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INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE IN THE MANAGEMENT OF PRIMARY LARGE MACULAR HOLE IN JEC PRIMASANA HOSPITAL: ANATOMIC AND VISUAL OUTCOME

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ABSTRACT

This descriptive study aimed to investigate the effectiveness of the internal limiting membrane (ILM) flap technique in treating primary large macular holes (MHs) in patients at JEC Primasana. A total of 24 patients with large MH (>400 um diameter) were included in this study. Patient demographics, including gender, age, laterality, tamponade used, lens status, macular hole index (MHI) and BCVA (logMAR) were recorded. Changes in visual acuity before and after treatment were assessed using the Wilcoxon test. Differences in MHI by closure type were analyzed using the Mann-Whitney test. The correlation between MHI and postoperative visual acuity was evaluated using Spearman's rank correlation. The main outcome measures were the anatomical MH closure and final BCVA (logMAR). This study found that the ILM flap technique resulted in significant improvements in anatomy and visual acuity post-treatment. A total of 19 patients (79.2%) had MH closure and a mean improvement in BCVA (logMAR) of 1.02±0.63. The correlation between MHI and postoperative visual acuity in the closure group was positive, the higher the MHI, the better the BCVA. The ILM flap technique showed fairly good effectiveness in improving functional and anatomical outcomes in patients with large MH at JEC Primasana.

Keywords: Large Macular Hole, Macular Hole Index, Internal Limiting Membrane Flap

INTRODUCTION

Macular hole (MHs) is a condition in which an anatomic opening or dehiscence develops in the fovea. The precise pathogenesis of macular hole formation remains controversial, but it probably involves tangential and/or anteroposterior vitreo-foveal traction.[1] A full-thickness macular hole (FTMH) is a sight-threatening condition which is defined as a retinal defect arising from the internal limiting membrane (ILM) extending up to the retinal pigment epithelium (RPE).[2]

According to the cause of the disease, it is divided into primary and secondary MHs. Primary MHs refers to macular hole without other induced eye diseases and the cause is unclear. Secondary MHs occur after ocular trauma, high myopia and so on.[3] Idiopathic MHs is one of the common forms of macular hole. Occurs in the macular area of a healthy eye, usually in the patients over 50 years old and cause marked reduction in vision.[4] MHs result in central vision loss, metamorphopsia and a central scotoma.[5]

The International Vitreomacular Traction Study (IVTS) classification (2013) is based on OCT appearance. It considers size (horizontal diameter at narrowest point) and status of the vitreomacular interface. Full-thickness MHs are categorized by size as small (≤250 μm), medium (>250 μm to ≤400 μm) or large (>400 μm). They are further characterized by vitreous status (with or without vitreomacular traction) and by cause (primary or secondary). Full- thickness

macular hole is primary if caused by vitreous traction, and secondary if the macular hole is caused by pathologic characteristics other than vitreomacular traction.[3]

Management of MH depends on the etiology, the size of the hole, and, in the case of trauma, the presence of associated ocular complications such as vitreous hemorrhage, choroidal ruptures, and commotio retinae. The decision was made to perform surgery because of the large size of the hole.[3]

It is widely used in the measurement and assessment of MHs characteristics like Macular Hole Index (MHI), facilitating treatment, decision-making and the expected surgical outcome. Preoperative horizontal measurements of macular hole may help to determine postoperative visual expectations and anatomical success, and predict the possibility of reopening.

The MHI that can reflect the prognosis of the surgery and its visual outcome has been gaining popularity among the publications on the macular hole and it's now been used as a useful predictor for the physiological outcome of MHs. MHI is a good predictive factor for FTMH surgery outcome 9Figure 1).[6]

