Vitreomacular interface disorders

Ghanbari MD
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Human vitreous after dissection of the sclera, choroid, and retina.
Lamellar structure of the posterior vitreous cortex (PVC) in the monkey. V = Vitreous; R = Retina; ILL = Internal Limiting Lamina.
Yellow lines represent vitreoretinal interface bonds constituted by laminin, fibronectin, and collagen types VI, VII, XVIII.
• Normal aging is accompanied by a number of physiological changes in the vitreous gel.

• After the age of 40, it undergoes progressive liquefaction (synchisis), with fluid escaping through defects in the posterior vitreous cortex, eg, those at the optic disc or prepapillary hole.
Most adherent

Least adherent

Moderately adherent


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Premacular Liquefied Lacuna
Begins Early in Life

27-year-old woman
Earliest Stage of PVD

Asymptomatic 64-year-old woman
Liquefied pocket and parafoveal vitreous separation
Early Stages of PVD

64-year-old woman
Early Stages of PVD

Asymptomatic 69-year-old woman
• Stage 0: No evidence of PVD
• Stage 1: Perifoveal vitreous detachment with vitreofoveal adhesion.
• Stage 2: Perifoveal vitreous detachment with no vitreofoveal adhesion.
• Stage 3: Complet PVD except for vitreopapillary adhesion
• Stage 4: Complete PVD
Acute PVD
Weiss Ring (Vogt Ring)
• Posterior vitreous detachment (PVD) is the result of a complex and inevitable set of events that occurs as the eye ages.

• It manifests as gel liquefaction and weakening of vitreoretinal adhesion.

• Imaging of the VMI with OCT reveals that PVD usually begins in the perifoveal macula.
YOUTH
GEL VITREOUS & VIT-RET ADHESION

AGING
Liquefaction & Vit-RET Dehiscence

COMPLETE PVD

Liquefaction without
Vitreo-Retinal Dehiscence

ANOMALOUS PVD

Partial Thickness = VITREOSCHISIS

PREMACULAR MEMBRANE

Centrifugal (outward) Contraction

Centripetal (inward) Contraction

MACULAR HOLE

MACULAR PUCKER

Full-thickness but only Partial PVD

Peripheral Separation Posterior Traction

Posterior Separation Peripheral Traction

MACULA

OPTIC DISC

VMTS
EXUD AMD

Vitreo-Papillary Traction

Retinal Tears & Detachment
The vitreous cortex temporally has a lamellar structure with two layers (arrows). The inner layer is detached from the outer lamellae. In this subject, the vitreous pocket is undetectable in both eyes.
Symptoms of PVDs

- Flashing lights
- Floaters
- Acute PVD have 15% retinal tear.
- PVD with vit. H emorrhage 50%- 70% have retinal tears.
• Spectral-domain optical coherence tomography images of early stages of posterior vitreous detachment (PVD) in asymptomatic individuals.

• (Top) Earliest detectable evidence for PVD (arrow) in a 64-year-old woman. (Second row) Evolving perifoveal PVD with broad residual macular adhesion in a 54-year-old man.

• (Third row) Perifoveal PVD with focal foveolar vitreous attachment in a 64-year-old woman (note premacular liquefied pocket).

• (Bottom) PVD extending through the entire macular region in a 69-year-old woman.
The International Vitreomacular Traction Study Group Classification of Vitreomacular Adhesion, Traction, and Macular Hole

Jay S. Duker, MD, Peter K. Kaiser, MD, Susanne Binder, MD, Marc D. de Smet, MD, Alain Gaudric, MD, Elias Reichel, MD, Srinivas R. Sadda, MD, Jerry Sebag, MD, Richard F. Spaide, MD, Peter Stalmans, MD, PhD

Objective: The International Vitreomacular Traction Study (IVTS) Group was convened to develop an optical coherence tomography (OCT)-based anatomic classification system for diseases of the vitreomacular interface (VMI).

Design: The IVTS applied their clinical experience, after reviewing the relevant literature, to support the development of a strictly anatomic OCT-based classification system.

Participants: A panel of vitreoretinal disease experts was the foundation of the International Classification System.

