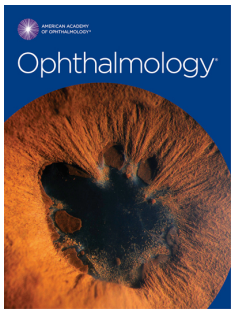
Journal Pre-proof



Idiopathic Macular Hole Preferred Practice Pattern®

Christina J. Flaxel, MD, Chair, Ron A. Adelman, MD, MPH, MBA, FACS, Steven T. Bailey, MD, Retina Society Representative, Amani Fawzi, MD, Macula Society Representative, Jennifer I. Lim, MD, Gurunadh A. Vemulakonda, MD, American Society of Retina Specialists Representative, Gui-shang Ying, MD, PhD, Methodologist

PII: S0161-6420(19)32093-7

DOI: https://doi.org/10.1016/j.ophtha.2019.09.026

Reference: OPHTHA 10934

To appear in: *Ophthalmology*

Received Date: 20 September 2019

Accepted Date: 20 September 2019

Please cite this article as: Flaxel CJ, Adelman RA, Bailey ST, Fawzi A, Lim JI, Vemulakonda GA, Ying G-s, Idiopathic Macular Hole Preferred Practice Pattern®, *Ophthalmology* (2019), doi: https://doi.org/10.1016/j.ophtha.2019.09.026.

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Idiopathic Macular Hole Preferred Practice Pattern®

Elsevier to replace this cover page with the color PDF.
Elsevier to renumber the pages and Table of Contents, as necessary.

Correspondence:
Ali A. Al-Rajhi, PhD, MPH, American Academy of Ophthalmology, P. O. Box 7424, San Francisco, CA 94120-7424. E-mail: aalrajhi@aao.org.
.

RETINA/VITREOUS PREFERRED PRACTICE PATTERN® DEVELOPMENT PROCESS AND PARTICIPANTS

The **Retina/Vitreous Preferred Practice Pattern® Panel** members wrote the Idiopathic Macular Hole Preferred Practice Pattern® ("PPP") guidelines. The PPP Panel members discussed and reviewed successive drafts of the document, meeting in person twice and conducting other review by e-mail discussion, to develop a consensus over the final version of the document.

Retina/Vitreous Preferred Practice Pattern Panel 2018–2019
Christina J. Flaxel, MD, Chair
Ron A. Adelman, MD, MPH, MBA, FACS
Steven T. Bailey, MD, Retina Society Representative
Amani Fawzi, MD, Macula Society Representative
Jennifer I. Lim, MD
Gurunadh A. Vemulakonda, MD, American Society of Retina Specialists Representative
Gui-shang Ying, MD, PhD, Methodologist

We thank our partners, the Cochrane Eyes and Vision US Satellite (CEV@US), for identifying reliable systematic reviews that we cite and discuss in support of the PPP recommendations.

The Preferred Practice Patterns Committee members reviewed and discussed the document during a meeting in June 2019. The document was edited in response to the discussion and comments.

Preferred Practice Patterns Committee 2019
Robert S. Feder, MD, Chair
Roy S. Chuck, MD, PhD
Steven P. Dunn, MD
Christina J. Flaxel, MD
Steven J. Gedde, MD
Francis S. Mah, MD
Randall J. Olson, MD
David K. Wallace, MD, MPH
David C. Musch, PhD, MPH, Methodologist

The Idiopathic Macular Hole PPP was then sent for review to additional internal and external groups and individuals in July 2019. All those returning comments were required to provide disclosure of relevant relationships with industry to have their comments considered (indicated with an asterisk below). Members of the Retina/Vitreous Preferred Practice Pattern Panel reviewed and discussed these comments and determined revisions to the document.

FINANCIAL DISCLOSURES

In compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies (available at www.cmss.org/codeforinteractions.aspx), relevant relationships with industry are listed. The Academy has Relationship with Industry Procedures to comply with the Code (available at http://one.aao.org/CE/PracticeGuidelines/PPP.aspx). A majority (88%) of the members of the Retina/Vitreous Preferred Practice Pattern Panel 2018–2019 had no financial relationship to disclose.

Retina/Vitreous Preferred Practice Pattern Panel 2018–2019
Christina J. Flaxel, MD: No financial relationships to disclose
Ron A. Adelman, MD, MPH, MBA, FACS: No financial relationships to disclose
Steven T. Bailey, MD: No financial relationships to disclose
Amani Fawzi, MD: No financial relationships to disclose
Jennifer I. Lim, MD: Alcon Laboratories—Consultant/Advisor
Gurunadh A. Vemulakonda, MD: No financial relationships to disclose
Gui-shang Ying, MD, PhD: No financial relationships to disclose

Preferred Practice Patterns Committee 2019
Robert S. Feder, MD, Chair: No financial relationships to disclose
Roy S. Chuck, MD, PhD: Novartis—Consultant/Advisor
Steven P. Dunn, MD: No financial relationships to disclose
Christina J. Flaxel, MD: No financial relationships to disclose
Steven J. Gedde, MD: No financial relationships to disclose
Francis S. Mah, MD: Novartis—Consultant/Advisor & Lecture Fees
Randall J. Olson, MD: No financial relationships to disclose
David K. Wallace, MD, MPH: No financial relationships to disclose
David C. Musch, PhD, MPH, Methodologist: IRIDEX, Notal Vision—Consultant/Advisor

Secretary for Quality of Care
Timothy W. Olsen, MD: No financial relationships to disclose

Academy Staff
Ali Al-Rajhi, PhD, MPH: No financial relationships to disclose
Andre Ambrus, MLIS: No financial relationships to disclose
Meghan Daly: No financial relationships to disclose
Flora C. Lum, MD: No financial relationships to disclose

The disclosures of relevant relationships to industry of other reviewers of the document from January to October 2019 are available online at www.aao.org/ppp.