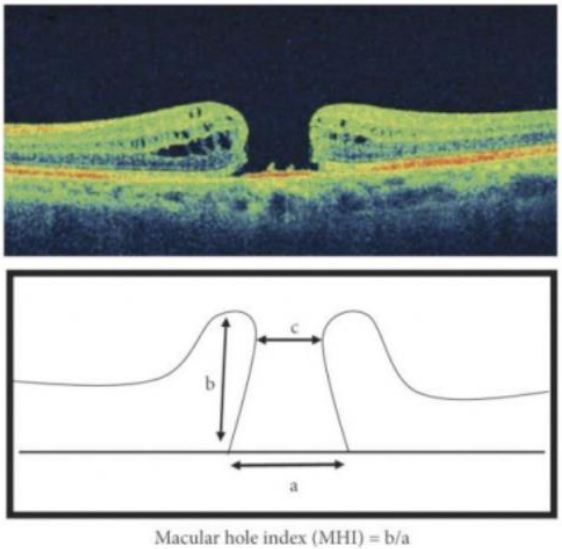


Figure 1: The macular hole index (MHI) [18]. Top: optical co- herence tomography (OCT) cross-sectional image of a macular hole.

Bottom diagram showing the base diameter of the hole (a), hole height (b), and minimum diameter of the hole (c), as measured by OCT. The MHI is defined as b/a.[7]

Vitrectomy combined with internal limiting membrane (ILM) peeling is popular for the treatment of macular hole (MHs). However, the improvements of MH closure rate and postoperative visual acuity are not satisfactory especially in large and refractory MHs. Currently, the ILM flap technique has gradually been applied for the treatment of MH and achieved high MH closure rate.[3]

Michalewska et al. were the first to describe a technique for the treatment of idiopathic large MHs by creating an inverted ILM flap in 2010. In this method, the ILM is not completely removed from the retina but is left attached to the edges of the MH, and then inverted to cover the macular hole. Using this technique, the authors reported that the large MH closure rate was improved to 98% compared with 88% with the conventional ILM peeling and resulted in a better functional outcome.[8]

The ILM flap technique has many variations, including the difference of the size, shape, number, and manner in which the flaps put on the MHs. The ILM flap technique also has some auxiliary means including perfluoro-n-octane (PFO), dye, autologous blood and adhesive viscoelastics. There is controversy about the effects between several technique variations of ILM flap, and it needs to be explored in the future.[4]

The aim of this study is to report anatomic and visual outcome after ILM flap in patient with primary large macular hole.

METHODS

In this study, we retrospectively reviewed the medical records of all patients diagnosed with primary MH at JEC Primasana Eye Hospital, Jakarta, Indonesia between January 2022 and

January 2023. Inclusion criteria were primary MH patients with a baseline diameter of >400um treated with pars plana vitrectomy (PPV) with ILM flap technique. Exclusion criteria were concomitant ocular pathology such as retinal vascular disease (e.g. diabetic retinopathy, retinal vascular occlusion), age-related macular degeneration, glaucoma, previous history of retinal surgery, history of trauma, uveitis, high myopia (history of refractive error greater than -6.00 diopters), or macular detachment, macular hole treated with ILM peeling technique.Patients were examined at baseline and 6 months after surgery. Before surgery, each patient underwent a comprehensive ophthalmologic examination including best- corrected visual acuity (BCVA) assessment, slit-lamp biomicroscopy, intraocular pressure (IOP) measurement, spectral domain structural OCT analysis with MH index measurement calculated using Image J. At follow-up, patients underwent a complete ophthalmologic examination including BCVA Snellen assessment and OCT analysis. We divided the surgeons into two groups. Senior surgeons were categorized if they held a consultant degree and had more than 5 years of service as a vitreoretinal surgeon. Final BCVA was categorized as improved if there was any improvement in BCVA
(logMAR) from before the ILM procedure. It was categorized as decreased if there was a decrease in BCVA (logMAR) after the procedure. Descriptive statistics were calculated using SPSS 20.0. During the study, 1 subject could not be followed and was excluded.

