Original Article

Macular morphometrics in foveal displacement following full thickness macular hole surgery

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Purpose: To investigate if the ratio of the preoperative nasal and temporal "arms" of the macular hole (MH) can have a predictive value in the magnitude of foveal displacement postoperatively. **Methods:** This is retrospective interventional case series of eyes of 40 patients with full-thickness macular hole (FTMH), which underwent vitrectomy with internal limiting membrane (ILM) peeling and had Type 1 closure.All subjects underwent pre and postoperative optical coherence tomography (OCT, Heidelberg, Spectralis, Germany). Their pre and postoperative foveo-papillary distance (FPD) was measured and the magnitude of shift was calculated. The nasal and temporal arm lengths, their ratio (N/T ratio), and the hole base diameter were measured in the preoperative OCTs.The main outcome measure was the correlation of the N/T ratio with the postoperative foveal displacement. **Results:** We observed that in 25% (n = 10) the fovea shifted temporally; in 75% (n = 30) it shifted nasally. The shift did not show a significant correlation with either N/T ratio (r = 0.155, $P = 0.34$) or with base diameter (r = -0.008, $P = 0.961$). The odds ratio (OR) was 4.92 ($P = 0.04$) and the relative risk (RR) was 3.12 ($P = 0.039$) for a longer temporal segment to predict a temporal shift. **Conclusion:** Both nasal and temporal shifts are possible after successful hole closure and temporal shifts can also occur in a significantly high proportion of patients. Temporal shifts are more likely in eyes with a longer temporal segment.

Access this article online
Website: www.ijo.in
DOI: 10.4103/ijo.IJO_1845_19
Quick Response Code:

Key words: Foveal shift, full-thickness macular holes, hole base diameter, nasal segment/temporal segment, post-operative optical coherence tomography

The displacement of the fovea towards the optic disc after vitrectomy and internal limiting membrane (ILM) peeling for full-thickness macular holes (FTMHs) has been previously reported.[1-6]

The ILM peeling can hypothetically cause microtubule depolymerization and thus shrinkage, which can, in turn, shorten the foveo-papillary distance (FPD) and cause a nasal shift of the fovea.[2] It is possible that this shift may cause alterations in the patients' visual processing and binocular vision and hence it is important to know if the magnitude of shift can be predicted preoperatively.

Ishida *et al*.[2] have studied the relationship between the ratio of retinal displacement in the temporal field to the hole base diameter and have found a significant positive correlation. They reported that the temporal vessels moved more than the nasal vessels and have hypothesized that the temporal retina being more flexible is the reason for this shift. It is interesting that the ILM peeling, which can hypothetically affect the microtubules of the axons of the inner retina and thus cause a nasal shift, correlates with the base diameter of the hole, which is a part of the outer retina. It must be kept in mind that the magnitude of ILM peeled need not necessarily correlate with the hole base diameter.

It can be hypothesized that the "arm length" of the nasal and temporal lips of the macular hole (MH) could play a part in the degree of shift of the hole. We thus aimed to retrospectively study the predictive value of the hole base diameter and its nasal and temporal components in predicting the magnitude of the foveal shift.

Methods

This is a retrospective case series including 40 consecutive eyes that underwent vitrectomy and ILM peeling for the treatment of a FTMH. The study was performed at a tertiary eye care center. The surgery was performed by two experienced vitreoretinal surgeons (UKN and MS); both having more than 10 years of surgical experience. The study was approved by the institutional review board and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all the patients. Since this was a retrospective review, all the patients were treated as per standard of care and no treatment was altered for the purpose of this study.

Design

Eyes with an idiopathic FTMH confirmed on spectral-domain optical coherence tomography (SD-OCT, Spectralis, Heidelberg,

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Received: 09-Oct-2019 Revision: 23-Dec-2019
Accepted: 18-Feb-2020 Published: 25-Jun-2020

Cite this article as: Nair U, Mohan A, Sheera KR, Indurkar A, Soman M. Macular morphometrics in foveal displacement following full thickness macular hole surgery. Indian J Ophthalmol 2020;68:1436-40.