TABLE OF CONTENTS

OBJECTIVES OF PREFERRED PRACTICE PATTERN® GUIDELINES

As a service to its members and the public, the American Academy of Ophthalmology has developed a series of Preferred Practice Pattern® guidelines that **identify characteristics and components of quality eye care.** Appendix 1 describes the core criteria of quality eye care.

The Preferred Practice Pattern® guidelines are based on the best available scientific data as interpreted by panels of knowledgeable health professionals. In some instances, such as when results of carefully conducted clinical trials are available, the data are particularly persuasive and provide clear guidance. In other instances, the panels have to rely on their collective judgment and evaluation of available evidence.

These documents provide guidance for the pattern of practice, not for the care of a particular individual. While they should generally meet the needs of most patients, they cannot possibly best meet the needs of all patients. Adherence to these PPPs will not ensure a successful outcome in every situation. These practice patterns should not be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the best results. It may be necessary to approach different patients' needs in different ways. The physician must make the ultimate judgment about the propriety of the care of a particular patient in light of all of the circumstances presented by that patient. The American Academy of Ophthalmology is available to assist members in resolving ethical dilemmas that arise in the course of ophthalmic practice.

Preferred Practice Pattern® guidelines are not medical standards to be adhered to in all individual situations. The Academy specifically disclaims any and all liability for injury or other damages of any kind, from negligence or otherwise, for any and all claims that may arise out of the use of any recommendations or other information contained herein.

References to certain drugs, instruments, and other products are made for illustrative purposes only and are not intended to constitute an endorsement of such. Such material may include information on applications that are not considered community standard, that reflect indications not included in approved US Food and Drug Administration (FDA) labeling, or that are approved for use only in restricted research settings. The FDA has stated that it is the responsibility of the physician to determine the FDA status of each drug or device he or she wishes to use, and to use them with appropriate patient consent in compliance with applicable law.

Innovation in medicine is essential to ensure the future health of the American public, and the Academy encourages the development of new diagnostic and therapeutic methods that will improve eye care. It is essential to recognize that true medical excellence is achieved only when the patients' needs are the foremost consideration.

All Preferred Practice Pattern® guidelines are reviewed by their parent panel annually or earlier if developments warrant and updated accordingly. To ensure that all PPPs are current, each is valid for 5 years from the approved by date unless superseded by a revision. Preferred Practice Pattern guidelines are funded by the Academy without commercial support. Authors and reviewers of PPPs are volunteers and do not receive any financial compensation for their contributions to the documents. The PPPs are externally reviewed by experts and stakeholders, including consumer representatives, before publication. The PPPs are developed in compliance with the Council of Medical Specialty Societies' Code for Interactions with Companies. The Academy has Relationship with Industry Procedures (available at www.aao.org/about-preferred-practice-patterns) to comply with the Code.

The intended users of the Idiopathic Macular Hole PPP are ophthalmologists.

METHODS AND KEY TO RATINGS

Preferred Practice Pattern® guidelines should be clinically relevant and specific enough to provide useful information to practitioners. Where evidence exists to support a recommendation for care, the recommendation should be given an explicit rating that shows the strength of evidence. To accomplish these aims, methods from the Scottish Intercollegiate Guideline Network[1] (SIGN) and the Grading of Recommendations Assessment, Development and Evaluation[2] (GRADE) group are used. GRADE is a systematic approach to grading the strength of the total body of evidence that is available to support recommendations on a specific clinical management issue. Organizations that have adopted GRADE include SIGN, the World Health Organization, the Agency for Healthcare Research and Policy, and the American College of Physicians.[3]

- All studies used to form a recommendation for care are graded for strength of evidence individually, and that grade is listed with the study citation.
- To rate individual studies, a scale based on SIGN[1] is used. The definitions and levels of evidence to rate individual studies are as follows:

I++	High-quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias
I+	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
I-	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
II++	High-quality systematic reviews of case-control or cohort studies High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
II+	Well-conducted case-control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
II-	Case-control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
III	Nonanalytic studies (e.g., case reports, case series)

- Recommendations for care are formed based on the body of the evidence. The body of evidence quality ratings are defined by GRADE[2] as follows:

Good quality	Further research is very unlikely to change our confidence in the estimate of effect
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Insufficient quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate Any estimate of effect is very uncertain

- Key recommendations for care are defined by GRADE[2] as follows:

Strong recommendation	Used when the desirable effects of an intervention clearly outweigh the undesirable effects or clearly do not
Discretionary recommendation	Used when the trade-offs are less certain—either because of low-quality evidence or because evidence suggests that desirable and undesirable effects are closely balanced

- The Highlighted Findings and Recommendations for Care section lists points determined by the PPP Panel to be of particular importance to vision and quality of life outcomes.
- All recommendations for care in this PPP were rated using the system described above. Ratings are embedded throughout the PPP main text in italics.
- Literature searches to update the PPP were undertaken in April 2018 and June 2019 in PubMed and the Cochrane Library. Complete details of the literature searches are available online at www.aao.org/ppp.

