10/11/2021 1:40PM

The Proteome of Preretinal Tissue in Proliferative Vitreoretinopathy and Epiretinal Membrane: Differential Expression of Extracellular Matrix

- Charles G Miller, MD, PhD
- Jonathan L. Prenner, MD
- Konstantin Astafurov, MD, PhD
- Todd Greco, PhD
- Jean Schwarzbauer, PhD

OBJECTIVE Characterize the proteome of preretinal membranes delaminated during surgery for retinal detachment with proliferative vitreoretinopathy (PVR) in comparison to idiopathic epiretinal membrane (ERM).

PURPOSE PVR complicates 5-10% of retinal detachments (RD), often causing recurrent RD. The molecular pathogenesis of PVR remains poorly understood. The proteome of PVR tissue, with a particular focus on those proteins differentially expressed in ERM, will help us to better understand the mechanism of disease and identify therapeutic targets to help prevent PVR from developing post-operatively.

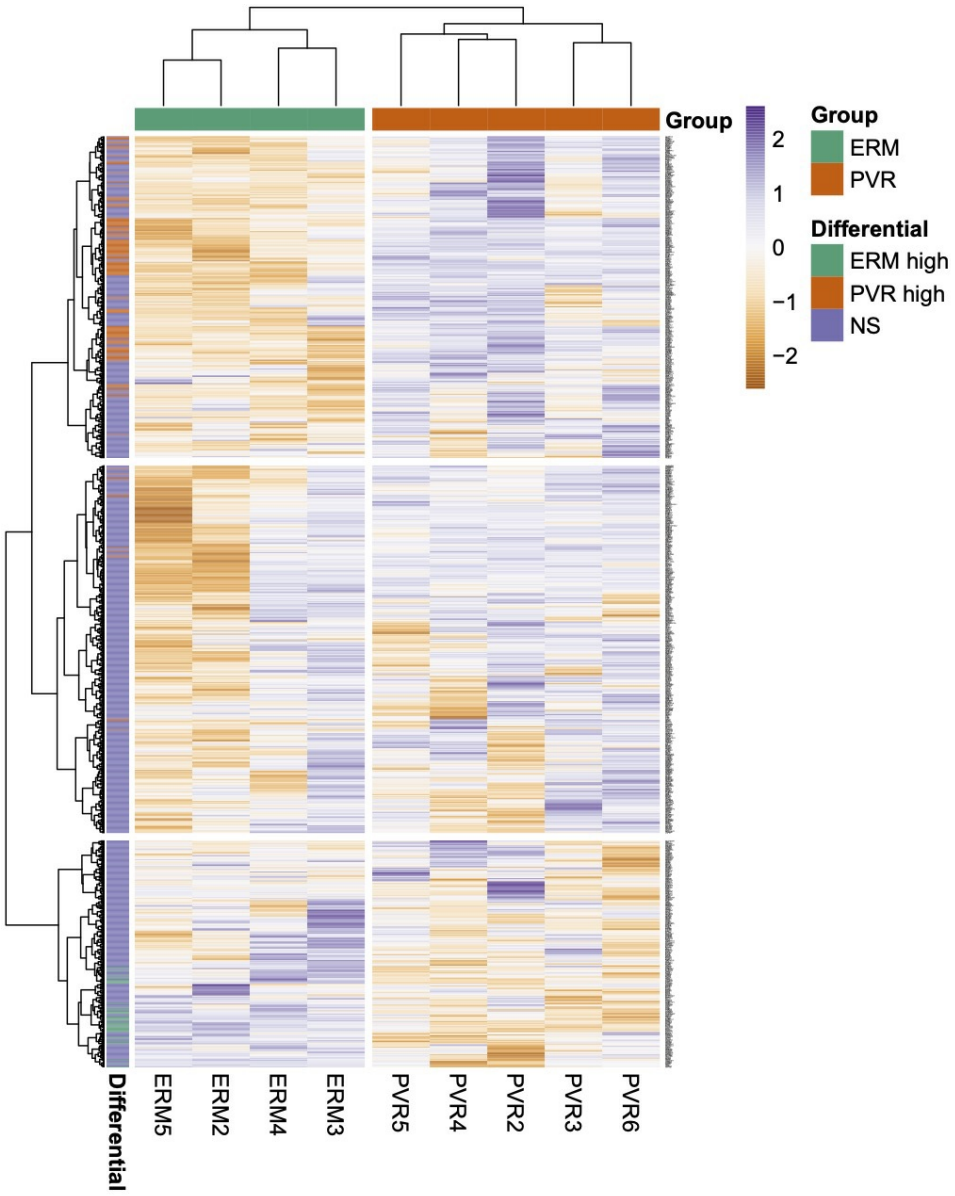
METHODS Preretinal tissue delaminated during pars plana vitrectomy for RD with PVR or idiopathic ERM were collected from 9 patients (5 PVR, 4 ERM). Trypsinized protein isolates were loaded into an Easy-nLC 1000 UPLC system mated to an Orbitrap Elite mass spectrometer with a 120,000 resolution MS1 scan (375–1500 m/z) followed by up to 20 MS/MS scans with collision-induced dissociation fragmentation. Byonic and Sequest HT algorithms were used to search the raw data files. MS/MS based protein identifications were validated using Scaffold software with peptide identification accepted at greater than 99% probability by the Scaffold Local FDR algorithm.