Germany), operated in the last two years (2017 June to 2019 May) and with a minimum follow-up of two months (were included in the study). Eyes with any other ocular co-morbidities like retinopathy, glaucoma, macular degeneration, or uveitis were excluded from the study. Eyes with a previous history of any other ocular surgery apart from cataract surgery with intraocular lens implantation were also excluded. Eyes with an inadequate follow-up of less than 2 months, unsuccessful closure, Type 2 closure or re-opening of the hole were also excluded. Eyes that underwent ILM peeling with an inverted ILM flap were also excluded.

Surgical technique

After a routine cleaning and draping, three pars plana vitrectomy ports were made. 23G or 25G was used based on surgeon preference. After core vitrectomy, a posterior vitreous detachment was induced with the cutter aided by triamcinolone staining if required. After a fluid gas exchange, the ILM was stained with Brilliant Blue G for 2 min. Complete ILM peeling was performed and the eye was filled with C_3F_8 or SF_6 based on surgeon's preference. None of the patients underwent any modified technique like an inverted ILM flap. All patients were advised strict postoperative prone positioning for at least one week. Some eyes also underwent simultaneous cataract surgery with intraocular lens implantation and as a result, visual acuity was not compared pre and post-op as it would not be possible to determine whether the change is due to the cataract surgery or the successful hole closure and foveal shift.

OCT measurements

The horizontal line scan passing through the center of the macula and its adjoining infrared reflectance image were used for the measurements. The FPD was measured by visually determining the foveal center and then drawing a line to any vessel at the optic disc margin. The foveal center was determined as described by Kawano *et al*.[4] and the vessel on the optic disc margin was marked as described by Ishida *et al*.[2] This was done pre and postoperatively and care was taken to use the same vessel for both the measurements [Fig. 1]. The post-op image was taken within two months of surgery at the earliest possible time when no gas artifacts were visible in any of the OCT sections. The base diameter was measured, and temporal and nasal segments were separately determined [Fig. 2]. The shift was defined as the difference between the post-op and pre-op FPD. Since these measurements can have subjective variations, two graders (SKR and AI) measured the OCT parameters and their values were averaged for the values. The N/T ratio was defined as the ratio of the nasal arm length to the temporal arm length.

Statistical analysis

The measurements were checked for reliability and consistency with an intra-class correlation and Cronbach's alpha [Table 1]. The values were then averaged to give one value. The variables with continuous data were checked for normality using the Shapiro–Wilk test. Means were compared using the Mann–Whitney U test, proportions were compared using the Chi-square test and Spearman's correlation was used to check for correlations. Odds ratio (OR) was calculated for studying the relationship between the direction of shift and the presence of a longer temporal or nasal segment.

Results

There were 40 eyes of 40 patients. During the study, significant numbers (n = 10) of eyes were noted to have a temporal shift, i.e., shift away from the disc. Hence, the results will be presented as a comparison of the two groups viz. nasal shift (NS, n = 30) and temporal shift (TS, n = 10)

Demographics

The mean age of 64.9 and 67.5 years (P = 0.469) and the male: female ratio of 11:19 and 1:1 (P = 0.456) was comparable in

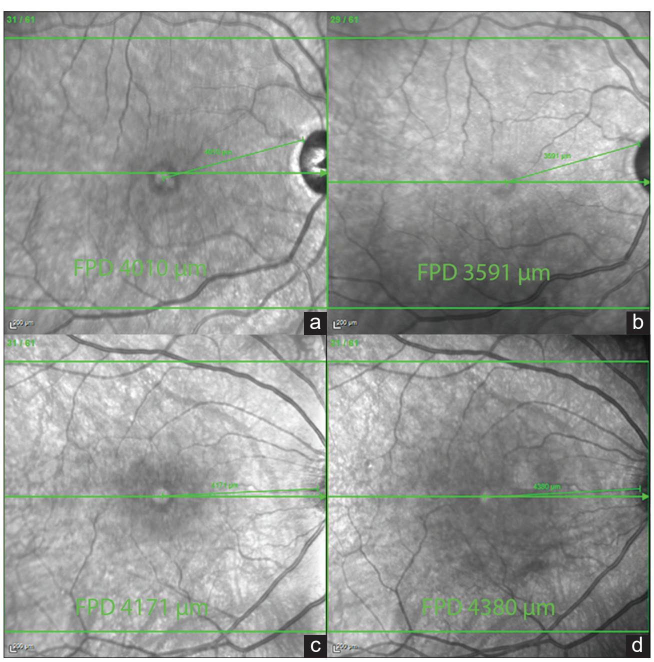

Figure 1: a and b show pre and postoperative infrared (IR) images of a representative case of nasal shift, c and d show pre and postoperative IR images of a representative case of temporal shift