HIGHLIGHTED FINDINGS AND RECOMMENDATIONS FOR CARE

Macular holes are more common in females than in males and usually occur after age 55. There is a high rate of macular hole formation in the fellow eye (10%-15%) in the 5-year period after a macular hole occurs in the first eye.

Patients with vitreous traction and no macular hole (stage 1-A or 1-B) should be observed without treatment, because they often remain stable or even improve. Currently, there is no evidence that treatment improves the prognosis.

Most patients with stage 2 to 4 macular holes will have a poor prognosis without treatment. The visual prognosis is good following successful macular hole closure. The benefits of treatment designed to achieve macular hole closure should be discussed.

Studies report that approximately 90% of recent macular holes that are $\leq$400 µm can be closed with vitrectomy surgery.

The early detection of a macular hole is associated with both a higher closure rate after vitrectomy surgery as well as better postoperative visual acuity.

Careful removal of the internal limiting membrane (ILM) during vitrectomy surgery increases the macular hole closure rate without adversely affecting the visual acuity.

Cataract is a frequent complication of vitrectomy surgery to repair macular holes. This risk should be discussed with patients preoperatively, and postoperative monitoring is advised.

INTRODUCTION

DISEASE DEFINITION

A macular hole is a discontinuity of the neurosensory retina, located at the fovea.

PATIENT POPULATION

The patient population consists of adults often 55 years of age or older, most of whom are women, who have idiopathic macular holes.

CLINICAL OBJECTIVES

- Identify patients at risk for macular hole
- Educate high-risk patients about the reason for periodic monocular self-assessment and follow-up examination, the symptoms of a macular hole, and the need to return promptly should symptoms occur
- Follow patients who are at risk for vision loss from macular hole
- Inform patients of the risks and benefits of the treatment options for macular hole
- Optimize recovery of visual function

BACKGROUND

A macular hole is an anatomic discontinuity of the neurosensory retina that develops in the center of the macula or fovea. Typically, the patient will experience metamorphopsia and decreased visual acuity, which may progress to a central scotoma as the macular hole enlarges.[4,5] Most investigators believe that macular holes are caused by pathologic vitreoretinal traction at the fovea. Uncontrolled series also suggest that trauma may be responsible for a minority of macular hole cases.[6,7] It is important to differentiate a full-thickness macular hole (FTMH) from a lamellar macular hole, which is a partial-thickness defect in the neurosensory retina. Another macular abnormality that can simulate an FTMH on clinical examination is a macular pseudohole, a circular or oval configuration of the foveal depression that can result in perifoveal fraction from an epiretinal membrane. A pseudohole has no retinal defect but can give the false clinical appearance of an FTMH.

EPIDEMIOLOGY

The Beijing Eye Study is a population-based cross-sectional study of 4346 subjects aged 40 or older, that found an FTMH in eight eyes of seven subjects, which corresponds to a prevalence of 1.6 per 1000 Chinese people having a macular hole in this age range.[8] Another population-based cross-sectional study in rural India of 4542 people aged 30 or older found a macular hole in 18 eyes of 13 subjects, which corresponds to a prevalence of 2.7 per 1000 people having a macular hole in this age

range.[9] In the United States, a population-based retrospective study of the largely Caucasian residents (>90%) of Olmsted County, Minnesota, estimated the age- and sex-adjusted incidence of macular holes to be 7.8 people and 8.7 eyes per 100,000 people (all ages) per year.[10] In a case-control study, the majority (72%) of idiopathic macular holes occurred in women; more than 50% of holes were found in individuals 65 to 74 years of age and only 3% in those under the age of 55.[11] The 5-year risk of a patient with an FTMH of developing an FTMH in the fellow eye was approximately 10% to 15%.[12-18] Fellow eyes with a complete posterior vitreous detachment have a lower risk of developing an FTMH. In one study, it was observed that no fellow eye with a complete posterior vitreous detachment developed an FTMH during a median follow-up period of 33 months (range, 9--99 months).[15]

NATURAL HISTORY

The formation of a macular hole typically evolves over a period of weeks to months through the clinically defined stages first described by Gass,[19] although some macular holes may develop more rapidly. In both cases, macular holes are frequently detected when the patient's symptoms change relatively abruptly.[19,20] The anatomic findings from optical coherence tomography (OCT) support Gass' original observations, and an updated classification of the stages of development of FTMH is described in Table 1.

Importantly, a full-thickness retinal defect is not present in stages 1-A and 1-B. Therefore, these stages may be better classified as impending macular holes.