RESULTS AND DISCUSSION

RESULTS

Table 1. Demographic Characteristic

Characteristic	Frequency	%
Gender		
Female	21	87.5
Male	3	12.5
Age		
(Men ± 60.92 ±7.45 Std.deviation)		
<= 50 years	3	12.5
51-60 years	5	20.8
>60 years	16	66.7
Lens Status		
Phakic	10	41.7
Pseudofakic	14	58.3
Tamponade		
Sulfur hexafluoride (SF6)	9	37.5
Perfluoropropane (C3F8)	5	20.8
Air	9	37.5
Silicon Oil	1	4.2
Pre-op P BCVA (LogMAR) (mean±STD.Deviation	1.02±0.63	
Pre-Op MHI (mean ±Std. Deviation)	0.75±0.24	

One hundred and forty-three patients were diagnosed with primary macular hole. A total of 83 patients underwent macular surgery, 58 of whom were treated with ILM peeling and 25 patients with ILM flap technique. A total of 25 patients met the inclusion criteria and were included in this study. However, during the study there was one patient lost from follow up and was excluded. The results showed that the majority of respondents were female (87.5%) with an average age of 60.92 years. At the beginning of the study, 10 patients (41.7%) were phakic and 14 patients (58.3%) were pseudophakic. Gas (SF6 and C3F8) was the most widely used tamponade in this study. The mean BCVA (logMAR) before surgery was 1.02+0.63 while the mean MHI before surgery was 0.75+0.24.

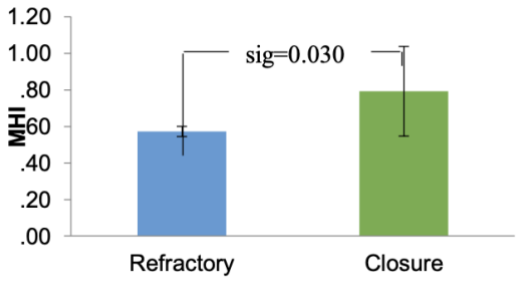


Figure 2. Macular Hole Index based on closure

A total of 19 out of 24 patients (79.2%) in our study had macular hole closure. Based on figure 2, the mean MHI in the refractory group was 0.57 ± 0.03 and the mean MHI in the closure group was 0.79 ± 0.25. The results of the mann whitney test obtained a significant value of 0.030. It can be concluded that there is a significant difference in MHI based on closure after the ILM flap procedure.

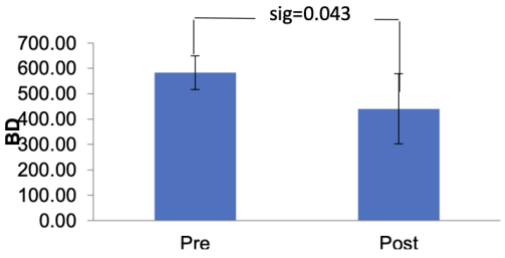


Figure 3. Base diameter in refractory group

The average base diameter (BD) in the refractory group before the ILM flap procedure was 583.20 ± 066.38 and after the ILM flap decreased to 441.20 ± 138.39 (Figure 3). The Wilcoxon test results obtained a sig value of 0.043. It can be concluded that there is a decrease in base diameter in the refractory group after the ILM flap procedure.

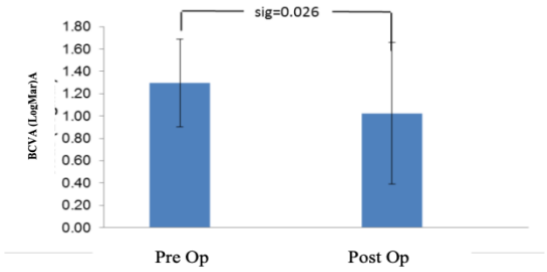


Figure 4. Visual Acuity Changes

Based on Figure 4, there was an improvement in BCVA (logMAR) after the ILM flap procedure. Before the ILM flap was performed, BCVA was 1.30 ± 0.39 and there was an improvement after the ILM flap of 1.02 ± 0.63. The Wilcoxon test results obtained a significant value of 0.026. It can be concluded that there is a significant difference in the improvement of BCVA (logMAR) before and after the ILM flap procedure.