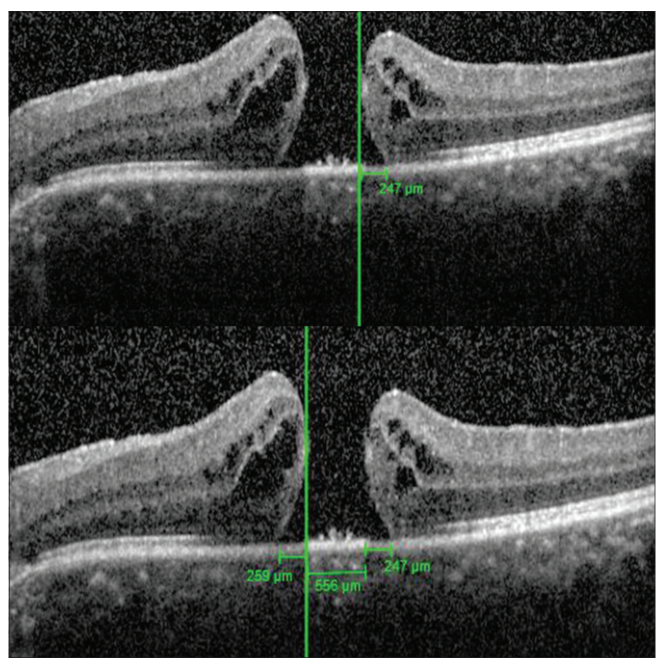

Figure 2: A horizontal optical coherence tomography line scan through the center of the macular hole that illustrates how the nasal, central, and temporal segments of the hole base were measured

the NS and TS groups, respectively [Table 2]. The laterality ratio of 3:2 and 1:1 ($P = 0.580$) and the phakic status (phakic: pseudophakic: combined cataract and vitrectomy with ILM peeling surgery) of 10:7:13 and 3:2:5 ($P = 0.934$) was also comparable in the NS and TS groups, respectively. The operating surgeons also had an equal distribution among the two outcome groups with 7:8 and 1:1 in the NS and TS groups, respectively.

OCT Measurements

The values are presented as mean (95% confidence interval). The pre-op FPD was 3770 (3676–3863) µm and 3729 (3601–3856) µm ($P = 0.508$), the post-op FPD was 3617 (3520–3713) µm and 3876 (3711–4042) µm ($P = 0.008$) and the shift was 152.9 (115.1–190.6) µm and -147.8 (-202.5–-93.1) µm ($P < 0.001$) in the NS and TS groups, respectively.

The mean base diameter was 946.2 (831.2–1061.1) and 900.4 (712.4–1088.3) ($P = 0.488$), nasal segment was 284.3 (215.5–353.2) and 193.8 (108.1–279.4) ($P = 0.083$), central segment was 443.1 (374.5–511.8) and 478.5 (371.6–585.3) ($P = 0.634$), the temporal segment was 218.7 (180.8–256.6) and 228.2 (157.8–298.5) ($P = 0.818$) and the N/T ratio was 1.36 (1.03–1.69) and 0.89 (0.61–1.17) ($P = 0.046$) in the NS and TS groups, respectively.

Shift did not show a significant correlation with either N/T ratio ($r = 0.155$, $P = 0.34$) or with base diameter ($r = -0.008$, $P = 0.961$).

Odds ratio and relative risk

There were 27 eyes with a longer nasal segment (segment ratio > 1) and 13 eyes with a longer temporal segment (segment ratio < 1). Of the ones with a longer nasal segment, 23 eyes had a postoperative nasal shift while four had a temporal shift. Of the eyes with a longer temporal segment, seven eyes had a nasal shift and six eyes had a temporal shift ($P = 0.032$) [Table 3].