TABLE 1 CLINICAL STAGES AND CHARACTERISTICS OF MACULAR HOLES

Stage*	Characteristics
1-A (impending)	• Loss of the foveal depression and a yellowish foveal spot (100–200 µm in diameter) • Localized shallow detachment of the perifoveal vitreous cortex with persistent adherence to the foveola • Vitreofoveolar traction may horizontally separate (split) the retina at the fovea (pseudocyst) that corresponds to the yellow spot[21] • Epiretinal membranes are uncommon • Visual acuity ranges from 20/25 to 20/80 • Surgical intervention is not recommended
1-B (impending)	• Yellow ring 200–350 µm in diameter • Posterior extension of the pseudocyst with disruption of the outer retinal layer[21-23] • The retinal roof remains intact with persistent adherence of the posterior hyaloid to the retina[21-23] • Epiretinal membranes are uncommon • Visual acuity ranges from 20/25 to 20/80 • Surgical intervention is not recommended
2	• Small full-thickness (<400 µm in diameter) retinal defect, often eccentric • Epiretinal membranes are uncommon • Visual symptoms include metamorphopsia and decreased vision • Visual acuity 20/25 to 20/80
3	• Full-thickness hole ≥400 µm in diameter • The posterior hyaloid is separated from the macula but may remain attached at the optic disc and be attached more peripherally[21] • An operculum or a flap is present on the posterior hyaloid over the hole and is visible clinically or by means of optical coherence tomography • A cuff of subretinal fluid may be detected along with intraretinal edema and cysts • Drusen-like deposits** may be occasionally seen in the base of the hole • A rim of retinal pigment epithelium hyper/hypopigmentation is often present at the junction between edematous or detached retina and normal-appearing attached retina in long-standing cases[24] • Epiretinal membranes may be present • Visual acuity usually ranges from 20/100 to 20/400[17,24]
4	• A full-thickness hole with a diameter usually larger than stage 3 (>400 µm in diameter) • A complete posterior vitreous detachment with a Weiss ring[20,23] • A cuff of subretinal fluid, intraretinal edema, and cystoid changes are usually present • Drusen-like deposits* may be occasionally seen in the base of the hole • Epiretinal membranes are more frequent[25] • Visual acuity is more profoundly affected to 20/100 to 20/400[17,24]

* For images of macular hole and abnormalities, please visit https://www.aao.org/image/macular-hole-abnormalities

** Drusen-like or yellow deposits may represent macrophages at the level of the retinal pigment epithelium, suggesting chronicity of disease.

Evidence provided by OCT,[21,22,26-29] retinal thickness analyzer,[30] scanning laser ophthalmoscopy,[31] and observations made during vitrectomy[32,33] suggests that vitreomacular traction (VMT) or vitreomacular adhesion (VMA) is likely responsible for a stage 1-A hole. Some impending holes may resolve spontaneously and completely,[34,35] while a few may evolve into lamellar or partial-thickness holes. About to 40% to 50% of pseudocysts characteristic of impending holes may progress over a period of weeks to months to an FTMH, often passing from stage 1-A through stage 1-B.[34,36] Approximately 75% of stage 2 macular holes progress to stage 3 or stage 4 macular holes.[16,36-39]

The prognosis of untreated FTMHs is poor. Only 5% will have 20/50 visual acuity or better, approximately 55% will have visual acuity of 20/100 or better, and 40% will have visual acuity of 20/200 or worse.[14,17,24,40,41] Sixty percent of eyes with an FTMH lose 2 or more lines of vision over 5 years of follow-up.[17,40] After a follow-up of 3 to 5 years, 70% to 80% of eyes will have 20/200 or worse visual acuity, and the visual acuity in the remaining 20% to 30% will usually be 20/70 to 20/100.[14,24,40,41] In about 3% to 11% of cases, an FTMH will close spontaneously.[16,17,42-44] If the hole closes spontaneously, the visual acuity may recover dramatically. The vast majority of eyes with untreated macular holes deteriorates to the 20/100 to 20/400 range and then stabilizes with good peripheral vision.

CARE PROCESS

PATIENT OUTCOME CRITERIA

Patient outcome criteria include the following:

- Prevention of visual loss and functional impairment
- Improvement of visual function
- Maintenance or improvement of quality of life

DIAGNOSIS

The initial evaluation of a patient with symptoms and signs suggestive of macular hole includes all features of a comprehensive adult medical eye evaluation, with particular attention to those aspects relevant to macular hole.[45] Conditions often mistaken for the various stages of macular hole include cystoid macular edema, central serous retinopathy, a subfoveal druse, lamellar macular hole, epiretinal membrane with pseudohole, and solar maculopathy.[46-48]

History

A complete history includes the following elements, although the exact composition varies according to the patient's particular symptomatology and specific needs.

- Duration of symptoms

- Ocular history: glaucoma, retinal detachment or tear, other eye disease, eye or head injuries, ocular surgery, or sun or eclipse gazing or use of a laser pointer or other type of laser
- Medication use that may be related to macular cystoid edema (e.g., systemic niacin, topical prostaglandin analogues, tamoxifen)

Examination

Examination includes the following elements:

- Slit-lamp biomicroscopy of the macula and vitreoretinal interface
- An indirect peripheral retinal examination
- Amsler grid test and/or Watzke-Allen test

Ancillary Tests

Optical coherence tomography is extremely helpful and offers detailed information about the macular anatomy size of the macular hole if an FTMH is present, and presence of any VMT or an epiretinal membrane. This information aids in the diagnosis, staging, and follow-up.[49,50] Optical coherence tomography images are also helpful with patient education. However, FTMHs are often readily apparent with slit-lamp biomicroscopy of the fundus.