RESULTS The proteome of PVR consists of 1119 proteins, which by principal component

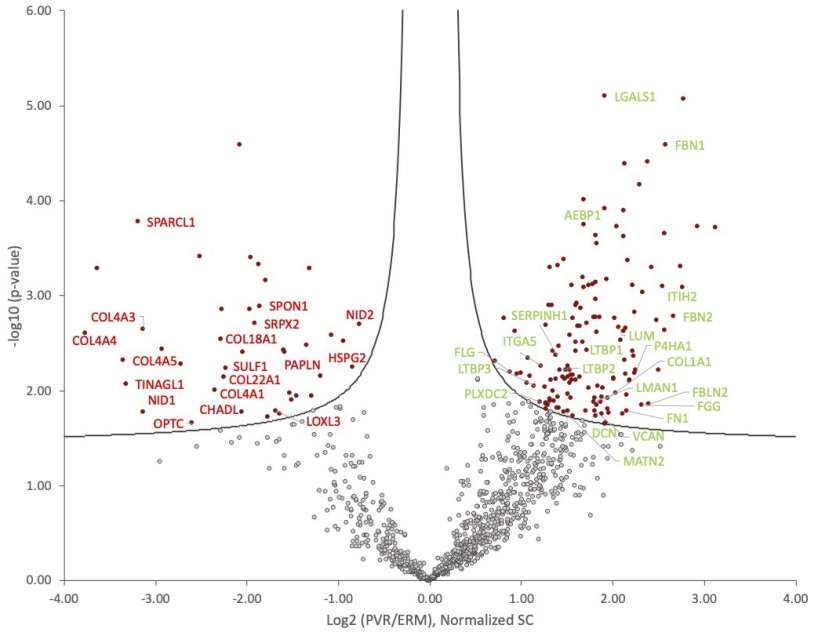
analysis and hierarchical clustering (Fig 1) delineate a proteomic signature. Idiopathic ERM proved more heterogenous. Gene set enrichment analysis revealed 4 biological processes from the gene ontology database that are overrepresented in PVR: extracellular matrix (ECM) organization, extracellular structure organization, supramolecular fiber organization, and cytoskeleton organization. The protein with highest relative mean spectral counts (a semi-quantitative value that allows for the comparison of protein quantity) in PVR tissue is fibronectin (FN1), a multidomain ECM glycoprotein. PVR was compared to ERM by fold change analysis. A volcano plot was constructed to visualize proteins for which there was a statistically significant ($p < 0.05$) difference in mean spectral counts between PVR and ERM (Fig 2). These encompassed 186 proteins, 42 of which are components of the matrisome (ECM-related proteins).

CONCLUSION ECM components are enriched in preretinal tissue derived from PVR and these data emphasize the importance of the fibrotic (acellular) component of PVR membranes. The ECM expression profile of PVR tissue differs significantly from that of idiopathic ERM. These insights supports a novel therapeutic strategy aimed at inhibiting ECM assembly to prevent PVR and subsequent RD.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



Heatmap demonstrating hierarchical clustering of the proteome of preretinal tissue samples derived from idiopathic ERM and PVR. Relative mean spectral counts (purple high, orange low) for each protein are indicated by horizontal bands, with differential expression levels indicated for those that reached statistical significance (green ERM high, orange PVR high, purple non-significant [NS]).



