was used as tamponade in 31 cases and sulfur hexafluoride (SF6) (20%) in five eyes.

Based on the shape of the inner foveal layers and their tomographic contour, four macular hole closure types have been distinguished: U-shaped with a contour similar to that of the healthy fovea; V-shaped as a steep foveal outline; an irregular type, presenting as a closed hole that cannot be defined either as U or V-shape; and a flat/open closure type with flat borders of the macular hole and bare RPE.

The patients were followed up at 1 week, 1 month, and 3 and 6 months/last follow-up visit post-surgery. Using the follow-up mode on SD-OCT, postoperative scanning was performed at the same levels on 1, 3, and 6 months to assess the following retinal features: 1) outer retinal defects (ORD) as focal foveal detachment (FFD) with the external limiting membrane (ELM) and ellipsoid zone (EZ) integrity; and 2) inner retina defects (IRD) at inner nuclear layer (INL), inner plexiform layer (IPL), ganglion cell layer (GCL), and dissociated optic nerve fiber layer (DONFL). On SD-OCT, DONFL was observed as shallow dimples in the optic nerve fiber layer bundle with the depth of the dimples less than the thickness of the optic nerve fiber layer and inner retinal depressions extending beyond the RNFL as GCL, IPL, and INL defects. Additionally, the number of perifoveal cystoids was also assessed pre and post-operatively.

Statistical Analysis: The Statistical analysis was performed by SPSS 23.0 version.

Results

In this prospective analytical study, we analyzed the demographics, hole indices, type of surgery, detailed anatomical and microstructural changes of all retinal layers, and corresponding visual improvement. The study included 26 females and 10 males (mean age: 68.17 ± 5.31 years) [Table 1].

Functional outcomes

The mean BCVA improved from logMAR 1.47 ± 0.42 before surgery to 1.24 ± 0.44 and 1.21 ± 0.51 at 1 and 6 months, respectively ($P = 0.009$) in 35 eyes [Table 1].

Surgical outcomes

The hole size was small (<250 μm) in three eyes, medium (250–650 μm) in 23 eyes, and large (>650 μm) in 10 eyes. Type 1 closure was achieved in 23 eyes (65.7%), type 2 in 11 eyes (31.42%), one eye showed persistent hole, and one patient was lost to follow-up. One case with persistent hole was re-injected with gas tamponade, achieving successful closure. U-shaped closure was observed in 15 eyes (42.85%), V-shaped in 10 eyes (28.57%), flat closure in nine eyes (25.71%), and an irregular closure in three eyes (8.57%).

Conventional ILM peeling was performed in 23 eyes (16 eyes achieved type 1 closure, and six eyes achieved type-2 closure), ILM peeling with free flap in eight eyes (six eyes achieved type-1 closure, and two eyes achieved type-2 closure), and ILM peeling with inverted flap in five eyes (one eye achieved type-1 closure, and four eyes achieved type-2 closure).

OCT parameters are shown in Table 2. The mean MLD was 539 ± 202.62 μm. Type-1 closure was achieved in cases with mean MLD of 482 ± 173.93 μm, and type-2 with 666.09 ± 216.49 μm ($P = 0.026$).

The overall mean base diameter was 1152.06 ± 245.59 μm. The mean BD of 1089.91 ± 224.76 μm and 1246.73 ± 245.25 achieved type-1 and type-2 closure, respectively.

Table 1: Demographic and visual acuity details

Baseline Variables		*n*=36
Age	Mean±SD	68.17±5.31
Gender		
Males		10 (25.7)
Females		26 (74.3)
Pre-op BCVA (logMAR)	Mean±SD	1.47±0.42
Post-op BCVA (logMAR) at 1 month	Mean±SD	1.24±0.44
Post-op BCVA (logMAR) at 6 months	Mean±SD	1.21±0.51

BCVA –Best-Corrected Visual Acuity

Table 2: Comparison of preoperative parameters between two closure types

Microstructural Analysis		Closure Type 1	Closure Type 2	*P*
Min Diameter	Mean±SD	482.91±173.93	666.09±216.49	**0.026**
Base Diameter		1089.91±224.76	1246.73±245.25	0.09
Height		433.61±61.61	368.18±93.52	0.053
MHI		0.41±0.11	0.29±0.08	**0.001**
HFF		0.82±0.18	0.59±0.12	**<0.001**
THI		1.02±0.4	0.6±0.25	**0.001**
DHI		0.8±0.39	0.65±0.23	0.158
Hole Sizes		482.91±173.93	666.09±216.49	**0.026**