MANAGEMENT

Prevention and Early Detection

At this time, there is no known prevention for the development of an idiopathic macular hole. The initial evaluation should include a careful assessment of the fellow eye. Fellow eyes are at higher risk of developing a macular hole when a definite posterior vitreous detachment cannot be confirmed. Early detection of a macular hole and intervention with vitrectomy surgery is associated with both a higher macular hole closure rate after vitrectomy surgery as well as better postoperative visual acuity, perhaps because of the smaller size of the hole and a more limited duration of compromise to the macula. For these reasons, it is important to diagnose a macular hole in the fellow eye as soon as possible. Thus, patients should be educated about early warning signs such as metamorphopsia or any changes in central vision. An OCT image of the macula of the fellow eye may also help to identify at-risk eyes, evident by the presence of vitreous traction at or near the center of the macula.

Early Stages

Some people with stage 1-A or 1-B macular holes have foveal cysts that may resolve completely without treatment.[34,35] One study reported that patients with foveal cysts can remain stable with good vision for up to 5 years.[16] The visual acuity of patients with stage 1 macular hole (i.e. impending macular hole) may improve spontaneously when the posterior vitreous

detaches from the central macula. Most patients who present with good central visual acuity can be followed and asked to return promptly if symptoms worsen.[34] Although stage 1-A and early stage 1-B lesions have been referred to as early or impending macular holes, only about 50% progress to an FTMH from persistent VMT.[36] When the vitreous attachment spontaneously separates from the fovea in the other 50%, the appearance of the fovea either returns to normal or appears as a reddish spot and there is often a rapid improvement in visual symptoms.[19,34,51] Vitrectomy surgery to prevent an FTMH has been explored and has been shown to have no effect on the rate of progression to an FTMH.[34]

Later Stages

When the macular hole progresses beyond stage 2, further vision loss will occur if the patient does not receive treatment. Moreover, as the macular hole enlarges, epiretinal membranes may develop and the success rate of macular hole closure with vitrectomy surgery may decrease.[52] A Cochrane systematic review and meta-analysis by Parravano in 2015 has demonstrated the benefit of vitrectomy on improving visual acuity outcomes and increasing macular hole closure rates.[53] *(I+, Moderate quality, Strong recommendation)*

Table 2 delineates management recommendations for each of the stages of macular hole.

TABLE 2 MANAGEMENT FOR MACULAR HOLE

Stage	Management	Follow-up
1-A and 1-B	Observation[34]	• Follow up at 2– to 4-month intervals in the absence of new visual symptoms • Recommend prompt return if new visual symptoms develop • Encourage monocular vision testing with Amsler grid
2	Pneumatic Vitreolysis*[54,55]	• Performed usually within 1 to 2 weeks of diagnosis • Follow up at 1-2 days, then 1 week or sooner if new visual symptoms • Frequency and timing of subsequent visits varies depending on the outcome of surgery and the patient's clinical course
2	Vitreoretinal surgery[39] '	• Performed usually within 1 month of diagnosis to minimize risk of progression of macular hole and vision loss • Routine postoperative follow-up at 1–2 days, then 1–2 weeks during which time strict face down positioning is advised • Frequency and timing of subsequent postoperative visits varies depending on the outcome of surgery and the patient's clinical course
2	Vitreopharmacolysis‡	• Performed usually within 1 to 2 weeks of diagnosis • Follow-up at 1 week and 4 weeks, or with new symptoms (i.e., retinal detachment symptoms)
3 or 4	Vitreoretinal surgery[39,43]	• Performed usually within 1 month of diagnosis • Postoperative follow-up at 1–2 days, then 1–2 weeks during which time strict face down positioning if advised • Frequency and timing of subsequent visits varies depending on the outcome of surgery and the patient's clinical course

* Several small case series have shown promising results with this technique for smaller holes

' Although surgery is usually performed, observation may also be appropriate in selected cases.

1 ‡ Ocriplasmin has been approved by the U.S. Food and Drug Administration for symptomatic vitreomacular adhesion. There is no
2 evidence to support its use for treatment of idiopathic macular hole without vitreomacular traction or adhesion, and this would be
3 considered off-label use.
4
5

Surgical Management

Preoperative Discussion

The preoperative discussion should include the following information:

- The natural history of most eyes with an untreated macular hole is progressive loss of central vision resulting in visual acuity in the 20/200 to 20/400 range. The peripheral vision is usually unaffected. Delays in repair of macular hole may result in reduced success of hole closure and visual benefit.
- Phaco-vitrectomy could be considered.[56]
- The risk of developing a macular hole in the fellow eye if the vitreous is attached to the macula is 10% to 15%; the risk is lower of the vitreous appears detached.
- There is a remote chance for spontaneous macular hole closure. If this happens, there may be visual gain depending on the duration and size of the macular hole.
- Vision does not typically return to "normal" even after successful hole closure.
- The option to use intravitreal ocriplasmin or expansile gas to treat a macular hole should be discussed if the eye has an associated VMT. The discussion should include detailed risks and benefits for each option relative to vitrectomy surgery and continued observation.[57,58]The expected visual outcome of successful hole closure should also be discussed, including residual visual blur and metamorphopsia that will likely persist after hole closure.