Volcano plot of the combined proteome of preretinal tissue plotting statistical significance versus normalized fold change of mean spectral counts in PVR compared to idiopathic ERM. Matrisome constituents whose differential expression levels reached statistical significance (black line) are labeled with corresponding gene symbols (red ERM high, green PVR high).

10/11/2021 1:46PM

Fovea-Sparing Versus Standard Internal Limiting Membrane Peeling for Myopic Traction Maculopathy

- Taku Wakabayashi, MD
- Nobuhiko Shiraki
- Yasushi Ikuno
- Hirokazu Sakaguchi, MD, phD

OBJECTIVE To investigate the efficacy of pars plana vitrectomy (PPV) with fovea-sparing internal limiting membrane (ILM) peeling (FSIP) for myopic traction maculopathy (MTM).

PURPOSE To report the surgical outcomes of pars plana vitrectomy (PPV) with fovea-sparing internal limiting membrane (ILM) peeling (FSIP) and standard ILM peeling for myopic traction maculopathy (MTM)

METHODS One hundred and two eyes of 96 consecutive patients who underwent primary PPV for MTM were included in this study. We retrospectively compared the surgical outcomes of eyes that underwent vitrectomy with FSIP from October 2012 through March 2017 with those of eyes that underwent vitrectomy with standard ILM peeling from June 2008 through September 2012. The main outcome measures were best-corrected visual acuity (BCVA) at 12 months after surgery, time to MTM resolution, and postoperative complications such as macular hole (MH) formation.

RESULTS There were 26 and 76 eyes in the FSIP and standard ILM peeling groups, respectively. The mean visual acuity at the 12 month follow-up was significantly improved compared with the mean preoperative visual acuity in both groups (P less than 0.001 for both groups). The pre and postoperative logMAR BCVA did not differ significantly between FSIP group and standard ILM peeling group (preoperativepreoperative: 0.60 ± 0.35 in the FSIP group and 0.61 ± 0.39 in the standard ILM peeling group, P = 0.935; postoperative BCVA: 0.32 ± 0.43 in the FSIP group and 0.37 ± 0.38 in the standard ILM peeling, P = 0.281). None of the eyes in the FSIP group and six (8%) eyes in the standard ILM peeling group developed postoperative MH. Consequently, the BCVA at 12 months deteriorated by three or more lines for four eyes (5%) in the standard ILM peeling group. The risk factors for postoperative MH formation were thinner choroidal thickness (P= 0.025) and worse preoperative visual acuity (P=0.035).

CONCLUSION The overall visual and anatomical improvements after vitrectomy with FSIP may be comparable with those after vitrectomy with standard ILM peeling. FSIP can prevent postoperative MH formation and a consequent significant impairment in vision. Eyes with thinner choroidal thickness and worse visual acuity preoperatively may most likely benefit from FSIP.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.

10/11/2021 1:52PM

Feasibilty and Validation of a Deep-Learning Algorithm for the Detection of Macular Holes With Spectral Domain Optical Coherence Tomography

- Jessica L. Cao, MD
- Hannah Kang
- Niranchana Manivannan, PhD
- Aneesha Kalur
- Amogh Iyer, BSE
- Carolina Carvalho Soares Valentim, MD
- Justin Muste
- Thais F Conti, MD
- Rishi P. Singh, MD

OBJECTIVE To determine the feasibility and validation of a deep-learning algorithm for the detection of macular holes (MH) and MH-related pathological findings on optical coherence tomography (OCT).

PURPOSE Artificial intelligence and deep-learning (DL) tools have the potential to improve diagnostic accuracy and clinical efficiency in the detection of various ocular disease states. The purpose of our study is to validate the reliability of a DL algorithm for MH and MH-related pathologies on OCT as a potential screening aid in the clinical setting.