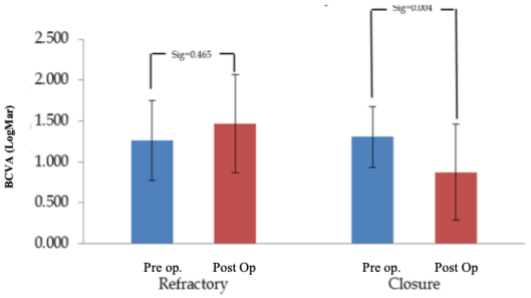


Figure 5. Visual acuity changes based on closure

In this study, the analysis conducted to determine changes in visual acuity before and after the ILM flap procedure based on closure was carried out Wilcoxon test. Based on Figure 5, it was found that in the refractory group the mean BCVA (logMAR) before ILM flap was 1.2156 ± 0.47 and there was a decrease after ILM flap at 1.467 ± 0.67. Wilcoxon test results obtained a significant value of 0.285. It can be concluded that there is no difference in BCVA (logMAR) before and after the ILM flap procedure in the refractory group. The average BCVA (logMAR) before the ILM flap procedure was 1.33 ± 0.38 in the closure group. There was an improvement after the ILM flap procedure of 0.91 ± 0.59. The Wilcoxon test results obtained a significant value of 0.003. It can be concluded that there is a significant increase in BCVA (logMAR) before and after the ILM flap procedure in the closure group.

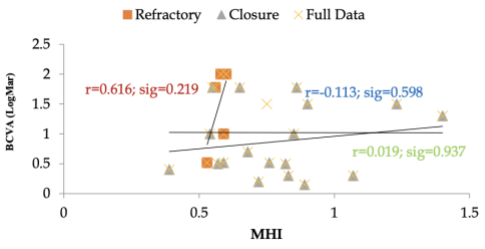


Figure 6. Correlation between MHI and post op BCVA (logMAR)

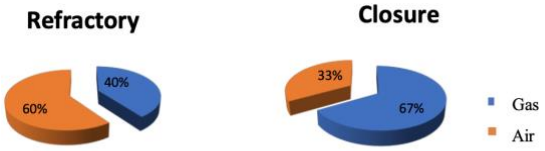
The correlation between MHI and postoperative BCVA (logMAR) was tested

with Spearman Rank correlation (figure 6). The correlation value between MHI and postoperative BCVA (logMAR) in the refractory group was 0.616 (61.6%). The correlation was positive, the higher the MHI, the better the BCVA. The results of the Spearman Rank correlation test obtained a significant value of 0.219, it can be concluded that there is no significant correlation between MHI and postoperative BCVA in the refractory group. The correlation value between MHI and postoperative BCVA in the closure group was 0.019 (1.9%), the correlation was included in the very low category. The correlation is positive, the higher the MHI, the higher the BCVA. The results of the Spearman Rank correlation test obtained a significant value of 0.883. It can be concluded that there is no significant correlation between MHI and postoperative BCVA (logMAR) in the closure group.

Tabel 2. Correlation between Tamponade and closure

Tamponade		Closure		Total
		Refractory	Closure	
Gas	Count	2	12	14
	% within Tamponade	14.3%	85.7%	100.0%
Air	Count	3	6	9
	% within Tamponade	33.3%	66.7%	100.0%
	Count	5	18	23
	% within Tamponade	21.7%	78.3%	100.0%
$\chi^2 = 1.168; sig = 0.280$				

In this study, 14 patients, 9 patients and 1 patient used gas (SF6 and C3F8), air and silicone oil as tamponade, respectively. We only examined subjects who used gas and air as tamponade because the number of patients who used silicone oil was too small. The correlation between tamponade and closure was tested with the Chi Square test shown in Table 2. From the Chi Square test results, a significant value of 0.280 was obtained. It can be concluded that there is no significant correlation between tamponade and closure of the macular hole.

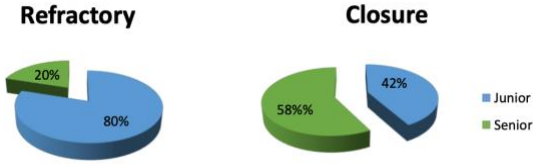


In the refractory group, 3 of 5 subject (60%) used air as a tamponade, while in the closure group 12 of 18 subject (67%) used gas (SF6, C3F8) tamponade. Although not statistically significant, it was seen that more patients had macular holes closed in the group that used gas as tamponade when compared to patients who used air tamponade.