Vitrectomy

For surgery, the discussion should include the following:

- The type of anesthesia required. (Usually, monitored anesthesia care is provided with a local anesthetic.) Macular hole surgery can be performed under general anesthesia for anxious or claustrophobic patients.
- The use of nitrous oxide gas. It should be avoided at least during the last 10 minutes of the air fluid exchange when general anesthesia is used because it may result in an unpredictable gas fill postoperatively.
- The risks (e.g., cataract, retinal tears) versus benefits of vitrectomy surgery.
- The role of positioning postoperatively. Detailed instructions about positioning postoperatively to tamponade the hole and minimize the risk of developing a cataract in phakic eyes should be discussed prior to scheduling surgery. Information can be given about equipment that can be rented and purchased for postoperative positioning.
- The possibility of an increase in postoperative intraocular pressure (IOP). The surgeon should inform patients about this possibility. In order to minimize the risk, patients should be advised about the importance of maintaining their scheduled postoperative examination

visits and avoiding travel to higher altitudes, especially above 2000 feet altitude. Severe and sustained elevations in IOP can result in permanent vision loss, especially in patients with glaucoma. The surgeon is responsible for formulating a postoperative care plan and should inform the patient of these arrangements.[57,58]

Detaching the Posterior Vitreous

An important anatomic goal of the pars plana vitrectomy (PPV) for macular hole closure is to separate the posterior cortical hyaloid from the retinal surface of the macula. Various surgeons have individual preferences or techniques to accomplish the surgical objectives. Triamcinolone acetonide can be injected into the vitreous following a core vitrectomy to highlight the posterior vitreous. Iatrogenic retinal breaks may develop in eyes with macular holes, often during the creation of a posterior vitreous detachment.[59] Thus, an intra-operative examination of the peripheral retina for breaks or tears should be performed intraoperatively prior to air-fluid exchange to minimize the risk of postoperative retinal detachment.

Internal Limiting Membrane Removal and Dyes

Another unsettled controversy is the value of removing the internal limiting membrane (ILM) during surgery. The ILM may act as a scaffold for cellular proliferation or attachment of contractile tissue elements that may cause persistent VMT after vitrectomy. Thus, failure of the original vitrectomy surgery to close the macular hole or late reopening of initially successfully closed holes may occur without removal of the ILM.[60] On the other hand, loss of its structural role or secondary collateral nerve fiber layer loss during removal may be detrimental.[60-62] In a recent large meta-analysis of 5480 cases, Rahimy and McCannell concluded that ILM peeling at the time of surgery significantly reduces the likelihood of the hole reopening but without better postoperative best-corrected visual acuities.[63] *(I++, Good quality, Strong recommendation)*

Table 3 summarizes large case series and randomized controlled trials that compared macular hole closure rates following vitrectomies when the ILM was either peeled or not peeled. Margherio et al found little difference with ILM removal,[64] whereas Tognetto et al found statistical evidence that ILM peeling is associated with higher rates of macular hole closure.[65] Brooks et al reported an 18% difference in favor of ILM peeling with a statistically significant difference in visual acuity between the peeling and non-peeling groups.[66] Interestingly, they noted a rather high rate (25%) of macular holes reopening in the non-peeled eyes compared with no reopening in ILM peeled macular holes.[66] In their randomized controlled trials, Christensen et al and Lois et al reported a greater difference in hole closure rates in favor of ILM peeling.[56,61] However, these trials were small and subject to some potential biases.

TABLE 3 MACULAR HOLE SURGICAL OUTCOMES – NO PEEL VS. PEEL OF ILM

Study (Author, Year)	Study Design	ILM Peeled/Not	Follow-up length (months)	% Macular Holes Closed	P Value
Margherio et al,[64] 2000	Case Series	No peel; n=59 Perifoveal tissue dissection; n=48	Mean 12.8 months Mean 13.4 months	92% 86%	P = 0.39
Tognetto et al,[65] 2006	Case Series	No peel; n=527 Peel; n=1100	Median 15 months Median 15 months	89% 94%	P<0.001
Brooks,[66] 2000	Case Series	No peel; n=46 Peel; n=116	18 months or greater	82% no peel (25% reopened) 100% (no reopening)	P<0.0001
Christensen et al,[61] 2009	RCT	No peel; n=25 Peel with ICG; n=34 Peel with TB; n=18	At 3 months	44% 94% 89%	P<0.001
			At 12 months	96% 97% 100%	P=1.0
Lois et al,[56] 2011	RCT	No peel; n=70 (randomized) Peel; n=71 (randomized)	At 1 month	48% (31/64) 84% (56/67)	P<0.001
			At 3 months	83% (52/63) 92% (61/66)	P=0.097
			At 6 months	89% (56/63) 94% (61/65)	P=0.33
Rahimy et al,[63] 2016	SR	No peel; n=1756 Peel; n=3724	Mean 38.6 months Mean 26.2 months	92.88% 98.82%	P<0.0001
Kwok et al,[67] 2005	RCT	No peel; n=25 Peel; n=26	Mean 12 months Mean 12 months	32% 92%	P<0.001