METHODS This was a retrospective study of patients of at least 18 years of age who were diagnosed with MH. Patients were excluded if they were diagnosed with any concomitant maculopathy. 346 OCT macular cube scans from eyes with a diagnosis of MH and 307 control scans without any vitreo-macular pathology were included. Two human graders analyzed all scans for the presence of pathology such as subretinal or intraretinal fluid, disturbance of vitreoretinal interface, or IS/OS disruption. The algorithm then graded all scans based on a set scale. The grading results of the algorithm and the 2 human graders were then compared to determine the level of agreement.

RESULTS When comparing human grader 1 to the algorithm, there was an 86.17% rate of

agreement for the detection of any pathology on the scan. For human grader 2 versus the algorithm, there was an 87.83% agreement rate. When combining the results of the two graders and at least one grader marked the macular cube as abnormal, there was an 87.61% agreement rate. There was an 86.39% agreement rate amongst the algorithm and the two human graders if cubes were marked as "abnormal" only if both graders individually marked them as abnormal. Further evaluation of macular hole size and classification with algorithm sensitivity and specificity is being completed.

CONCLUSION DL algorithms may be reliable tools for the early detection of MH on OCT and, by extension, could be useful screening aids that help improve clinical efficiency.

IRB APPROVAL Not applicable — I responded "No" to previous question regarding human subjects.

10/11/2021 1:58PM

Large Operative Case Series of Degenerative Lamellar Macular Holes

- Chirag M. Shah, MPH
- Mathew W. MacCumber, MD, PhD
- Naryan S Sabherwal, MD
- John S. Pollack, MD
- Joseph M. Civantos, MD
- Kirk H. Packo, MD, FACS
- Kourous A. Rezaei, MD
- Pauline T. Merrill, MD, FASRS
- Zac B. Ravage, MD
- Jack A. Cohen, MD
- Sohail J. Hasan, MD, PhD
- Vivek Chaturvedi, MD

OBJECTIVE This study examines the anatomic and visual outcomes of pars plana vitrectomy with membranepeeling for a large case series of degenerative lamellar macular holes.

PURPOSE Previous, smaller-sample case series have shown mixed visual outcomes after vitrectomy with membrane peel for degenerative lamellar holes. This study hopes to better clarify these outcomes in one of the largest case series of surgical cases of degenerative lamellar holes published to date.

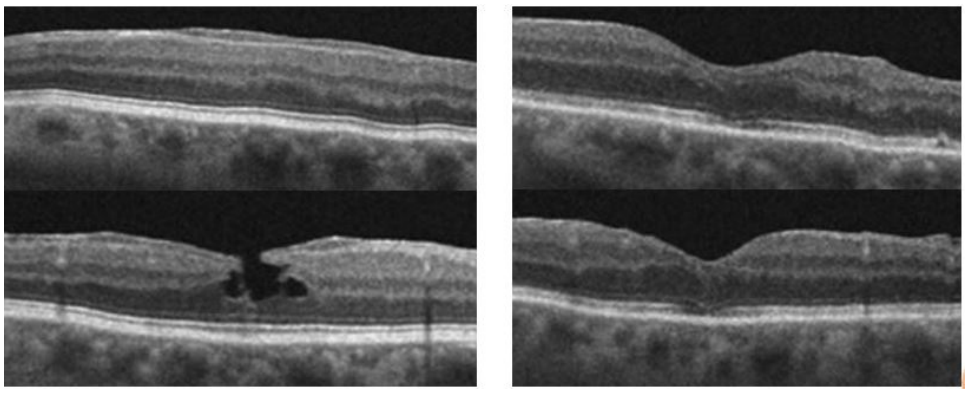
METHODS A retrospective chart review was conducted on 5 years of surgeries performed at a large hybrid retina practice in the Chicagoland area. All pre- and post-operative OCTs over the study period were examined for all patients who had vitrectomy with a concomitant diagnosis of a lamellar hole. Two authors (VC and CMS) used these OCTs to categorize lamellar holes as degenerative as opposed to tractional or pseudoholes. Pre-operative best corrected visual acuity (BCVA), post-operative BCVA (6 to 12 months after membrane peel), and hole closure, were documented. ANOVA and mixed effects regression models were used to compare pre- and post-operative visual and anatomic outcomes with an alpha of 0.01.

