Pre-operative optical coherence tomography predictors: Do they hold any relevance in the era of inverted internal limiting membrane flap in large macular holes?

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Purpose: To study the relevance of preoperative OCT predictors in large macular holes (MH) treated using the inverted ILM peel technique. Methods: Prospective study of 95 patients undergoing vitrectomy for large MH between January 2019 and December 2020 was performed by dividing the patients into groups depending on various quantitative parameters and indices of MH such as base diameter (BD), hole form factor (HFF), macular hole index (MHI), diameter hole index (DHI), and tractional hole index (THI) by using parameters such as minimal hole diameter, hole height, nasal and temporal arm lengths. Depending upon the duration of symptoms, patients were divided into three groups: <3 months, 3–6 months, and >6 months. Anatomical success rate, type of closure, and postoperative vision gain were analyzed in relation to the above-mentioned diameters, indices, and duration to see if any significance existed. Results: The mean age of patients included in the study was 60.48 ± 13.88 years, with female preponderance (males: females = 37:58). Change in logMAR was statistically significant individually with all studied parameters (P < 0.0001) without influence of size of hole and other indices. BD and DHI levels showed significant association with type of closure as indicated by P values of 0.017 and 0.048, respectively. Duration of symptoms showed no significance in terms of anatomical and functional success. Conclusion: OCT predictors of MH success seem to have lost relevance with inverted flap surgeries as 100% anatomical success is achieved with this technique, with 95.78% (91/95) achieving type I closure with statistically significant equivalent functional gain across the indices with no effect of duration of symptoms.

Key words: Anatomical success, inverted ILM Peel, large MH, OCT predictors, type of closure, functional success

The incidence of idiopathic full-thickness macular hole (FTMH) ranges from 0.3% to 0.8%,[1] which is defined as a defect in neurosensory retina caused by tangential traction by internal limiting membrane (ILM) or antero-posterior traction by vitreous. Based on the shortest horizontal diameter on OCT, the International Vitreomacular Traction Study has classified MH into three groups, namely small: ≤250 µm, medium: 250–400 µm, and large: >400 µm.[2] Evolution in surgical techniques from just posterior hyaloid separation to total ILM peel with tamponade have improved the success rate from 58%[3] to >90%[4–7] and using inverted ILM peel technique, even in cases of large MH, closure rate is achieved in 98%–100%.[8–11]

Though anatomic closure has reached the zenith, functional recovery is often not at par. Previous studies have shown a correlation between certain preoperative OCT predictors in relation to anatomic closure and/or visual gain.[12,13] The preoperative predictive factors that were studied previously are BD, MHI, THI, area ratio factor, VRF, and HFF, of which some showed predictive value of anatomical and/or functional success. Wakely et al.[14] reported BD as the only factor predicting the anatomical and functional success, with better functional results in small MH only. Other studies also demonstrated the role of other preoperative indices such as MHI, HFF, THI, DHI, macular hole closure index, and central subfield retinal thickness in predicting the anatomical outcomes.[14–17] Along with the above factors, the type of closure is also considered as a predictor of functional success by various studies.[18,19]

All these pre- and postoperative predictive factors have been studied in the era of the pre-inverted flap technique. With the introduction of the inverted flap technique by Michalewska...
the anatomical success rate for large MH has increased to 98% from 88% with conventional ILM peel; moreover, the functional success rate has increased by reducing the number of patients with “flat-open,” that is, type 2 closure.[15] With significant increase in anatomical and functional success with inverted peel, would these OCT predictors have a say in predicting anatomical and functional success, or have they been reduced to oblivion, is the debate. In the current study, we aim to study whether previously established indices, namely BD, HFF, MHI, DHI, and THI, have any role in predicting anatomical and functional success in MH closure with inverted ILM peel technique.

**Methods**

**Study design**
Prospective, observational study on 95 eyes of 95 patients with idiopathic large MH who underwent surgery at a tertiary care center by a single retinal surgeon between July 2019 and December 2020. Patients were divided into groups depending on various macular hole indices. After obtaining informed consent, all patients underwent PPV + inverted ILM peel + C3F8 tamponade. For the purpose of the study, patients undergoing vitrectomy for IFTMH were included in the study. Patients with history of trauma, small- and medium-sized MH, secondary MH, history of any previous retinal surgery, associated significant cataract needing combined surgery, and patients with incomplete follow-up were excluded from the study. All patients underwent thorough preoperative ophthalmological examination, including best-corrected visual acuity (BCVA), slit-lamp examination, and dilated indirect ophthalmoscopy examinations. Demographic data and lens status at the time of surgery were recorded. Preoperatively, staging of MH was done according to OCT classification.[2] Spectral-domain (SD) OCT (Zeiss–Cirrus 5000) was done preoperatively [Fig. 1a and b] and 6 weeks later [Fig. 2a and b] to document the status of MH. Post surgery, BCVA and macular status were recorded at 6 weeks. Also, vision improvement was recorded according to the duration of symptoms. All patients were followed up to 6 months for any recurrence. Anatomical success is defined as either type 1 or type 2 closure on OCT, while functional success is defined as more than or equal to 0.3 logMAR improvement in visual acuity postoperatively. Study was performed according to ethical standards of the Declaration of Helsinki and was approved by the institutional ethics committee.