Methods: Before the meeting, panel participants were asked to review 11 articles and to complete 3 questionnaires. The articles were preselected based on searches for comprehensive reviews covering diseases of the VMI. Responses to questionnaires and the group's opinions on definitions specified in the literature were used to guide the discussion.

Main Outcome Measures: Optical coherence tomography-based anatomic definitions and classification of vitreomacular adhesion, vitreomacular traction (VMT), and macular hole.

Results: Vitreomacular adhesion is defined as perifoveal vitreous separation with remaining vitreomacular attachment and unperturbed foveal morphologic features. It is an OCT finding that is almost always the result of normal vitreous aging, which may lead to pathologic conditions. Vitreomacular traction is characterized by anomalous posterior vitreous detachment accompanied by anatomic distortion of the fovea, which may include pseudocysts, macular schisis, cystoid macular edema, and subretinal fluid. Vitreomacular traction can be subclassified by the diameter of vitreous attachment to the macular surface as measured by OCT, with attachment of 1500 μm or less defined as focal and attachment of more than 1500 μm as broad. When associated with other macular disease, VMT is classified as concurrent. Full-thickness macular hole (FTMH) is defined as a foveal lesion with interruption of all retinal layers from the internal limiting membrane to the retinal pigment epithelium. Full-thickness macular hole is primary if caused by vitreous traction or secondary if directly the result of pathologic characteristics other than VMT. Full-thickness macular hole is subclassified by size of the hole as determined by OCT and the presence or absence of VMT.

Conclusions: This classification system will support systematic diagnosis and management by creating a clinically applicable system that is predictive of therapeutic outcomes and is useful for the execution and analysis of clinical studies.

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Table 1. The International Vitreomacular Traction Study Classification System for Vitreomacular Adhesion, Traction, and Macular Hole

<table>
<thead>
<tr>
<th>Classification</th>
<th>Subclassification</th>
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</thead>
<tbody>
<tr>
<td>Vitreomacular adhesion</td>
<td>Size: focal ($\leq 1500$ μm) or broad ($&gt;1500$ μm)</td>
</tr>
<tr>
<td></td>
<td>Isolated or concurrent</td>
</tr>
<tr>
<td>VMT</td>
<td>Size: focal ($\leq 1500$ μm) or broad ($&gt;1500$ μm)</td>
</tr>
<tr>
<td></td>
<td>Isolated or concurrent</td>
</tr>
<tr>
<td>Full-thickness macular hole</td>
<td>Size: small ($&lt;250$ μm), medium ($250-\leq 400$ μm),</td>
</tr>
<tr>
<td></td>
<td>or large ($&gt;400$ μm)</td>
</tr>
<tr>
<td></td>
<td>Status of vitreous: with or without VMT</td>
</tr>
<tr>
<td></td>
<td>Cause: primary or secondary</td>
</tr>
</tbody>
</table>

VMT = vitreomacular traction.
VITREOMACULAR ADHESIONS
Table 2. Correlation between Commonly Used Clinical Macular Hole Stages and the International Vitreomacular Traction Study Classification System for Vitreomacular Adhesion, Traction, and Macular Hole

<table>
<thead>
<tr>
<th>Full-Thickness Macular Hole Stages in Common Use</th>
<th>International Vitreomacular Traction Study Classification System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>VMA</td>
</tr>
<tr>
<td>Stage 1: impending macular hole</td>
<td>VMT</td>
</tr>
<tr>
<td>Stage 2: small hole</td>
<td>Small or medium FTMH with VMT</td>
</tr>
<tr>
<td>Stage 3: large hole</td>
<td>Medium or large FTMH with VMT</td>
</tr>
<tr>
<td>Stage 4: FTMH with PVD</td>
<td>Small, medium, or large FTMH without VMT</td>
</tr>
</tbody>
</table>

FTMH = full-thickness macular hole; PVD = posterior vitreous detachment; VMA = vitreomacular adhesion; VMT = vitreomacular traction.
OCT Based Definition and Classification of Vitreomacular Adhesion

• VMA is the equivalent of a stage 1 PVD
• Most eyes have complete vitreoretinal adhesion at birth, so the concept of vitreoretinal adhesion and VMA is a normal state.
VMA