RESULTS 23 degenerative lamellar holes in 22 patients, 59 tractional lamellar holes in 55

patients, and 9 pseudoholes in 9 patients were operated on over the study period. 100% of our degenerative hole cases had lamellar hole-associated epiretinal proliferation. Five patients' degenerative holes had transformed to full-thickness macular holes prior to surgery. None of our cases developed full thickness holes after surgery. Only 2 patients had a one line loss in BCVA in the post-operative period, and 100% of the degenerative lamellar holes closed post-operatively. The degenerative holes were found to have a statistically significant improvement of 2.5 lines in BCVA ($p < 0.01$). Post-operative visual acuity was significantly associated with better pre-operative visual acuity ($p < 0.01$). Change in visual acuity was significantly associated with change in Elipsoid Zone and worse pre-operative visual acuity ($p < 0.01$).

CONCLUSION Others have suggested avoiding peeling degenerative lamellar holes due to worse post-operative vision and the absence of tractional membranes. Our results point to benefits of peeling LHEP and ILM in selected cases of degenerative lamellar holes, given the significant visual benefit we found. Earlier peeling may result in better final BCVA by protecting the elipsoid zone prior to loss.

IRB APPROVAL No — I received a determination that the study/activity qualified for **exempt status or that it did not require IRB approval** from an IRB or another authorized oversight body *(IRB Exemption Letter may be requested)*.



A degenerative lamellar hole with epiretinal proliferation before and after membrane peel

10/11/2021 2:20PM

Superior Wide-Base Internal Limiting Membrane Flap Transposition (SWIFT) for Macular Holes

- Homayoun Tabandeh, MD
- Andy Morozov, BS
- Kourous A. Rezaei, MD
- David S. Boyer, MD

OBJECTIVE To report on the the surgical outcomes for superior wide-base internal limiting membrane flap transposition (SWIFT) for macular holes.

PURPOSE To study the outcomes of SWIFT for macular holes.

METHODS Retrospective consecutive case series including eyes undergoing SWIFT for MH. High-risk characteristics were defined as high myopia, chronicity, prior MH surgery with ILM removal, and large (>650 microns) MH. Main Outcome Measures were visual acuity and the status of the MH.

RESULTS 22 eyes of 22 patients, mean age 67.2 years, with mean follow-up of 11.9 months, were included in the study. 17 eyes had one or more high-risk characteristics. 6 (27%) eyes were highly myopic, 9 (41%) eyes had chronic MH, 3 (14%) eyes had history of prior MH surgery and ILM removal. The mean MH basal diameter was 880 microns and the mean inner diameter was 519 microns. The MH inner diameter was greater that 450 microns in 14 (64%) eyes, and greater than 650 microns in 8 (36%) eyes. The baseline mean logMAR visual acuity equivalent was 0.85. The MH closed in 21 (95%) eyes. At the last follow-up visit the mean logMAR visual acuity equivalent was 0.58. The mean change in vision was 0.3 logMAR equivalents.

CONCLUSION SWIFT is a useful surgical technique for the management of high-risk MHs including persistent MHs with previously removed ILM. The presentation will report on the surgical technique and visual and anatomic outcomes.

IRB APPROVAL No — I received a determination that the study/activity qualified for **exempt status or that it did not require IRB approval** from an IRB or another authorized

oversight body *(IRB Exemption Letter may be requested)*.

10/11/2021 2:24PM

ILM Peel, Retinal Hydration, Fibrin Glue, and C3F8 Gas for Recalcitrant Macular Holes

- Kamal Kishore, MD, MBBS
- Kurt Hanebrink
- Lukman Faniyi

OBJECTIVE Can the combination of ILM peel, retinal hydration, fibrin glue, C3F8 gas followed by one week of face-down positioning successfully close recalcitrant macular holes?

PURPOSE There is no consensus on the management of difficult macular holes (large, chronic, flat, associated with retinal detachment, post-traumatic, high myopes etc). We report our initial experience with ILM peel, retinal hydration, fibrin glue, C3F8 gas and one week of face-down positioning in the management of difficult macular holes.