MHI- Macular Hole Index, HFF- Hole Form Factor, THI- Tractional Hole Index, DHI- Diameter Hole Index; values shown in bold are statistically significant

Table 3: Comparison of Post-operative anatomical parameters at 1 month versus 6 months

Microstructural changes OCT Analysis			1 month	6 months	*P*
DONFL	Present	Number (Percentage)	17 (48.6)	18 (51.4)	1
	Absent		18 (51.4)	17 (48.6)	
FFD	Present		35 (100)	3 (8.6)	<0.001
	Absent		0 (0)	32 (91.4)	
INL, IPL, GCL defects	Present		17 (48.6)	19 (54.3)	0.687
	Absent		18 (51.4)	16 (45.7)	
ELM Regeneration	Intact		17 (48.6)	28 (80)	0.001
	Not Intact		18 (51.4)	7 (20)	
EZ Regeneration	Intact		7 (20)	23 (65.7)	<0.001
	Not Intact		28 (80)	12 (34.3)	

DONFL-Dissociated Optic Nerve Fibre Layer, INL-inner nuclear layer, IPL- inner plexiform layer (IPL), GCL- ganglion cell layer, FFD- focal foveal detachment, ELM-External Limiting Membrane, EZ-Ellipsoid Zone

Table 4: Comparison of postoperative functional outcomes at 1 month versus 6 months

Microstructural Changes analyzed	Follow-up visits at	Absent		Present		*P* between the groups
		BCVA Mean±SD	*P* within the group	BCVA Mean±SD	*P* within the group	
ELM (Disruption)	1 month	0.87±0.19	NA	1.52±0.53	NA	0.002
	6 months	0.87±0.18	1	1.43±0.49	0.331	<0.001
EZ (Disruption)	1 month	0.95±0.13	NA	1.43±0.49	NA	0.001
	6 months	0.84±0.19	0.034	1.37±0.59	0.512	<0.001
FFD	1 month	1.2±0.43	NA	1.6±0.53	NA	0.346
	6 months	1.14±0.49	0.031	1.87±0.11	0.423	<0.001
INL, IPL and GCL defects	1 month	0.96±0.13	NA	1.48±0.48	NA	<0.001
	6 months	0.87±0.18	0.035	1.51±0.52	0.576	<0.001
DONFL	1 month	0.99±0.29	NA	1.51±0.45	NA	<0.001
	6 months	0.94±0.33	0.068	1.39±0.62	0.393	0.001

DONFL- Dissociated Optic Nerve Fibre Layer, INL- Inner Nuclear Layer, IPL- Inner Plexiform Layer, GCL- Ganglion Cell Layer, FFD- Focal Foveal Detachment, ELM- External Limiting Membrane, EZ- Ellipsoid Zone

The mean macular hole height was 416.46 ± 80.81 μm. The mean HH of 433.61 ± 61.61 μm showed type-1 closure, and the mean HH of 368.18 ± 93.52 μm showed type-2 closure.

The derived macular hole indices were as follows:

1. Mean MHI was 0.37 ± 0.11; the mean MHI for type-1 and type-2 closures was 0.41 ± 0.11 and 0.29 ± 0.08, respectively (P = 0.001).
2. Mean HFF was 0.75 ± 0.19; the mean HFF for type-1 and type-2 closures was 0.82 ± 0.18 and 0.59 ± 0.12, respectively ($P \leq 0.001$).
3. Mean THI was 0.89 ± 0.41; the mean THI for type-1 and type-2 closures was 1.02 ± 0.4 and 0.6 ± 0.25, respectively (P = 0.001).
4. Mean DHI was 0.76 ± 0.35. Macular holes with DHI of 0.8 ± 0.39 achieved type-1 closure, and DHI of 0.65 ± 0.23 achieved type-2 closure (P = 0.158).

Overall, MLD, MHI, THI, and HFF showed statistical significance with respect to the type of hole closure.