ICG = indocyanine green; ILM = internal limiting membrane; TB = trypan blue

A meta-analysis of 4 randomized control trials which included 317 patients with stage 2-4 idiopathic full thickness macular holes by Spiteri et al found that ILM peeling achieves higher anatomical success with a reduced need for additional surgical interventions when compared with non-peeling in treating patients at stages 2, 3, and 4.[68,69] One study in 2016 evaluated a small group of eyes that compared the extent of the ILM peel and evaluated outcomes. This study did show there was less metamorphopsia associated with wider ILM peel.[70] The use of inverted ILM flaps has been shown to be an effective technique for addressing idiopathic, myopic, and large macular holes, improving both functional and anatomical outcomes.[71-73] In general, it is thought that large, chronic, and myopic macular holes may benefit from ILM peeling, while small, recent macular holes may not need ILM peeling in all cases.[74]

A cost-effectiveness analysis was also performed alongside a RCT and concluded that ILM peeling is a cost-effective treatment for FTMH compared to no-peeling technique over a 6-

month period and was based on the higher number of reoperations required in the no-peel arm of the trial.[75]

Indocyanine green (ICG), trypan blue (TP), brilliant blue (BB), and other dyes, as well as triamcinolone acetonide (TA), have been reported to optimize visualization of the ILM during surgery.[76-80] When ICG was used initially, reports of visual field defects and retinal pigment epithelium abnormalities in the foveal center raised concerns about possible toxicity.[81,82] Subsequent studies have suggested either a slight decrease in postoperative visual acuity using ICG compared with using no dye or no difference between the various dyes.[77,78,80,82-88] A meta-analysis concluded that there is no difference in the rate of macular hole closure between eyes with ILMs that were peeled without dye or with the use of ICG or BB.[88] The authors found a slight decrease in visual acuity outcomes using ICG for ILM peeling during the first postoperative year; however, there was no difference thereafter and no difference even during the first year when a concentration of ≤0.05% ICG was used.[88] A recent retrospective study of 351 patients found that the closure rate of ICG-assisted ILM peels (73.2%) was statistically lower than the closure rate using BB, but this closure rate is lower than that seen in most other studies of ILM peeling in FTMH.[89] One study compared cone electroretinograms after ILM peeling using BB, ICG, or TA and found no difference in visual acuity at 6 months among the groups but it found a decreased photopic negative response with ICG compared with the other agents, indicating possible subclinical impairments of the retinal ganglion cell layer.[88] However, a similar paper, reporting on 48 eyes of 48 patients with a macular hole in which, the same three agents were used (16 per agent) found no differences in focal macular electroretinogram outcomes between agents; it concluded that none of the three agents is toxic to the macula.[90] Triamcinolone acetonide has been safely used to visualize residual vitreous to facilitate removal of the ILM with good results and low concerns for toxicity.[76,80]

Importantly, when the surgeon prefers ICG to stain the ILM, efforts should be made to avoid unnecessarily high concentrations of ICG or prolonged exposure. And, in summary, definitive recommendations about the use of specific dyes to peel the ILM in macular hole surgery simply do not exist in the literature. Unfortunately, there has not been a large randomized trial comparing dyes in ILM peeling.

Seal

Retinal tamponade may be created by intravitreal injection of different agents at the conclusion of macular hole surgery to achieve anatomic closure of the macular hole. In general, there is no consensus about the best choice of tamponade agent. Tamponade options include the use of air (lasting days), SF_6 (lasting about 2 weeks), C_3F_8 (lasting about 6 weeks), or silicone oil (long term). Two early studies found that better results were achieved by using C_3F_8 gas when compared with SF_6 gas.[91,92] A later study found no

difference in results when comparing the use of these two gases.[93] A recent study found a 98% rate of closure using SF_6 gas.[94] High closure rates have been reported when air tamponade and ILM peeling are used,[66] though this may not apply to larger macular holes (>400 µm).[95]

Silicone oil may be used for patients who cannot position facedown.[96,97] In one study, 86% of 40 holes were closed using silicone oil;[96] however, these same investigators later concluded that the anatomic and visual results are better with gas tamponade.[98] Using silicone oil also requires a second operation to remove oil. Postoperative, patients may have ellipsoid zone loss in the area of the previous macular hole and may note distortions centrally, even after surgical repair.[98]

Positioning

In the early days of macular hole surgery, patients were instructed to maintain a face-down position for 10 to 14 days postoperatively to optimize macular hole closure. Postoperative prone positioning is uncomfortable for the patient. In some cases, positioning may be extremely difficult or even lead to pressure sores or neuropathy.[99-101] Recent studies have reported excellent results using face-down positioning for 1 to 3 days.[94,102,103] Surgeons have reported closure rates with no face-down positioning that are similar to the rates seen in series requiring face-down positioning.[104-110] Longer positioning may be required for holes larger than 400 µm or those with inadequate gas fill.[63,108]

A small comparative study was published comparing facedown positioning to not being face down and found that differences in positioning had no effect on the macular hole closure rate.[111] In all of these studies, however, the patient was told to avoid the face-up or supine positioning. Specifically, recommendations were for an upright position that avoided the head tilting back.[108,110] Additionally, some advocates of this approach have emphasized the importance of a good postoperative gas fill to allow for tamponade of the macular hole without prone positioning.[112] Longer positioning may be required for holes larger than 400 µm or those with inadequate tamponade.[63,108] This minimizes the risk of cataract progression and provide some tamponade of the macular hole.