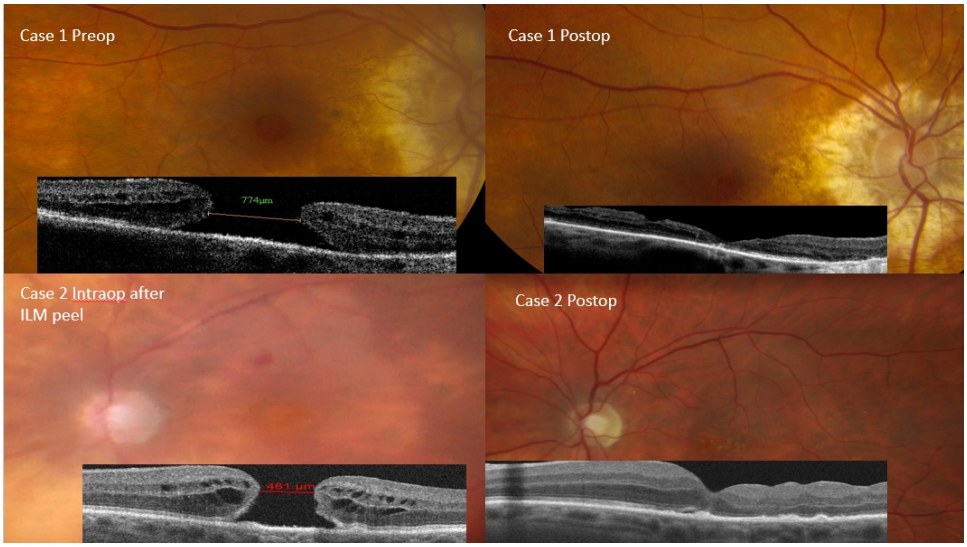
METHODS Surgery: 25 g ppv, ilm peel (BBG or ICG), fax, injection of fibrin glue, 18% C3F8 gas. Face down for 1 week. Age/Sex Size (min diameter, µm) Vision Age of hole Other features Case 1 93/F 774 CF >1 year Flat on OCT Case 2 76/M 461 CF >3 years Case 3 63/M 633 CF >1 year Flat on OCT MH discovered during RD surgery (25 g ppv, SB, laser, oil) four months ago, for RD with PVR (8 months old) Case 4 59/M 652 CF 11 months MH discovered during RD surgery (25 g ppv, SB, laser, gas) 7 months prior to MH surgery. RD 4 months old at the time of surgery

RESULTS All holes closed successfully. Case 1: 20/200, one-year FU Case 2: 20/60, 3 months FU Case 3: 20/200, 3 months FU Case 4: 20/200, 6 months FU All eyes were pseudophakic. No complications.

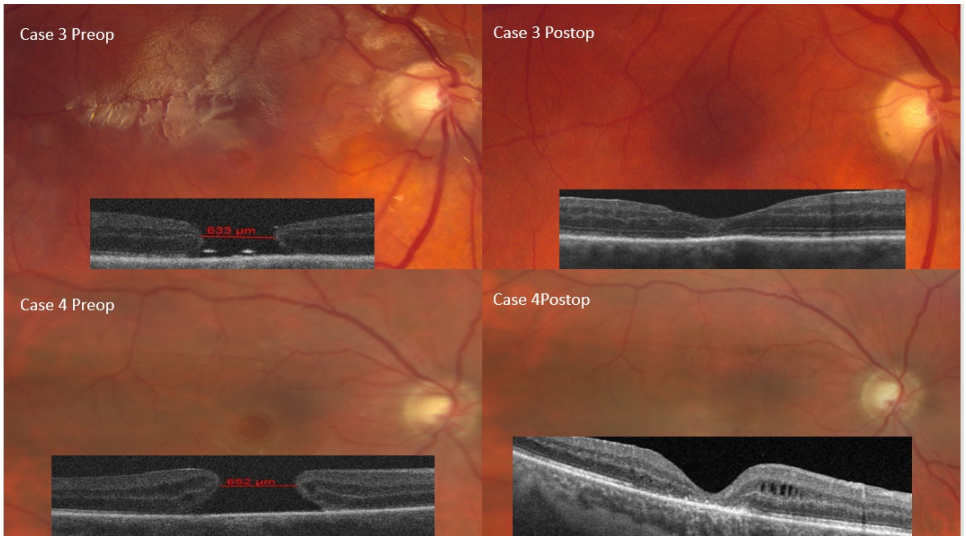
CONCLUSION ILM peel, retinal hydration, Fibrin glue and C3F8 gas followed by one week of face-down positioning may be helpful in closing difficult macular holes. ILM peel

improves retinal compliance and relieves tangential traction, retinal hydration creates retinal redundancy, fibrin glue brings the edges of the hole together, and gas keeps the hole closed by lateral surface tension.