- (1) Focal ($\leq 1500 \mu m$)
- (2) Broad ($>1500 \mu m$)
If detectable retinal anatomic changes occur on OCT, with concurrent vitreous status showing perifoveolar PVD, the eye is characterized as having VMT.
<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Abnormal Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased visual acuity</td>
<td>Cystoid macular edema</td>
</tr>
<tr>
<td>Scotomata</td>
<td>Retinoschisis</td>
</tr>
<tr>
<td>Photopsia</td>
<td>Tractional retinal detachment</td>
</tr>
<tr>
<td>Micropsia</td>
<td>Macular hole</td>
</tr>
<tr>
<td>Metamorphopsia</td>
<td>Retinal folds</td>
</tr>
<tr>
<td></td>
<td>Retinal tears</td>
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<tr>
<td></td>
<td>Retinal vessel avulsion</td>
</tr>
<tr>
<td></td>
<td>Optic disc edema</td>
</tr>
</tbody>
</table>
OCT Based Definition and Classification of Vitreomacular Traction

• (1) Evidence of perifoveal vitreous cortex detachment from the retinal surface;
• (2) macular attachment of the vitreous cortex within a 3-mm radius of the fovea; and
• (3) Association of attachment with distortion of the foveal surface, intraretinal structural changes, elevation of the fovea above the RPE, or a combination there of, but no full-thickness interruption of all retinal layers.
VMT Size:

- Focal ($\leq 1500$ mm) or
- Broad ($> 1500$ mm)
- Isolated or concurrent
• Broad areas of attachment with traction can cause:
  • **generalized thickening of the macula**
  • **vascular leakage on FA**
  • **macular schisis,**
  • **cystoid macular edema.**
Focal areas of vitreous attachment

- Foveal surface distortion.
- Elevate the foveal floor,
- pseudocysts within the central macula
- Combination
• The presence of pseudocysts usually is associated with diminished visual acuity and visual distortion.

• After release of traction, pseudocysts generally resolve over time with little remaining visual deficit.
Spectral-domain optical coherence tomography scan from an eye with neovascular age-related macular degeneration showing associated stage 1 posterior vitreous detachment with broad vitreomacular adhesion zone.
Relationship to Epiretinal Membrane Formation.

• Autopsy studies reveal that residual vitreous remains on the surface of the retina in nearly half of all eyes with PVD.

• This condition is called vitreoschisis
The vitreous cortex temporally has a lamellar structure with two layers (arrows). The inner layer is detached from the outer lamellae. In this subject, the vitreous pocket is undetectable in both eyes.
Epiretinal membrane

• This residual vitreous may proliferate to form an epiretinal membrane (ERM) at any stage of vitreous separation.

• Clinical studies uniformly show a high incidence of apparent PVD in eyes with macular pucker.
• ERM composed of:
  1. Glial cells
  2. Laminocytes (histiocytes).
CLASSIFICATION OF ERM

• Grade 0: Cellophane Maculopathy A transparent membrane without distortion of the underlying retina is observed.
• Grade 1: Crinkled Cellophane Maculopathy

• As the disease progresses, shrinkage or contraction of the iERM results in irregular wrinkling of the inner layers of the retina.
Grade 2: Preretinal Macular Fibrosis

• The iERM is characterized by a thicker and more opaque membrane obscuring the underlying retinal vasculature and a marked full-thickness retinal distortion.
• Retinal edema,
• Small retinal hemorrhages,
• Cotton-wool spots,
• Exudates
• Opaque membranes.
Approximately 80% of patients with Grade 2 iERM will have symptoms of blurred vision and/or metamorphopsia.
• In general, iERM is a chronic disease, and its onset and progression are usually slow. **According to the BlueMountain Eye study, the 5-year cumulative progression rate from Grade 0 to Grade 2 iERM was reported as 9.3%,** and the overall progression, regression, and stable rates were 28.6, 25.7, and 38.8%, respectively.
INDICATIONS OF TREATMENT

- Decreased vision
- Visual symptoms
Management

• Surgical Management of Idiopathic Epiretinal Membrane

• *Trans pars plana vitrectomy and epiretinal membrane peeling have been used in patients with symptomatic visual disturbances as a standard procedure.*

• However, in 10% to 21% of cases, the ERMs recurred, and 3% of recurrent cases required a second surgical intervention.
• Therefore, additional ILM peeling is advised to achieve the complete removal of epi-ILM and sub-ILM proliferation, thus eliminating the scaffold for further proliferation.

