

**Re: Ishida et al: Risk Factors, Onset, and Progression of Epiretinal Membrane after 25-Gauge Pars Plana Vitrectomy for Rhegmatogenous Retinal Detachment**



**TO THE EDITOR:** We read the study by Ishida et al<sup>1</sup> investigating epiretinal membrane (ERM) formation after pars plana vitrectomy for rhegmatogenous retinal detachment. The authors found a higher prevalence of ERM in eyes with vitreous hemorrhage and in those without inner limiting membrane (ILM) peeling. Premacular membrane is the preferable term to *epiretinal membrane*, because *epi* means adjacent (could be subretinal) and *retina* is not specific (includes peripheral proliferative vitreoretinopathy membranes), whereas *premacular membrane* specifically refers to the presence of a membrane in front of the macula that causes macular pucker.<sup>2</sup>

Previous studies<sup>3</sup> found that a substantial proportion of eyes with rhegmatogenous retinal detachment had residual cortical vitreous adherent to the retina despite clinical evidence of posterior vitreous detachment. When this phenomenon is the result of a split between the lamellae of the posterior vitreous cortex it is called *vitreoschisis*.<sup>4</sup> Studies have found that vitreoschisis is prevalent in eyes with macular pucker and is believed to be important in its pathogenesis (Fig 1). Vitreoschisis occurs when vitreous gel liquefaction exceeds the degree of weakening of vitreoretinal adherence, such that anomalous posterior vitreous detachment causes vitreoschisis by splitting between the lamellae of the posterior vitreous cortex (Fig 1), leaving the outer layer of the posterior vitreous cortex attached to the retina.<sup>5</sup> It has been hypothesized that macular pucker can result when vitreoschisis occurs at a level of the vitreous cortex anterior to the hyalocytes (located 20–50 μm anterior to the ILM), which then remain attached to the macula and stimulate the migration and

proliferation of circulating monocytes and retinal glial cells, later inducing the membrane contraction that puckers the macula.<sup>5</sup> In the study of Ishida et al,<sup>1</sup> vitreous hemorrhage was shown to be a risk factor for development of postoperative macular pucker, with blood cells, platelets, cytokines, and growth factors thought to be contributing factors. Because a high prevalence of vitreoschisis has been found in other circumstances with reason to believe a role exists for vitreoschisis in the pathogenesis of macular pucker, what information do the authors have concerning vitreoschisis as a risk factor for postoperative macular pucker developing in their patients with rhegmatogenous retinal detachment? Specifically, how many patients showed evidence of vitreoschisis from preoperative OCT, intraoperative visualization or imaging, or both and what is the correlation with development of postoperative macular pucker?

Should vitreoschisis be an important factor, as we suspect it is, then preoperative identification would be important in guiding management. Such cases may well benefit from preventative ILM peeling in the macula, a maneuver that Ishida et al<sup>1</sup> found was not associated with postoperative macular pucker. Alternatively, preoperative or intraoperative pharmacologic vitreolysis with interfactant agents, such as ocriplasmin and nattokinase, could separate the entire posterior vitreous cortex from the ILM, preventing macular pucker by eliminating hyalocyte adherence to the macula as well as the collagenous substrate for monocyte and glial cell migration and proliferation into contractile membranes.

“An ounce of prevention is worth a pound of cure.”