**OCT Image measurements**
Preoperative OCT image [Fig. 3] was analyzed by two independent observers to test for inter-observer variations. Following measurements were made in microns: A: basal hole diameter; B: minimum hole diameter; C: distance between base diameter and minimum hole diameter; D: hole height; E: left arm length; F: right arm length.

From these measurements, the following indices were derived:

a) Hole forming factor (HFF):
\[
\frac{\text{Left arm length (E)} + \text{Right arm length (F)}}{\text{Basal hole diameter (A)}}
\]

b) Macular Hole Index (MHI):
\[
\frac{\text{Hole height (D)}}{\text{Basal hole diameter (A)}}
\]

c) Tractional Hole Index (DHI):
\[
\frac{\text{Hole height (D)}}{\text{Minimum hole diameter (B)}}
\]

d) Diameter Hole Index (THI):
\[
\frac{\text{Minimum hole diameter (B)}}{\text{Basal hole diameter (A)}}
\]

**Surgical procedure**
In all cases, 23-G PPV with Alcon constellation was performed using a noncontact wide-angle viewing system (Oculus BIOM 5) on a 3D viewing system (Ngenuity). After obtaining informed consent from patients, surgery was performed under local anesthesia in all cases. Further, 23-G cannulae were placed 3 and 3.5-mm away from the limbus in pseudophakic and phakic patients, respectively. Core vitrectomy was done. Remaining adherent posterior hyaloid was removed by posterior vitreous detachment (PVD) induction using vitrectomy cutter. Membranes (Epi-retinal membrane, if present) were peeled using peeling forceps. ILM peel (arcade to arcade) was done after staining with brilliant blue dye (0.05%) by pinch and peel technique by using ILM peeling forceps (Grieshaber, Alcon). ILM equivalent to the size of the hole was peeled at the macula (multiple flower petal-like flaps) and flaps were stuffed.
in the hole (inverted flap technique) under perfluorocarbon liquid (PFCL). PFCL–air exchange was done and the vitreous cavity was filled with 14% C3F8 at the end of the procedure. Patients were given head down position for 1 week. Patients were examined postoperatively at day 1, 2, 7, 3 weeks, 6 weeks, 3 months, and 6 months. Patients were considered “lost to follow up or incomplete follow up” if they did not turn up till 3 months after surgery.

**Statistical methods**

The continuous variables, such as age, were summarized in terms of mean, median, and standard deviation, while gender was represented in terms of frequency and percentage. The pre- and post-logMAR values corresponding to each level of parameters were expressed in terms of mean and standard deviation and compared using paired t test. Also, the change in logMAR was determined for each patient and summarized as mean and standard deviation according to the levels of the parameters. The comparison of mean change across levels of each parameter was performed using one-way analysis of variance (for more than two levels) and t test for independent samples (for two levels). On similar lines, the analysis was performed for the duration of symptoms. The association between the levels of parameters and types was tested for statistical significance using Pearson’s Chi-square test. All the analyses were carried out using SPSS ver. 20.0 (IBM Corp, USA), and the statistical significance was tested at 5% level.

**Results**

The mean age of patients included in the study was 60.48 ± 13.88 years with a median of 64 years as shown in Table 1. There was female preponderance with 58 (61.06%) females and 37 (38.94%) males. The comparison of pre- and post-logMAR values was performed with the results shown in Table 2. The level-wise comparison of each parameter revealed that the mean difference of logMAR was significantly different than zero (P < 0.0001). The mean for pre-stage was higher than post-stage, suggesting that there was a significant improvement in vision in each level. The mean change in the logMAR was compared across the levels of each parameter as shown in Table 3. The difference in the mean change was statistically insignificant for all the parameters. The comparison of the mean duration of symptoms and visual gain is shown in Table 4. Further, the association of type of closure associated with each parameter is given in Table 5. A significant association was observed between base diameter and DHI and the type of closure with P values of 0.017 and 0.048, respectively.