The OR was 4.92 ($P = 0.04$) and the relative risk (RR) was 3.12 ($P = 0.039$) for an eye with a longer temporal segment seen preoperatively to result in a temporal foveal shift post-surgery.

Discussion

We report the first observation of a temporal shift seen postoperatively after vitrectomy and ILM peeling for FTMHs. We did not find any association between the magnitude of the foveal shift and the N/T ratio or the hole base diameter. We found a significant difference in the ratio of the nasal and temporal segments of the hole base between the groups that showed a nasal and temporal shift. We also found that eyes with a longer temporal segment were more likely to have a temporal shift than eyes with a longer nasal segment.

All the previous reports[1-6] have reported a nasal shift with the temporal retina being more relaxed as a possible explanation. We saw that there is a temporal shift in 25% of the eyes and hence there may be other unknown factors in the postoperative remodeling process.

Table 1: Reliability indicators for OCT measurements

Parameter	Cronbach's Alpha	Interpretation*	Intra-class correlation#	Interpretation#
Pre-op FPD	0.838	Good	0.721	Moderate
Post-op FPD	0.933	Excellent	0.874	Good
Nasal Segment	0.938	Excellent	0.884	Good
Central Segment	0.955	Excellent	0.914	Excellent
Temporal Segment	0.883	Good	0.790	Good

*A value between 0.8 and 0.9 was considered good and above 0.9 was considered excellent. #ICC Single measures was used and a value below 0.75 was considered moderate, between 0.75 to 0.9 was considered good and above 0.9 was considered excellent. FPD: foveo-papillary distance; OCT: optical coherence tomography

Table 2: Demographics and OCT parameters (Significant associations are in bold)

Parameter	Nasal Shift (*n*=30)	Temporal Shift (*n*=10)	*P**
Age (years)	64.9 (61.6-68.1)	67.5 (61.8-73.2)	0.469
Sex (male: female)	11:19	1:1	0.456
Phakic Status#	10:7:13	3:2:5	0.934
Laterality (right: left)	3:2	1:1	0.580
Surgeon (UKN: MS)	7:8	1:1	0.855
Pre-op FPD (µm)	3770 (3676-3863)	3729 (3601-3856)	0.508
Post-op FPD (µm)	**3617 (3520-3713)**	**3876 (3711-4042)**	**0.008**
Shift (µm)	**152.9 (115.1-190.6)**	**-147.8 (-202.5 to -93.1)**	**<0.001**
Base Diameter	946.2 (831.2-1061.1)	900.4 (712.4-1088.3)	0.488
Nasal Segment (µm)	284.3 (215.5-353.2)	193.8 (108.1-279.4)	0.083
Central Segment (µm)	443.1 (374.5-511.8)	478.5 (371.6-585.3)	0.634
Temporal Segment (µm)	218.7 (180.8-256.6)	228.2 (157.8-298.5)	0.818
Segment Ratio	**1.36 (1.03-1.69)**	**0.89 (0.61-1.17)**	**0.046**

Values are presented as mean (95% confidence interval) for continuous variables. *Mann-Whitney U test was used for continuous variables; Chi-square test was used for categorical data. #Three possible situations were observed for lens status - phakic, pseudophakic and combined surgery (phakic pre-op, pseudophakic post-op). FPD: Foveo-papillary distance; OCT: Optical coherence tomography

Table 3: 2×2 Table for determining Odds Ratio (OR) and Relative Risk (RR)

	Nasal Shift	Temporal Shift
Nasal Segment Longer	23	4
Temporal Segment Longer	7	6

The OR was 4.92 (P=0.04) and the RR was 3.12 (P=0.039) for a longer temporal segment to lead to a temporal foveal shift post-surgery