IRB APPROVAL Yes — *IRB Approval Letter may be requested*.



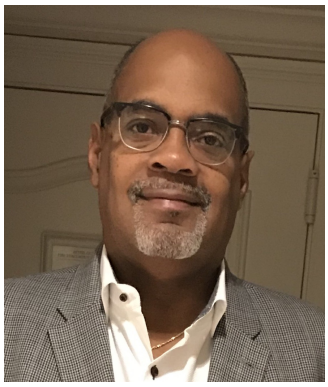
Case 1 and Case 2. Preop Fundus photos and OCT left, and post-op fundus photos and OCT right



Case 3 and Case 4. Preop fundus photo and OCT, left and post-op fundus photos and OCT, right.

10/11/2021 2:28PM

The Role of Face Down Positioning in the Successful Repair of Full Thickness Macula Holes



- Keith A. Warren, MD
- Alexis Warren, MD
- Thai Lor, BS

OBJECTIVE Is face down positioning necessary for successful macular hole repair?

PURPOSE The buoyancy effect of intraocular gas has long been proposed to be critical to successful macula hole repair. Recent studies have suggested a role of internal limiting membrane peeling in the successful closure without face down positioning. We analyzed a retrospective consecutive case series of patients treated with pars plana vitrectomy, ILM peel and gas tamponade without face down positioning.

METHODS 35 eyes in 33 patients diagnosed with Stage 3 or 4 idiopathic macular hole (2016-2019) were treated by 23 gauge pars plana vitrectomy, ILM peel and SF6 gas tamponade by a single surgeon. Phakic patients underwent combined phacoemulsification and vitrectomy surgery. Patients were instructed not to position face down but were permitted to assume any position except supine. Patients with other ocular comorbidities, previous vitrectomy or with traumatic macular were excluded. Average length of follow up was 18 months. The primary outcome measured was successful closure of the macula hole by a single operation. Other variable evaluated were visual acuity and diameter of macular hole.

RESULTS There were 25 (71.4%) female and 10(28.6%) male. Mean age was 72.3 years. There were 21 right eyes (60.0%) and 14 (40.0%) left eye. 20 (57.1%) eyes underwent combined phaco-vitrectomy. Mean pre-operative vision was 0.64 LogMar with a mean post-operative vision of 0.14 LogMar. The average pre operative macular hole diameter was 520 +/- 197µ. 32 of 35 (91.42%) eyes closed with a single operation. Early posterior capsular opacity was noted in 3 eyes (15.0%) that underwent combined phaco-vitrectomy. No other complications were noted. While the average hole base diameter (BD) of the 3 eyes was 935µ, there did not appear to be a statistically significant relationship between the diameter

of the macula hole, duration of symptoms or lenticular status and hole closure. Eyes that underwent combined phaco-vitrectomy had a slightly decreased final vision when compared to those who underwent vitrectomy alone, but this difference was not statistically significant.

CONCLUSION Primary macular hole repair without facedown positioning was successful in 91% of eyes. The average BD, and duration did not have a significant effect on successful repair. Visual acuity improvement was associated with hole closure, shorter duration (< 6 months) and smaller BD (<400µ). This study may suggest that ILM peel plays an important role in macular hole closure, not gas tamponade.

IRB APPROVAL No — I **did not receive IRB approval** or a determination that the study/activity was exempt or that it did not require IRB approval. **Complete a Human Subject Research application** for review by the ASRS Human Research Committee. **Your abstract will not be considered without a completed application.** The ASRS HRC will review the information provided to determine whether the study qualifies as exempt or otherwise not requiring IRB approval. The ASRS HRC is not constituted as an IRB and thus cannot provide IRB approval for activities that require such.