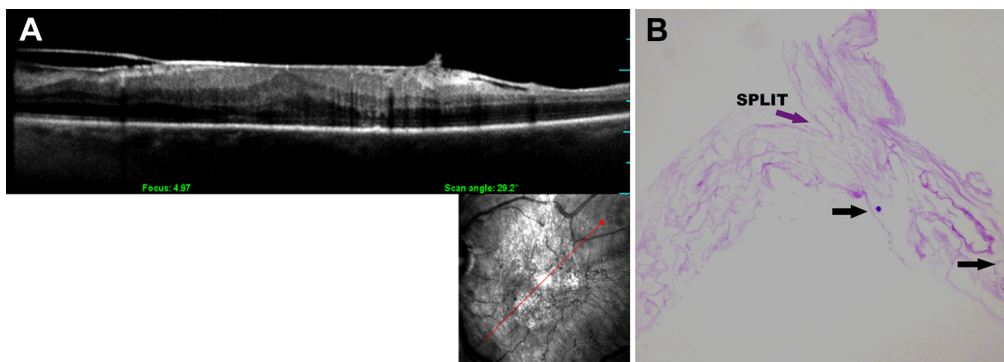
—Benjamin Franklin, 1736

WEI GUI, MD

J. SEBAG, MD, FRCOPHTH

VMR Institute for Vitreous Macula Retina, Huntington Beach, California

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**Figure 1.** A, OCT/Scanning Laser Ophthalmoscopy imaging of a premacular membrane (PMM) with vitreoschisis. B, Photomicrograph showing the very same PMM removed at surgery for macular pucker. A split in the membrane (purple arrow) consistent with the preoperative imaging is visible and hyalocytes are present in the posterior aspect of the PMM (black arrows; stain, periodic acid–Schiff; original magnification, × 225). (From Gupta P, Yee KMP, Garcia P, et al. Vitreoschisis in macular diseases. *Br J Ophthalmol*. 2011;95:376–380. © 2011 Reprinted with permission.)

Correspondence:

J. Sebag, MD, FRCOphth, VMRI Institute for Vitreous Macula Retina, Huntington Beach, CA 92647. E-mail: [jsebag@VMRIinstitute.com](mailto:jsebag@VMRIinstitute.com).

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**REPLY:** We thank Drs Gui and Sebag for their comments on our work.<sup>1</sup> Their recommended term, *premacular membrane*, may be the most suitable expression here.



However, in our study, we defined epiretinal membrane (ERM) as a hyperreflective line above the inner retinal surface, accompanied by deformation of the foveal pit, and we described it in the Abstract and Methods. Therefore, we believe that this word would not be misleading to the readers.

In our study, we excluded patients with preoperative ERM (see the exclusion criteria), and no patients showed preoperative vitreoschisis that was detected on OCT findings, as Drs Gui and Sebag pointed out in their figure.<sup>1,2</sup> Although we agree with their opinion that residual cortical vitreous adherents to the retina resulting from vitreoschisis would cause the postoperative macular pucker or ERM, it would be difficult to detect all of them by OCT before ERM formation. Additionally, the intraoperative evidence of vitreoschisis was not investigated in our study, and unfortunately, we do not have such data. Apart from vitreoschisis, some hypothetical causes of ERM formation were reported, such as microbreaks in the internal limiting membrane (ILM) resulting from posterior vitreous detachment.<sup>3</sup> That is, various factors would be associated with the development of ERM after pars plana vitrectomy for rhegmatogenous retinal detachment (RRD).

The preoperative or intraoperative use of interfacant agents like ocriplasmin or nattokinase was not discussed in our study, and we would appreciate if further study is conducted to elaborate on this.

However, there would be some problems. The primary disease of our study is RRD and its surgery is usually an emergency; therefore, there would not be enough time for these drugs to be effective in some cases. Regarding the intraoperative use of these agents, their effectiveness is unknown because the vitreous body is removed and drug metabolism may be altered. Further, regarding the cost issue, it is not certain whether these drugs can be used for patients requiring pars plana vitrectomy simultaneously. Although the use of interfacant agents like ocriplasmin would cause posterior vitreous detachment,<sup>4</sup> further studies are required to determine whether that can resolve vitreoschisis and associated residual vitreous cortex.

Currently, ILM peeling for only high-risk cases during pars plana vitrectomy for RRD would be the most effective and reasonable strategy to prevent postoperative ERM. That is, ILM peeling should be considered in RRD patients with vitreous hemorrhage, which was detected as the risk factor of postoperative ERM in our study.<sup>1</sup> However, as we described in the study's limitations, the surgeon's arbitrariness regarding ILM peeling possibly was associated with our results, and further studies would be needed in the future.

YASUAKI IWAMA, MD<sup>1,2</sup>  
YUICHIRO ISHIDA, MD<sup>1,3</sup>  
HIROSHI NAKASHIMA, MD<sup>1</sup>  
TOSHIHIDE IKEDA, MD<sup>1</sup>  
KAZUYUKI EMI, MD, PhD<sup>1</sup>

<sup>1</sup>Department of Ophthalmology, Osaka Rosai Hospital Clinical Research Center for Optical Sensory Organ Disability, Osaka, Japan;

<sup>2</sup>Department of Ophthalmology, Osaka University Graduate School of Medicine, Osaka, Japan; <sup>3</sup>Department of Ophthalmology, Aichi Medical University, Nagakute, Japan

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