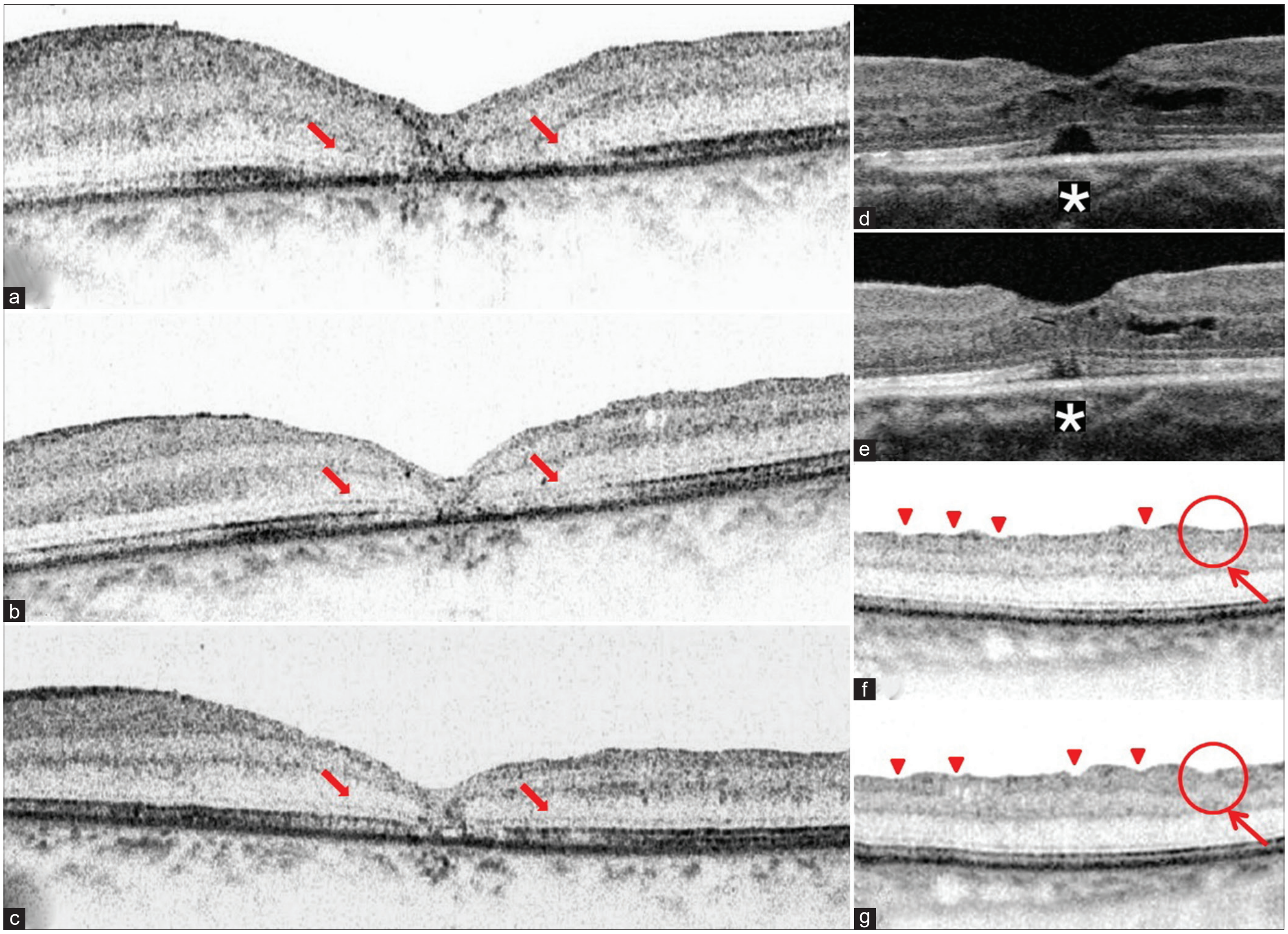

Figure 1: Postoperative SD-OCT showing (a-c) disrupted ELM and EZ at 1 month with subsequent regeneration at 3 and 6 months (red arrows), (d and e) FFD at 1 month with significant resolution at 3 months (white asterisk), (f and g) multiple dimples due to DONFL (red arrowheads) and INL, IPL, and GCL defects (red circle with arrow) at 1 and 6 months

Postoperative anatomical and functional outcomes

FTMH with everted edges (73.91%) showed type-1 closure. Resolution of cystoid spaces post-surgery at 6 months was observed in 28 (80%) eyes with residual cystic cavities in seven eyes. In 18 eyes with ≤10 cystoids, 13 eyes had type-1 and five eyes had type-2 closure, and in 10 eyes with >10 cystoids, six eyes had type-1 and four eyes had type-2 closure.

Visual acuity and ELM-EZ integrity outcomes

The ELM was restored in 48.6% (18 eyes) at 1 month and in 80% (20 eyes) at 3 and 6 months ($P = 0.001$). Pre-op BCVA of 1.47 ± 0.42 improved to 0.87 ± 0.18 at 1 and 6 months in 20 eyes with an intact ELM compared to 1.52 ± 0.52 at 1 month in 17 eyes and 1.43 ± 0.49 at 6 months in 15 eyes with disrupted ELM. Eyes with intact ELM had better BCVA at 1 and 6 months compared to eyes with disrupted ELM ($P = 0.002$ and $P < 0.001$, respectively).