• Several clinical series reported that ILM peeling seems to give better results than non-ILM peeling.
• In both groups, equivalent efficacy and safety profiles in terms of final visual outcomes were found, whereas the ERM recurrence rate was lower in the ILM peeling than in the non-ILM peeling group.
Pharmaceutical Management of iERM and Associated Ocular Disorders

- Recent clinical data showed that preoperative cystoid macular edema is correlated to the presence of postoperative, persistent intraretinal cysts,
- whereas an increased, preoperative central retinal thickness is correlated to an increased, postoperative central retinal thickness.
• Topical antiinflammatory agents, including nonsteroidal antiinflammatory drugs, and dorzolamide might possibly be beneficial in the resolution of macular edema after vitrectomy for iERM.

• Schoenberger et al.\textsuperscript{90} reported that the administration of topical nonsteroidal antiinflammatory drugs as compared with a placebo, resulted in more rapid reduction in macular volume.
Full-Thickness Macular Hole

- Introduction and Definition:
  - Full-thickness macular hole is an anatomic defect in the fovea featuring interruption of all neural retinal layers from the ILM to the RPE.
Optical Coherence Tomography Based Full-Thickness Macular Hole Classification System

• Size of Hole,
• Presence or Absence of Vitreomacular Traction,
• Cause.
• The OCT-based measurements of minimum hole width (aperture size) predict anatomic treatment with both medications and surgery.
• A small FTMH features an aperture size of less than 250 µm
The cutoff for small FTMHs at 250 µm is derived from studies showing that these holes are associated with a small rate of spontaneous closure, have a very high closure rate with vitrectomy.
• A medium FTMH is defined by aperture size from 250 to 400 µm
• Studies exploring postsurgical FTMH closure rates by aperture size consistently show a very high anatomic closure rate (>90% in all recent series) with complete removal of residual hyaloid, with or without ILM peeling.
• Nearly half of FTMHs are large (diameter >400 mm) at the time of diagnosis.

• Vitrectomy with ILM peel is associated with high closure rates (90%-95%), even for these large holes. Without an ILM peel, the vitrectomy success rate is closer to 75%.

• In the few eyes with large FTMH that have undergone pharmacologic vitreolysis, no anatomic success has been recorded.
Status of the Vitreous: Presence or Absence of Vitreomacular Traction.

• In the OCT-based anatomic system, FTMHs are categorized secondarily according to absence or presence of vitreous attachment.

• Only macular holes with concurrent VMT should be considered for pharmacologic vitreolysis.
• Primary Versus Secondary Full-Thickness Macular Hole.
• Full-thickness macular hole can be subdivided into primary and secondary forms.
• Primary FTMH (VMT)idiopathic) results anomalous PVD (VMT).
• A secondary FTMH is caused directly by other pathology.
secondary FTMH

- (1) blunt trauma,
- (2) lightning strike,
- (3) high myopia
- (4) macular schisis,
- (5) macular telangiectasia type 2,
- (6) wet macular degeneration,
- (7) macroaneurysm,
- (8) surgical trauma.
- (9) diabetic macular edema,
- (10) retinal vascular occlusions
- (11) uveitis.
It recently was shown that fovea destabilization resulting from traction-induced damage to the inner fovea, occurring before or coincident with spontaneous vitreofoveal separation, may predispose some eyes to macular hole formation.
Impending Macular Hole

• A special circumstance exists when an individual develops FTMH in one eye and OCT reveals VMA or VMT in the fellow eye.

• Studies show that these fellow eyes are at increased risk for development of FTMH.
LMH

• Definition:
• Irregular foveal contour
• Defect in the inner fovea (may not have actual loss of tissue)
• Intraretinal splitting (schisis), typically between the outer plexiform and outer nuclear layers
• Maintenance of an intact photoreceptor layer
Lamellar macular hole usually progresses slowly and is thought to arise from incomplete FTMH formation, centripetal traction from ERM, or both, although current understanding of LMH evolution and surgical indications remains incomplete.