Correlation between surgeon factor and closure

Tabel 3. Correlation between surgeon factor and closure

Surgeon factor		Closure		Total
		Refractory	Closure	
Junior	Count	4	8	12
	% within Surgeon factor	33.3%	66.7%	100.0%
Senior	Count	1	11	12
	% within Surgeon factor	8.3%	91.7%	100.0%



In this study, we also investigated the surgeon factor on the macular hole closure rate. In the refractive group, 80% (4 out of 5) were performed by 5 junior surgeons, while in the closure group, 91.7% (11 out of 19) were performed by 3 senior surgeons. The correlation between surgeon and closure factors was tested using the Chi Square test shown in Table 3. The Chi Square correlation test results showed a significant value of 0.132, so it can be concluded that there is no significant correlation between the surgeon factor and closure.

Correlation between surgeon factor and BCVA (logMAR)

Tabel 4. Correlation of surgeon factor and final BCVA (logMAR)

Surgeon factor		Visus		Total
		Decrease	Improve	
Junior	Count	3	9	12
	% within Surgeon factor	25.0%	75.0%	100.0%
Senior	Count	1	11	12
	% within Surgeon factor	8.3%	91.7%	100.0%
Total	Count	4	20	24
	% within Surgeon factor	16.7%	83.3%	100.0%
$Chi\ Square\ (\chi^2) = 1.200;\ sig = 0.273$				

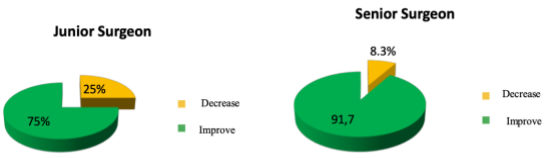


Table 4 shows the Chi Square test showed a significant value of 0.273. It can be concluded that there is no significant correlation between the surgeon factor and BCVA (logMAR). In junior surgeons, the final BCVA (logMAR) was 75% improved and 25% decreased. Meanwhile, in the senior group 91.7% had improved and 8% had decreased. Although not statistically significant, more patients in both groups had improvement in BCVA after the ILM flap procedure.

Discussion

In a healthy retina, neurons are surrounded by Müller cells. If the retina is detached orotherwise damaged, macrophage-like cells from the vitreous may infiltrate the retina. These cells may activate Müller cells via tissue necrosis growth factor- inducing gliosis. Moreover,the peeled-off ILM itself contains Müller cell fragments; therefore, ILM peeling alone can induce gliosis. Thus, if a segment of peeled-off ILM is left attached, it may provoke gliosis both inside the retina and on the surface of the ILM.

The ILM also may be a scaffold for tissue proliferation. [9] The mechanism by which the inverted ILM flap technique works is not fully understood. The inverted ILM flap technique may induce glial cell proliferation, resulting in the macular hole filling with proliferating cells that enhance closure. 10 Histopathologic studies confirmed that ILM being a base membrane acts as a scaffold for gliosis to close large MHs.

Besides gliosis, the ILM flap seals the MH by secluding communication between the vitreous and subretinal space, creating a closed compartment enabling the RPE to pump out fluid effectively, preventing further seepage of fluid and, hence, keeping the hole dry. Shiode et al. experimentally proved that some of the constituents of ILM enhance the proliferation and migration of Müller cells in vitro.

Moreover, neurotrophic factors and basic fibroblast growth factor (bFGF) retained on the surface of the ILM flap and secreted by the migrating Müller cells could stimulate the survival of retinal cells. Thus, it is likely that Müller cell gliosis, and humoral factors could contribute to the closure of large MHs.[9] Many articles mentioned that the spontaneous closure occurred in MHs with a relatively small diameter.