Foveal dystopia has been observed in cases of epiretinal membranes that returned close to normal after surgery.[7,8] We know that ILM peeling can cause significant trauma to the inner retina[9-11]; however, the fovea still has a tendency to return to its original location post-surgery. The nasal shifts post MH surgery are visible as early as two weeks from surgery[2] and persist to as late as 12 months.[3] Hence, we may hypothesize that only inner retinal changes are not enough for the fovea to shift, there must be changes in the outer as well. It is also possible that this observation namely the temporal shift has been observed by other investigators but the smaller number of eyes with such an event possibly do not influence the overall mean values. In fact, data from Ishida *et al*.[2] reveals that the mean change of the temporal shift ranged between -608 μm and 69 μm. Also corroborating is their observation that the nasal displacement ranged from -316 μm to 16 μm. Even though they used a different method of assessment, this data does offer some evidence to the fact that some eyes did have a temporal shift. Also, what is interesting is that though the above authors found a significant association between larger holes and nasal displacement, eyes with temporal shift were not holes with a large basal diameter or larger minimal diameter clearly underlying the fact that hole diameter had no relationship to this unusual phenomenon as was also observed in our series.

The presence of a longer temporal segment increasing the odds for a postoperative temporal shift is very interesting. A possible explanation could be that a larger temporal segment indicates more temporal contraction and hence upon approximation with the rating of perceived exertion (RPE) there is a resultant shift of the less contracted nasal segment in the temporal direction especially the outer retina. Itoh *et al*.[3] have reported an asymmetrical recovery of the cone outer segment tips post-surgery with the temporal side taking longer than the nasal. It stands to reason that more the area of the detached neurosensory retina from the RPE more would be the duration and degree of recovery. Also, as mentioned earlier epiretinal membrane (ERM) peel induced segmental macular sliding predominantly involving the superficial layers at the level of the outer plexiform layers have been reported[8] and can be a possible explanation as to why eyes with longer temporal segments have a higher odd for a temporal shift.

We did not find a significant correlation between the magnitude of shift and the hole base diameter, which is in agreement with the findings of Kawano *et al*.[4] Ohta *et al*.[5] compared the site of the pre-opened MH with the center of the opened hole and the postoperative closed hole. It would be interesting to see if the center shifts upon hole opening towards the side with the longer or shorter segment and how it affects the postoperative shift of the closed hole. Faria *et al*.[1] reported the presence of temporal thinning and nasal thickening. We did not perform this as it would have been difficult to draw any reliable conclusions with small sample size.

The reliability statistics showed good to excellent values for most of the parameters. The two observers differed maximally in the preoperative FPD. This could be because there would be subjective variations in determining the foveal center. We have averaged their values for the final calculations to minimize any subjective bias.

In eyes with DME, removal of the posterior hyaloid without ILM peeling does not lead to foveal displacement, but eyes with ILM peeling show obvious nasally foveal displacement.[12] The area of ILM peeled can hypothetically influence the microtubular damage and hence the magnitude of the shift. Since this was a retrospective study, there was no data for us to evaluate the same. The two surgeons could have potentially differed in the area, the commencement and direction of ILM peeling; however, there were no statistically significant differences seen in their outcomes. A significant number of subjects underwent cataract surgery with intraocular lens implantation in the same sitting; however, there were no statistically significant differences between the eyes that underwent combined surgery and the ones that had only vitrectomy and ILM peeling. We also could not compare visual acuity pre and post-op because the change in visual acuity could be due to the change in lens status.

Undue importance is probably given to the nasal shift of the retina post MH surgery. Data from Ishida *et al*. reveal that the differences in the changes of temporal and nasal were smaller than the MH diameter itself implying that displacement of the fovea might not be exactly equal to the displacement of retinal vessels or specifically the superficial retina alone as all the holes closed in that series. Moreover, even after closure of the hole, the shift continued beyond two weeks clearly indicating multiple mechanisms and planes of the shift in these eyes.

The limitations of the study are the small number of eyes having a temporal shift. A prospective study with larger sample size, preferable disc to foveal distance pre-opening the hole, measurement of ILM peeled area, temporal and nasal segments length and thickness, and their correlation with the amount of shift can provide valuable insights.

Conclusion

Both nasal and temporal shifts are possible after successful macular hole closure. Our study challenges the current belief of a nasal shift. The eyes with a longer temporal arm have higher odds of a temporal shift than the eyes with a longer nasal arm.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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