Forces acting on the central macula include an ERM in some patients and varying anteroposterior and tangential forces from the vitreous in others.
Lamellar macular hole

- Most patients with LMH have mild metamorphopsia, limited central vision loss, and stable visual acuity.
• Surgery for LMH remains controversial, and patient selection is crucial.
• Results of surgical interventions for LMH are variable, with anywhere between 25% and 75% of patients achieving improved visual outcomes, typically because of peeling of the associated ERM.
• Pseudomacular hole
OCT confirms the diagnosis on the basis of the following 4 characteristics

- (1) invaginated or heaped foveal edges,
- (2) concomitant ERM with central opening,
- (3) steep macular contour to the central fovea with near-normal central foveal thickness,
- (4) no loss of retinal tissue.
Perhaps the most characteristic feature of macular pseudohole is the presence of a concomitant ERM on the surface of the macula that distorts the foveal contour into a shape with a steep slope; altered light reflex also is observed commonly.
• Management of macular pseudohole typically is conservative.
• If the ERM is associated with a significant decline in vision,
• pars plana vitrectomy with membrane peeling can be performed.
• Dr Kaiser presented six-month follow-up data on “Ocriplasmin for the Treatment of Macular Hole: Phase III Results.” The main points included:
• Approximately 40.6% of patients with full thickness macular hole (FTMH) achieved closure compared with 17% on placebo (p=0.004)
• Approximately 58% of patients with FTMHs smaller than 250 μm saw closure with ocriplasmin compared with just 20% in placebo patients
• 27% of patients gained ≥ 3 lines in visual acuity after six months of treatment with ocriplasmin, compared with 13% on placebo
Cost Evaluation of Surgical and Pharmaceutical Options in Treatment for Vitreomacular Adhesions and Macular Holes

Jonathan S. Chang, MD, William E. Smiddy, MD

Objective: To evaluate cost-effectiveness and cost utilities for treatment options for vitreomacular adhesions (VMAs) and full-thickness macular holes (MHs).


Participants: There were no participants.

Methods: Outcomes of published clinical trials (index studies) of surgical treatment of VMAs and MHs and a prospective, multicenter clinical trial of pharmaceutical vitreolysis with intravitreal ocriplasmin with saline control were used to generate a model for costs of treatment and visual benefits. All techniques were assumed to result in a 2.5-line visual benefit if anatomy was resolved. Markov analysis, with cost data from the Centers for Medicare and Medicaid Services, was used to calculate imputed costs for each primary treatment modality in a facility setting, with surgery performed in an ambulatory surgery center serving as the highest end of the range and nonfacility setting with surgery performed in an ambulatory surgery center serving as the lowest end of the range.

Main Outcome Measures: Imputed costs of therapy, cost per line saved, cost per line-year saved, cost per quality-adjusted life years (QALYs).

Results: When pars plana vitrectomy (PPV) was selected as the primary procedure, the overall imputed cost ranged from $5802 to $7931. The cost per line was $2368 to $3237, the cost per line-year saved was $163 to $233 and the cost per QALY was $5444 to $7442. If intravitreal injection of ocriplasmin was the primary procedure, the overall imputed cost was $8767 to $10977. The cost per line ranged from $3549 to $4456, the cost per line-year saved was $245 to $307, and the cost per QALY was between $8159 and $10244. If intravitreal saline injection was used as a primary procedure, the overall imputed cost was $5828 to $8098. The cost per line was $2374 to $3299, the cost per line-year saved was $164 to $227, and the cost per QALY was $5458 to $7583.

Conclusions: As a primary procedure, PPV was the most cost-effective therapy in this model. The other treatments had similar costs per QALY saved and compare favorably with costs of therapy for other retinal diseases. Ophthalmology 2014;121:1720-1726 © 2014 by the American Academy of Ophthalmology.
Pathologies inducing contraction or shrinkage of the vitreoretinal interface

- Vitreoretinal macular adhesion
- Vitreomacular traction syndrome
- Macular epiretinal membranes
- Macular holes
- Lamellar Macular holes
- Proliferative microangiopathies (DR, RVO)
- Ocriplasmin: Indications?