EZ regeneration was noted in 20% (7 eyes) at 1 month ($P = 0.001$) and in 65.7% (23 eyes) at 3 and 6 months ($P < 0.001$). BCVA improved to logMAR 0.95 ± 0.13 and 0.84 ± 0.19 at 1 month (7 eyes) and at 6 months (23 eyes) ($P = 0.034$) with continuous EZ. BCVA with disrupted EZ was logMAR 1.43 ± 0.49 at 1 month (28 eyes) and 1.37 ± 0.59 at 6 months (15 eyes). Whenever the EZ was regenerated, simultaneous ELM recovery was observed.

FFD was noted in 100% (35 eyes) at 1 month, 34.3% (12 eyes) at 3 months, and 8.6% (3 eyes) at 6 months ($P < 0.001$). BCVA of logMAR 1.6 ± 0.43 at 1 month improved to 1.14 ± 0.43 in 32 eyes with resolution of defects at 6 months. The BCVA was better by log MAR 0.46 ± 0.43 ($P \leq 0.001$) in patients with resolution of defects.

INL, IPL, and GCL defects were noted in 48.6% (17 eyes) at 1 month, 51.4% (18 eyes) at 3 months, and 54.3% (19 eyes) at 6 months. In the absence of defects, the mean BCVA was logMAR 0.96 ± 0.13 at 1 month (18 eyes) and 0.87 ± 0.18 at 6 months (16 eyes) ($P = 0.035$), whereas in the presence of defects, the BCVA was 1.48 ± 0.48 (17 eyes) and 1.51 ± 0.52 (19 eyes) at 1 and 6 months, respectively. There was a significant difference in BCVA in eyes with and without these defects at 1 and 6 months.

DONFL was noted in 48.6% (17 eyes) at 1 month and in 51.4% (18 eyes) at 3 and 6 months. In eyes with DONFL the mean BCVA was 1.51 ± 0.45 at 1 month and 1.39 ± 0.62 at 6 months. BCVA without DONFL was 0.99 ± 0.29 at 1 month (18 eyes) and 0.94 ± 0.33 at 6 months (17 eyes). BCVA was significantly better at 1 month ($P \leq 0.001$) and 6 months ($P = 0.001$) in eyes without

DONFL. Above mentioned all microstructural anatomical and functional outcomes are summarized in Tables 3 and 4.

Discussion

The detailed analysis of various hole indices and microstructural changes with more accuracy is possible due to advanced SD-OCT scanning quality. Multiple studies in the past have published various macular hole parameters and indices as functional outcome predictors.

This prospective study highlights the detailed evaluation of hole indices along with microstructural changes of all retinal layers simultaneously influencing the postoperative functional outcomes.

We analyzed 36 eyes of 36 patients, the mean age being 68.14 ± 5.31 years (74.3% females and 27.7% males). The studies conducted by Kaźmierczak *et al*.[12] and Venkatesh *et al*.[13] on 40 and 47 eyes found the mean age to be 68.75 ± 6.05 and 62.5 ± 7.3 years, respectively.

In our study, hole closure was achieved in 34 eyes (97.14%): type-1 in 23 eyes (67.64%) and type-2 in 11 eyes (32.35%), and 67.64% with type-1 closure had everted edges preoperatively. Anatomically successful MH closure was noted in 58 eyes (85.29%) by Michalewska *et al*.[14] and in 42 eyes (95.45%) in a study done by Kaźmierczak *et al*.,[12] comparable with our patients.

In a study conducted by Chhablani J *et al*.,[15] the mean MLD was 559.5 ± 201.9 μm, demonstrating that the minimum diameter between the edges significantly correlates with the type of closure with a predicted probability of type-1 closure being 100% in holes with a minimum diameter of <300 μm with a drop to <20% if the minimum diameter is >1000 μm. Similarly, in our study, the mean MLD was 539 ± 202.62. Type-1 closure was achieved with a mean MLD of 482 ± 173.93 μm and type-2 with a mean MLD of 666.09 ± 216.49 μm (P = 0.026). Similar studies done by Ch'ng *et al*.[16] and Gupta *et al*.[17] also reported MLD to be a significant preoperative factor.