Sugiyama et al. suggested that MHs of less than 250 μm diameter have more opportunity to close spontaneously. Privat et al. believed that the diameter of MHs is probably the main factor for the spontaneous closure, since the diameters in their study are between 70 and 250 μm in 13 patients, except in one patient who had a 350 μm macular hole. The macular hole with the diameter of less than 400um may have chance to close spontaneously.[11]

Michalewska et all reports their study that show the improved anatomic and functional results in patients with large macular holes which a piece of inverted ILM was overlying the macular hole.[10] Narayanan R et al report their study that showed inverted ILM flap technique did not lead to significantly higher anatomical closure rates than conventional ILM peeling in large macular holes more than 800 mm in diameter. [12]

In a previous study conducted by Unsal et al. showed that basal diameter and macular hole volume could be used as strong predisposing factors of OCT parameters for postoperative visual acuity prognosis.[5]

In our study, all subjects had a diameter of more than 400um. The anatomical success after surgery reached 79.2%. Previous theory says that Macular Hole Index of more than 0.5 will give a good prognosis. All patients in our study had MHI >0.5 but 5 patients were refractory. However, there is a tendency for higher MHI to have a better closure rate.

We found that there was a significant difference in MHI based on closure in the closure group. MHI diameter had a significant correlation with hole closure. However, this was not significant in the refractory group. This could be due to operator factors, use of different tamponade agents, macular hole shape, duration of symptoms, etc. for which we did not observe the correlation that may have a confounding effect on the results, which cannot be ruled out.

Further studies with a larger sample size should validate these results.In the first few months after macular hole surgery with the inverted ILM flap technique, SOCT demonstrated improvement in the foveal contour and increased tissue coverage of the macular hole. Glial cells proliferate producing an environment for the photoreceptors to assume new positions in direct proximity to the fovea. These findings explain why inducing Müller cell proliferation improves not only the macular hole closure rate but also postoperative visual acuity.[9]

Some previous studies have shown changes in visual acuity before and after therapy with ILM flaps in line with the closure rate. Liang xida et all reports their study that shows that the spontaneous closure of MH may gain a well visual acuity, and the influencing characteristic needs to be explored. Cases with a spontaneous closure of MHs acquired progress in visualacuity. The average initial BCVA was 0.36 ± 0.20, and the average final BCVA after spontaneous closure of MH was 0.70 ± 0.17.13 Sborgia G. et al report their study that showed high closure rate and visual acuity improvement supported the effectiveness of the inverted ILM flap technique for LMH.[14]

We also found this in our study. Postoperative BCVA improved statistically significant over all measurement time points and the MH closure rate was 79.2%. Regarding to the MHI parameter, we found a significant correlation between MHI and post operatif BCVA in the closure group but not in the refractory group. There are a number of potential causes for this, including age and visual acuity prior to surgery, among other factors, which may require further investigation.

In this study, we noted that patients in the refractory group appeared to be older and/or had poorer initial visual acuity compared to patients in the closure group. The exact pathogenesis for cataract development after vitrectomy has not been fully elucidated and is often multifactorial. Prior research has identified factors including oxidation of lens proteins, length of operative time, light toxicity, and use of intraocular gas. More recent studies have suggested that vitrectomy leads to increased oxygen tension in the eye, allowing for cataract progression due to oxidation of the lens fibers.[11]

3 out of 5 patients in refractory group were phakic eye patients. This may explain why there was a decrease in visual acuity in 3 out of 5 patients in the refractory group. Cataract formation leads to decreased BCVA after ILM flap procedure. In our study, we also looked for the correlation between closure rate, tamponade used and surgeon factors. The results showed that there was no significant correlation between tamponade use with closure rate, surgeon factors with closure rate and surgeon factor with final BCVA.

However, it was seen that patients who had macular hole closure used gas as tamponade more than those who used air, and there was a tendency that the closure rate in the senior surgeon group was higher than the junior surgeon group and the final BCVA (logMAR) improved more in the senior surgeon group. All of the above are due to the many variabel that can affect the closure rate of macular holes.

Among them are the length of time experiencing complaints before surgery, sleeping position after surgery and many other things that can affect the results of surgery. The limitations of this study are the variety of surgeon, the tamponade used and the lack of anamnesis regarding to the duration of complaints and the post operative face-down position that can affect the results of surgery. Due to the inconsistency between different reports, a long-term prospective study with a large homogenous sample is needed to give a more reliable results and to minimize bias.

CONCLUSION

The results of this study especially in closure group suggest that ILM flap is an effective technique for large macular hole management. This is evidenced by the fairly good closurerate. MHI can be a predictor of closure and anatomical and functional improvement of a macular hole.

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