Commentary: Indistinct retinal outer layers in the walls of idiopathic full thickness macular hole - A potential predictive biomarker for surgical outcomes

Pars plana vitrectomy (PPV) with an internal limiting membrane (ILM) peeling and gas tamponade is widely accepted as the gold standard for the primary repair of full-thickness macular holes (MH) resulting in the overall MH closure in 80 to 100% of cases.[1] However, predicting postoperative visual outcomes in MH can be difficult. Eyes with a shorter duration of symptoms and better preoperative visual acuity have been recognized to have better visual outcomes after MH surgery.[1]

With the advent of optical coherence tomography (OCT), many parameters that can prognosticate success in MH surgery have been proposed. The minimum diameter of MH or minimum linear dimension of MH is one of the easily understood OCT parameters. Commonly, a smaller minimum diameter is associated with better postoperative visual acuity.[2] The basal hole diameter is a linear dimension of MH at the level of the retinal pigment epithelium layer. The predictive trend of the basal hole diameter for visual outcomes is almost the same as the minimum diameter. The smaller the basal hole diameter, the better the postoperative visual acuity.[2] The hole height, defined as the greatest distance between the retinal pigment epithelium layer and the vitreoretinal interface has been studied only to find no significant relationship between the hole height and postoperative visual outcomes.[2]

The relationship between the length of photoreceptor inner segment/outer segment (IS/OS) junction defect and visual outcomes has also been investigated. The predictive performance of the IS/OS junction defect length for visual outcomes varies across studies, with some reporting an association with postoperative macular sensitivity and visual acuity.[3]

The hole form factor (HFF) was the first calculated OCT index used as a prognostic factor.[3] The HFF is the quotient of the summation of the left and right arm lengths divided by the basal hole diameter. The HFF is reported to be positively correlated with postoperative visual acuity; however, the correlation is weaker than those for the minimum diameter and the basal hole diameter.[2] The Macular Hole Index (MHI) – is defined as the ratio of the hole height to the basal hole diameter and is reported to be positively correlated to postoperative visual acuity in several studies.[4] The tractional hole index (THI), defined as the ratio of the hole height to the minimum diameter, is another OCT index tested as a predictor for visual outcome only to be refuted by subsequent studies.[3,4] Other OCT parameters such as the external limiting membrane (ELM) line defect length and the cone outer segment tips line defect length have been studied. A larger baseline ELM defect may mean more damage and hence suggest a poorer prognosis, due to greater difficulty in achieving complete reformation.[3,4]

There have been recently many newer indices that have been proposed as good predictors of prognosis in MH.[3] Some of these are:

1) macular hole area index (MAI), which is the MH area divided by the total area of the macular hole.

2) macular hole tissue area index (MTAI): this is essentially, the MH tissue area divided by the total area of the MH.
3) macular hole cystoid space area index (MCSAI): this refers to the MH cystoid space area divided by the total area of the MH.

Many of these require the image to be exported out of the OCT machine to be analyzed by software such as ImageJ, which may not be readily possible in a clinic. Also, results for OCT-based predictors that have been proposed so far, vary across the studies and therefore their utility has often been questioned.[3,5]

Shimozono *et al*.[5] demonstrated ellipsoid zone (EZ) integrity correlated well with the best-corrected visual acuity (BCVA). Kitao *et al*.[6] evaluated long-term microstructural and visual changes over time after MH repair. Restoration of the photoreceptor layer was defined as the continuous back-reflection line corresponding to the ELM, EZ, and Cone interdigitation zone (CIZ). They had demonstrated that most eyes in their study had glial proliferation at the fovea in the early postoperative period, but thereafter glial cells gradually decreased over time. The disappearance of the glial cells was first observed in the outer nuclear layer just above the ELM, and the remaining glial cells migrated upward to the inner retinal layer and eventually disappeared. During this process, the EZ was concomitantly reconstructed with subsequent restoration of the CIZ. The foveal microstructure regenerated in the order ELM, EZ, and then CIZ. Concomitantly, visual acuity was noted to improve over 3 years, indicating that both microstructure and visual acuity improve continuously for up to 3 years after surgery. Müller apical processes are connected by continuous heterotypic *adherens* junctions to other Müller apical processes and to photoreceptors, generating the so-called ELM. Alterations in Müller cells during different retinal pathologies may affect the state of ELM and involve hyper-reflective changes in the first outer OCT band.[7] ELM represents junctional complexes between Müller cells and rod–cone photoreceptor cells, thus its presence is essential throughout the affected area for the regeneration of the photoreceptor outer segment.[8] The growth of Müller 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.[9]

In the present article, [IJO_1215_20] the authors have proposed that the indistinct retinal outer layer (I-ROL) observed in the walls of MH is likely to be activated Müller cells and the circumferential extent of I-ROL may provide a quantitative estimate of Müller cells' response. Therefore, the presence of I-ROL can have prognostic importance in MH closure. A larger study with a control group may prove or disprove the utility of I-ROL in prognosticating MH.

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