In the current study, macular holes with a mean BD of 1089.91 (SD = 224.76 μm) and 1246.73 μm (SD = 245.25) showed type-1 and type-2 closures, respectively. The mean height of the macular holes for type-1 and type-2 was 433.61 ± 61.61 and 368.18 ± 93.52 μm, respectively (P = 0.053). In a retrospective study done by Demir *et al*.[18] on 183 patients, BD was 924.72 ± 341.58 μm (range: 118–2148) in eyes observed to have type-1 closure and 1153.58 ± 399.86 μm (range: 401–2303) with type-2 closure (P = 0.04), and hole height was noted to be 464.5 ± 92.86 μm in type-1 closure and 506.67 ± 196.27 μm in type-2 closure (P = 0.239).

In our study, the mean MHI was 0.37 ± 0.11 (type-1 closure: 0.41 ± 0.11, type-2 closure: 0.29 ± 0.08), (P = 0.001). Wakely *et al*.,[19] in a study on 50 eyes, noted a mean MHI of 0.673 (SD: 0.336, P = 0.011), which was significantly associated with anatomical success.

The mean THI was 0.89 ± 0.41 in the present study (type-1 closure: 1.02 ± 0.4, type-2 closure: 0.6 ± 0.25). This derived index was found to be statistically significant between the two groups (P = 0.001), similar to a study done by Venkatesh *et al*.[13]

The mean HFF was found to be 0.75 ± 0.19 in our study (type-1 closure: 0.82 ± 0.18, type-2 closure: 0.59 ± 0.12) (P ≤ 0.001), which was comparable to the mean HFF of 0.7 ± 0.2 noted in the study by Chhablani J *et al*.[15] Ullrich *et al*.[20] on a study on 94 eyes found that macular holes with HFF > 0.9 closed following one surgical procedure, whereas in the case of HFF ≤ 0.5, the anatomical success rate after one operation was 67%.

The mean DHI in our study was 0.76 ± 0.35 (type-1 closure: 0.8 ± 0.39, type-2 closure: 0.65 ± 0.2) (P = 0.158). Similarly, a study on 46 eyes by Ruiz-Moreno *et al*.[10] showed DHI being not a significant predictive factor. Qi *et al*.[21] in their study on 101 patients with stage-3 and stage-4 holes found HDR (P = 0.01) to be significantly different in the two groups (hole closed and un-closed), influencing closure rate with larger holes.

Based on the size of the macular hole, we performed three different surgical techniques: conventional ILM peeling for holes size ≤650 μm in 22 eyes [16 eyes (69.6%) had type-1 and six eyes (45.5%) had type-2 closure], ILM peeling with free flap for holes size >650–900 μm in eight eyes [six eyes (26.1%) achieved type-1 and two eyes (18.2%) achieved type-2 closure], and ILM peeling with inverted flap in five eyes for hole size >900 μm [one (4.3%) had type-1 closure and four (36.4%) had type-2 closure]. Velez-Montoya *et al*.[22] showed no difference in anatomical closure rates by conventional ILM peeling (91.67%), inverted-flap (91.67%), and free-flap techniques (85.71%), but this may have been due to randomization into three groups without considering the hole size in their study.

Considering the perifoveal number of cystoids, an observation was made that the macular holes with a higher number of intra-retinal cysts showed type-1 closure. This was supported by a study done by Venkatesh *et al*.[13] in which a higher macular hole cystoid space area (MCSA) index was considered as a predictor of type 1 closure, that is, the more the cystic space, the higher the chance of better anatomical outcomes. The study hypothesized that the presence of retinal cysts is indicative of greater anteroposterior tractional forces and taller macular holes.

Along with the abovementioned indices, the postoperative integrity of all retinal layers also plays a significant role in predicting functional outcomes. ELM represents junctional complexes between muller cells and rod–cone photoreceptor cells thus its presence is essential throughout the affected area for the regeneration of the photoreceptor outer segment.[23] We found ELM to be continuous in 48.6% (17 eyes) at 1 month and in 80% (28 eyes) at 3 and 6 months (P = 0.001). Bottoni *et al*.[23] in their study found intact ELM in 53% of patients at 1 month and 79% at 3 months in 19 eyes post-operatively. Improvement in visual acuity was evident when comparing BCVA at 1 month (P = 0.002) and 6 months (P ≤ 0.001) with intact versus disrupted ELM in our study. We also observed that eyes with EZ regeneration had intact ELM, which was consistent with the findings of Wakabayashi *et al*.[24] [Fig. 1: a-c].