**Discussion**

Kelly and Wendel were the first to define the role of PPV and removal of posterior hyaloid in MH with a limited success rate of 58%. Subsequently, various advancements in surgical techniques led to an increase in the success rate from 75.6% to 100%. PPV when combined with ILM peel and tamponade has reported the success rate of >90%. Lately, the inverted ILM peel technique has shown an increase in the success rate to up to 98%.

Basal hole diameter is the linear dimension of MH at the level of the retinal pigment epithelium layer. As evident by various studies, preoperative hole size was the only predictor of postoperative VA, which is inversely proportional to VA gain. A retrospective study on 50 eyes showed a decrease in VA by 10% for every 26-µm increase in the BHD. However, in our study, despite including extremes of BD, ranging from 464 to 9778 microns, no such trend was seen and the odds of VA change associated with BD were negligible. However, VA

| Parameter | Statistic | Value |
|-----------|-----------|-------|
| Age (years) | n | 95 |
| | Mean | 60.48 |
| | Median | 64 |
| | Standard deviation | 6.85 |
| | Minimum | 51 |
| | Maximum | 84 |
| Gender | Male No. (%) | 37 (38.94) |
| | Female No. (%) | 58 (61.06) |
Table 2: Comparison of pre and post LogMAR for each category of parameter

| Parameter   | Categories | Pre-LogMAR | Post-LogMAR | P* |
|-------------|------------|------------|-------------|----|
|             |            | n   | Mean | SD   | n   | Mean | SD   |     |
| Base diameter | <1000     | 29  | 0.87 | 0.39 | 29  | 0.61 | 0.29 | <0.0001 |
|             | 1000-1500 | 47  | 1.01 | 0.35 | 47  | 0.70 | 0.29 | <0.0001 |
|             | >1500     | 19  | 1.01 | 0.41 | 19  | 0.74 | 0.40 | <0.0001 |
| MHI         | <0.5      | 69  | 1.02 | 0.38 | 69  | 0.72 | 0.33 | <0.0001 |
|             | >0.5      | 26  | 0.83 | 0.35 | 26  | 0.57 | 0.26 | <0.0001 |
| DHI         | <0.5      | 46  | 0.98 | 0.39 | 46  | 0.68 | 0.31 | <0.0001 |
|             | >0.5      | 49  | 0.95 | 0.37 | 49  | 0.68 | 0.33 | <0.0001 |
| THI         | <1.41     | 74  | 0.99 | 0.39 | 74  | 0.69 | 0.32 | <0.0001 |
|             | >1.41     | 21  | 0.88 | 0.32 | 21  | 0.64 | 0.29 | <0.0001 |
| HFF         | <0.5      | 20  | 1.05 | 0.43 | 20  | 0.80 | 0.31 | <0.0001 |
|             | 0.5-0.9   | 55  | 0.95 | 0.38 | 55  | 0.65 | 0.32 | <0.0001 |
|             | >0.9      | 20  | 0.95 | 0.32 | 20  | 0.67 | 0.31 | <0.0001 |

*Obtained using paired t-test

Table 3: Comparison of change in logMAR before and after intervention in different parameters

| Parameter   | Categories | Change in logMAR | P* |
|-------------|------------|------------------|----|
|             |            | n   | Mean (SD) |     |
| Base diameter | <1000     | 29  | 0.25 (0.28) | 0.656* |
|             | 1000-1500 | 47  | 0.31 (0.31) |     |
|             | >1500     | 19  | 0.27 (0.23) |     |
| MHI         | <0.5      | 69  | 0.30 (0.30) | 0.536* |
|             | >0.5      | 26  | 0.26 (0.24) |     |
| DHI         | <0.5      | 46  | 0.30 (0.31) | 0.678* |
|             | >0.5      | 49  | 0.28 (0.27) |     |
| THI         | <1.41     | 74  | 0.30 (0.31) | 0.446* |
|             | >1.41     | 21  | 0.25 (0.20) |     |
| HFF         | <0.5      | 20  | 0.25 (0.35) | 0.793* |
|             | 0.5-0.9   | 55  | 0.30 (0.29) |     |
|             | >0.9      | 20  | 0.28 (0.20) |     |

*Obtained using one-way ANOVA; *Obtained using t-test for independent samples

Table 4: Duration of symptoms and change in logMAR

| Duration (in months) | Change in logMAR | P* |
|----------------------|------------------|----|
|                      | n   | <0.3 | >=0.3 |     |
| <3                   | 36  | 22   | 14    | 0.572 (NS)* |
| 3-6                  | 25  | 16   | 09    |     |
| >6                   | 34  | 18   | 16    |     |

*Obtained using Pearson’s Chi-square test, NS: Not Significant

gain was relatively poor (though not significant), with BHD exceeding 1500 microns, as they had type 2 closure.