The mean BCVA improved significantly in eyes with intact EZ in comparison to disrupted EZ at 1 month (P = 0.001) and 6 months (P ≤ 0.001) in our study. EZ regenerated in 20% at 1 month and in 65.7% at 3 and 6 months (P < 0.001) postoperatively. BCVA improved to logMAR 0.95 ± 0.13 and 0.84 ± 0.19 at 1 month (7 eyes) and at 6 months (23 eyes) (P = 0.034). BCVA in 28 eyes with disrupted EZ was logMAR 1.43 ± 0.49 at 1 month and 1.37 ± 0.59 6 months in 15 eyes. Shimozono *et al*.[25] and Baba *et al*.[26] demonstrated EZ integrity correlated well with BCVA. Similar to the eyes in our study, Inoue *et al*. showed mean BCVA (logMAR) improvement from 0.67 ± 0.25 to 0.16 ± 0.22 postoperatively ($P < 0.001$) in eyes with intact EZ.[27]

Growth of Muller cells and astrocytes into the hole to fill in the photoreceptor cell layer follows the re-approximation of the edges of the hole to RPE.[28,29] There is a possibility for anterior shift of tissue creating a space between migrating glial and photoreceptor cells from the RPE in the central area forming focal foveal detachment, EZ disruption, or both (ORD).[30] In our study, eyes with the absence of FFD had better BCVA at 6 months ($P \leq 0.001$) while 8.5% of eyes ($P \leq 0.001$) showed FFD at 6 months with compromised BCVA postoperatively [Fig. 1:d and e]. Chawla *et al*.[31] noted a median BCVA gain of logMAR 0.5 (range: logMAR 0.2–1) from 4 months to 6 months postoperatively. Itoh Y *et al*.[32] showed mean BCVA improvement from logMAR 0.56 to 0.11 at the last follow-up visit with resolution of ORD.

In our study, INL, IPL, and GCL defects seen in 54.3% at 6 months. BCVA without defects was 0.87 ± 0.18 ($P > 0.035$) and with defects was 1.51 ± 0.52 ($P = 0.393$) ($P < 0.001$ between the two groups). Similarly, Nukada *et al*. also found IRD in 80.6% of the eyes; an improvement in BCVA (logMAR 0.2 to 1) was noted at 6 months after surgery with resolution of IRD.[33]

Tadayoni *et al*.[34] showed DONFL appearance as numerous slightly dark arcuate striae following ILM peeling within the posterior pole. Mitamura *et al*.[35] reported that DONFL was created as shallow dimples on OCT in the optic nerve fiber layer bundle. Ito *et al*. hypothesized that DONFL may be a spontaneous and delayed morphologic change, whereas some other studies identified that these changes are related to tractional forces from membrane peeling and direct instrument-tissue interaction and toxicity of ICG dye used for ILM staining.[36-38]

In our study, 48.6% (17 eyes) at 1 month and 51.4% (18 eyes) at 3 and 6 months had DONFL, demonstrating that no new patients developed DONFL after 3 months [Fig. 1:f and g]. The mean BCVA of eyes with DONFL was 1.51 ± 0.45 at 1 month and 1.39 ± 0.62 at 6 months. Similarly, Ito *et al*.[38] found DONFL only in 54% (36 of 67 eyes) of the ILM-peeled eyes at 1 and 3 months, with improvement in BCVA from logMAR0.46 ± 0.25 to 0.39 ± 0.27 at 6 months; however, according to previous studies, no significant difference was found in visual acuity, microperimetry results, and macular sensitivity on Humphrey (10-2) visual field testing in cases with or without DONFL.[39,40]

The limitation of our study was the smaller sample size.

Conclusion

In summary, various hole indices determine the closure type, postoperative regeneration of outer retinal layers, and resolution of retinal defects, significantly influencing the final visual outcomes. Additionally, we found the effect of duration on intraretinal remodeling wherein we noted immediate postoperative ELM recovery as the prerequisite for EZ regeneration, and no new IRD were seen after a period of 3 months. However, future longitudinal studies with a larger sample size are needed to corroborate this observation.

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Conflicts of interest

There are no conflicts of interest.

References

1. Gass JD. Idiopathic senile macular hole. Its early stages and pathogenesis. Arch Ophthalmol 1988;106:629-39.
2. McCannel CA, Ensminger JL, Diehl NN, Hodge DN. Population-based incidence of macular holes. Ophthalmology 2009;116:1366-9.
3. Lewis ML, Cohen SM, Smiddy WE, Gass JD. Bilaterality of idiopathic macular holes. Graefes Arch Clin Exp Ophthalmol 1996;234:241-5.
4. Trempe CL, Weiter JJ, Furukawa H. Fellow eyes in cases of macular hole. Biomicroscopic study of the vitreous. Arch Ophthalmol 1986;104:93-5.
5. la Cour M, Friis J. Macular holes: Classification, epidemiology, natural history and treatment. Acta Ophthalmol Scand 2002;80:579-87.
6. Christensen UC, Krøyer K, Sander B, Larsen M, Henning V, Villumsen J, *et al.* Value of internal limiting membrane peeling in surgery for idiopathic macular hole stage 2 and 3: A randomised clinical trial. Br J Ophthalmol 2009;93:1005-15.
7. Lois N, Burr J, Norrie J, Vale L, Cook J, McDonald A, *et al.* Internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole: A pragmatic randomized controlled trial. Invest Ophthalmol Vis Sci 2011;52:1586-92.
8. Chin EK, Almeida DR, Sohn EH. Structural and functional changes after macular hole surgery: A review. Int Ophthalmol Clin 2014;54:17-27.
9. Kusuhara S, TeraokaEscaño MF, Fujii S, Nakanishi Y, Tamura Y, Nagai A, *et al*. Prediction of postoperative visual outcome based on hole configuration by optical coherence tomography in eyes with idiopathic macular holes. Am J Ophthalmol 2004;138:709-16.
10. Ruiz-Moreno JM, Staicu C, Piñero DP, Montero J, Lugo F, Amat P. Optical coherence tomography predictive factors for macular hole surgery outcome. Br J Ophthalmol 2008;92:640-4.
11. Lee MW, Kim TY, Song YY, Baek SK, Lee YH. Changes in each retinal layer and ellipsoid zone recovery after full-thickness macular hole surgery. Sci Rep 2021;11:11351. doi: 10.1038/s41598-021-90955-4.
12. Kaźmierczak K, Stafiej J, Stachura J, Żuchowski P, Malukiewicz G. Long-term anatomic and functional outcomes after macular hole surgery. J Ophthalmol 2018;2018:3082194.
13. Venkatesh R, Mohan A, Sinha S, Aseem A, Yadav NK. Newer indices for predicting macular hole closure in idiopathic macular holes: A retrospective, comparative study. Indian J Ophthalmol 2019;67:1857-62.
14. Michalewska Z, Michalewski J, Cisiecki S, Adelman R, Nawrocki J. Correlation between foveal structure and visual outcome following macular hole surgery: A spectral optical coherence tomography study. Graefes Arch Clin Exp Ophthalmol 2008;246:823-30.
15. Chhablani J, Khodani M, Hussein A, Bondalapati S, Rao HB, Narayanan R, *et al.* Role of macular hole angle in macular hole closure. Br J Ophthalmol 2015;99:1634-8.
16. Ch'ng SW, Patton N, Ahmed M, Ivanova T, Baumann C, Charles S, *et al.* The Manchester large macular hole study: Is it time to reclassify large macular holes? Am J Ophthalmol 2018;195:36-42.
17. Gupta B, Laidlaw DA, Williamson TH, Shah SP, Wong R, Wren S. Predicting visual success in macular hole surgery. Br J Ophthalmol 2009;93:1488-91.
18. Gümüş G, Demir G, Tülü Aygün B, Demircan A, Alkın Z, Öztornacı O. Prognostic factors affecting macular hole closure

types. Ther Adv Ophthalmol 2021;13:25158414211009007. doi: 10.1177/25158414211009007.