HFF is the ratio between the addition of two side arms of MH and BHD. The lower the ratio, the poorer the chances of hole closure. In a prospective study of 94 patients, all the patients with HFF >0.9 had closed macular holes after single surgery compared to 67% when HFF was <0.5.[21] However, none of these studies were done with inverted ILM technique. In our study, HFF varied from 0.324 to 1.015 microns, and irrespective of the HFF, our cases achieved 100% success rate with inverted flap technique.

The predictive value of MHD for visual outcomes is similar to BHD. MHD is the minimum linear dimension of MH and is one of the most studied OCT parameters after BD.[13-15,21,22] Retrospective study by Gupta et al. predicted that if MHD is <350 µm and if preoperative VA is ≥0.6, a probability of visual success of >20/40 is seen in 93% of patients.[22] Another retrospective case series by Haritoglou et al. showed a significant correlation in terms of visual gain with minimum diameter but not with BHD.[15] In our study, only 13% of cases have MHD <350 µm, and we found no correlation between MHD and VA gain.

Another parameter is hole height (HH), that is, the greatest distance between retinal pigment epithelium layer and the vitreoretinal interface. Except in the study by Haritoglou et al., which showed negative correlation between HH and VA,[10] other studies found no correlation between the two.[13,14] MHI, which takes into account both the hole height and BHD, is considered as an intuitive predictor for visual outcome following MH surgery.[12,23] The ratio of HH and BHD, that is, MHI is reported to be positively correlating to postoperative VA, as also shown in the study by Kusuhara et al.[34] and review article by Sentaro Kusuhara et al.[23] where a significant improvement in postoperative VA was seen when MHI ≥0.5, while no such correlation was seen by Liu P et al.[29] In our study, more than 70% of cases have MHI <0.5, but P value of 0.536 signifies no statistical difference between the two groups, suggesting no role in determining the functional success. In our study too, like Peipei et al.[34] we found statistically insignificant correlation between the HH or MHI and VA gain.

Another OCT index tested as a VA predictor was THI, which is defined as the ratio of HH to MHD and represents primarily the anteroposterior vitreomacular traction. According to one retrospective study, the THI value of >1.41 has a positive predictive value with improvement by 2/> Snellen line.[13] However, later studies failed to prove the significant predictive performance of THI.[34] Similar findings were noted in our study, where 22% of cases had THI >1.41; still, no significant
predictive value of THI was seen as shown by the P value of 0.446.

The strength of tangential traction at the fovea, which is the ratio between MHD and BD, is defined as DHI, which postulates that strength of traction is maximum when the inner diameter of MH is equal to the base diameter. This index mainly predicts the type of closure. Previous studies by Ruiz et al. and Liu P et al. failed to show any such correlation. However, according to recent study by Venkatesh et al., when DHI was >0.5, type 2 closure was mostly seen. The present study showed no significance in terms of visual gain with reduced index value of DHI. However, going in sync with Venkatesh et al.’s study, even in our study, when DHI was more than 0.5, significantly more cases of type 2 closure were seen, signifying that type of closure is affected by this factor.

In this study, besides OCT parameters and indices, we also studied the effect of duration of symptoms on anatomical closure and functional improvement. Duration of symptoms can predict anatomic closure and thus visual improvement as shown by Kelly and Wendel. According to them, a better visual outcome was seen when duration of symptoms was less than 6 months. However, according to Thompson et al. and Jaycock et al., patients with duration of symptoms up to 3 years showed better anatomical outcomes, though not clinically significant. In our study, 100% of the patients achieved macular hole closure irrespective of the duration of symptoms. Also, the visual gain was symmetric in the three groups irrespective of the duration of symptoms.

With an increase in the size of the diameter of the hole, the type of closure may be affected and DHI is the only factor that depends on the minimal hole and basal hole diameter of the macular hole. In this study, more cases of type 2 closure were seen when base diameter exceeded 1500 microns and when DHI was less than 0.5.

## Conclusion

Large MH (>400 µm) pose surgical challenges with relatively poor anatomical and visual prognosis with standard ILM Peel technique. Various preoperative OCT parameters were defined to predict success in such cases. With the advent of the inverted flap technique, both anatomical and functional successes have increased. In our series of large MH, the anatomical success was 100% cases with inverted flap technique, irrespective of the OCT parameters and indices. Similarly, the functional success rate was independent of OCT predictors and duration of symptoms.

## Limitations

Short follow-up and small sample size. A study with a larger sample and longer follow-up is needed to assess if visual changes are sustained over time.

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## Conflicts of interest

There are no conflicts of interest.

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