19. Wakely L, Rahman R, Stephenson J. A comparison of several methods of macular hole measurement using optical coherence tomography, and their value in predicting anatomical and visual outcomes. Br J Ophthalmol 2012 Jul; 96:1003-7.
20. Ullrich S, Haritoglou C, Gass C, Schaumberger M, Ulbig MW, Kampik A. Macular hole size as a prognostic factor in macular hole surgery. Br J Ophthalmol 2002;86:390-3.
21. Qi Y, Yu Y, You Q, Wang Z, Wang J, Liu W. Hole diameter ratio for prediction of anatomical outcomes in stage III or IV idiopathic macular holes. BMC Ophthalmol 2020;20:351.
22. Velez-Montoya R, Ramirez-Estudillo JA, Sjoholm-Gomez de Liano C, Bejar-Cornejo F, Sanchez-Ramos J, Guerrero-Naranjo JL, *et al.* Inverted ILM flap, free ILM flap and conventional ILM peeling for large macular holes. Int J Retina Vitreous 2018;4:8.
23. Bottoni F, De Angelis S, Luccarelli S, Cigada M, Staurenghi G. The dynamic healing process of idiopathic macular holes after surgical repair: A spectral-domain optical coherence tomography study. Invest Ophthalmol Vis Sci 2011;52:4439-46.
24. Wakabayashi T, Oshima Y, Fujimoto H, Murakami Y, Sakaguchi H, Kusaka S, *et al.* Foveal microstructure and visual acuity after retinal detachment repair: Imaging analysis by Fourier-domain optical coherence tomography. Ophthalmology 2009;116:519-28.
25. Shimozono M, Oishi A, Hata M, Kurimoto Y. Restoration of the photoreceptor outer segment and visual outcomes after macular hole closure: Spectral-domain optical coherence tomography analysis. Graefes Arch Clin Exp Ophthalmol 2011;249:1469-76.
26. Baba T, Yamamoto S, Arai M, Arai E, Sugawara T, Mitamura Y, *et al.* Correlation of visual recovery and presence of photoreceptor inner/outer segment junction in optical coherence images after successful macular hole repair. Retina 2008;28:453-8.
27. Inoue M, Watanabe Y, Arakawa A, Sato S, Kobayashi S, Kadonosono K. Spectral-domain optical coherence tomography images of inner/outer segment junctions and macular hole surgery outcomes. Graefes Arch Clin Exp Ophthalmol 2009;247:325-30.
28. Moshfeghi AA, Flynn HW Jr, Elner SG, Puliafito CA, Gass JD. Persistent outer retinal defect after successful macular hole repair. Am J Ophthalmol 2005;139:183-4.
29. Ip MS, Baker BJ, Duker JS, Reichel E, Baumal CR, Gangnon R, *et al.* Anatomical outcomes of surgery for idiopathic macular hole as determined by optical coherence tomography. Arch Ophthalmol 2002;120:29-35.
30. Mehrdad M, Akshay ST, Justin W, Steven TB, Dongseok C, Christina JF. Long term follow-up of persistent outer retinal defects following macular hole surgery. JOJ Ophthalmol 2017;3:555608.
31. Chawla A, Barua A, Patton N. Long-term structural and functional outcomes after macular hole surgery. Retina 2016;36:321-4.
32. Itoh Y, Inoue M, Rii T, Hiraoka T, Hirakata A. Correlation between length of foveal cone outer segment tips line defect and visual acuity after macular hole closure. Ophthalmology 2012;119:1438-46.
33. Nukada K, Hangai M, Ooto S, Yoshikawa M, Yoshimura N. Tomographic features of macula after successful macular hole surgery. Invest Ophthalmol Vis Sci 2013;54:2417-28.
34. Tadayoni R, Paques M, Massin P, Mouki-Benani S, Mikol J, Gaudric A. Dissociated optic nerve fiber layer appearance of the fundus after idiopathic epiretinal membrane removal. Ophthalmology 2001;108:2279-83.
35. Mitamura Y, Suzuki T, Kinoshita T, Miyano N, Tashimo A, Ohtsuka K. Optical coherence tomographic findings of dissociated optic nerve fiber layer appearance. Am J Ophthalmol 2004;137:1155-6.
36. Ehlers JP, Dupps WJ, Kaiser PK, Goshe J, Singh RP, Petkovsek D, *et al.* The prospective intraoperative and perioperative ophthalmic ImagiNg with optical CoherEncE TomogRaphy (PIONEER) study: 2-year results. Am J Ophthalmol 2014;158:999-1007.
37. Iriyama A, Uchida S, Yanagi Y, Tamaki Y, Inoue Y, Matsuura K, *et al.* Effects of indocyanine green on retinal ganglion cells. Invest Ophthalmol Vis Sci 2004;45:943-7.
38. Ito Y, Terasaki H, Takahashi A, Yamakoshi T, Kondo M, Nakamura M. Dissociated optic nerve fiber layer appearance after internal limiting membrane peeling for idiopathic macular holes. Ophthalmology 2005;112:1415-20.
39. Mitamura Y, Ohtsuka K. Relationship of dissociated optic nerve fiber layer appearance to internal limiting membrane peeling. Ophthalmology 2005;112:1766–70.
40. Imai H, Ohta K. Microperimetric determination of retinal sensitivity in areas of dissociated optic nerve fiber layer following internallimiting membrane peeling. Jpn J Ophthalmol 2010;54:435–40.