Some studies have monitored the timeline of macular hole closure by obtaining OCT imaging of the macula within days of vitrectomy surgery (through the gas-filled vitreous cavity) and used that information to curtail positioning.[113-117] In a recent meta-analysis of 251 cases by Hu et al. concluded that no face down positioning was similar to face down positioning for holes smaller than 400µm, but face-down positioning may be beneficial for holes larger than 400µm.[118] *(I+, Good Quality, Discretionary Recommendation)*

Outcomes of Surgery

Two multicenter, randomized, controlled trials provide evidence for the efficacy of surgery compared with observation for FTMH.[39,43] One study of 120 patients with stage 3 and stage

4 macular holes reported a benefit from vitrectomy surgery in the closure rate and visual acuity 6 months after randomization.[43] However, results with stage 2 macular holes did not demonstrate a similar benefit.[39] Nevertheless, the consensus of the vitreoretinal community is to recommend surgery for a stage 2 macular hole, not only because the visual acuity results are good with surgery but also to minimize further visual loss that accompanies progression to a stage 3 or stage 4 macular hole. However, observation with close follow-up is also recommended for early-stage macular holes. For a stage 1 macular hole, a randomized controlled study showed that 60% may not progress to an FTMH and that vitrectomy surgery did not prevent the progression of stage 1 macular holes.[34] With OCT imaging, the physician is able to monitor the progress of early-stage macular holes and make appropriate treatment recommendations.

Surgical studies have reported closure rates of 91% to 98% for FTMHs.[83,94,102,110] Most articles have reported that the median postoperative visual acuity of sealed macular holes is approximately 20/40,[77,83,94,102,110,119-121] clearly better than the visual acuity of untreated macular holes.[14,17,24,40,41] However, post-operatively patients may have elliptical zone loss in the area of the previous macular hole and may note some distortion in central vision even after successful surgical repair of the macular hole.

Predictors of Visual Results

In case series, many authors have reported better closure rates and better final visual acuities when the duration of symptoms is less than 6 months.[122-126] Findings from case series indicate that a macular hole that has been present for more than 2 to 3 years may be closed, yet the success rate is lower (63%) and visual acuity outcomes are worse than for a macular hole of shorter duration.[66,122,127-132]

Patients whose macular holes fail to seal after the first surgery usually have a less favorable visual acuity outcome when compared with primary closure. Two studies have shown that up to 70% of the macular holes close following additional vitrectomy surgery but visual gain may be reduced. An improvement of only 1 line in visual acuity and an approximate visual acuity of 20/100 were reported.[133,134] On the other hand, patients whose macular holes closed following the initial surgery but then required additional vitrectomy for reopened hole did better than those who required additional surgery.[133]

Complications of Vitrectomy

Cataract

The vast majority of phakic eyes in adults develop cataracts after macular hole surgery. Clinically significant cataract develops in over 80% of phakic eyes within the first few years after vitrectomy.[135,136] One study found that the median time to cataract surgery after vitrectomy for a macular hole was 14 months and that 98% of eyes needed cataract

surgery when followed for a mean of 91 months after vitrectomy.[137] One study showed a high rate of 11% of closed macular holes reopening after cataract surgery and that the development of cystoid macular edema after surgery increased the risk by sevenfold.[138] Given the rate of cataract formation and risk of reopening of the macular hole, some surgeons advocate combining macular hole surgery with phacoemulsification and placement of an intraocular lens.[104,138-140] A combined procedure eliminates the need for two operations and may allow for a more complete gas fill.[104,138,139] The potential complications of combining cataract surgery with vitrectomy include hypotony, intraocular lens-iris capture, and possibly an increased risk of macular edema in some patients. Up to 10% of successfully closed macular holes later reopen, although the risk might be less when the ILM is peeled during the vitrectomy to close the hole.[18,137,141-146]

Retinal Tears

Intraoperative retinal tears have been reported in 3% to 17% of macular hole operations, and most occur inferiorly.[144,145,147-151]

Retinal Detachment

Although postoperative retinal detachment has been reported to be as high as 14% of cases, most series report an incidence of 1% to 5%.[64,77,104,144,145,147-149,152] The detachment is typically located inferiorly and caused by small flap tears at the posterior vitreous base. Fortunately, most detachments can be repaired without reopening of the hole.[150]

Visual Field Loss

In the past, up to 20% of patients were noted to have a permanent temporal visual field loss after macular hole surgery.[153-157] Most ophthalmologists believe that this field loss is caused by either mechanical injury (such as trauma to the peripapillary retinal vasculature or nerve fiber layer[156]) or dehydration damage to the retina as a result of air streaming from the temporally placed infusion cannula during the air-fluid exchange.[158] It is unknown whether the following recommendations for the surgeon have reduced the incidence of visual field loss:

- To minimize direct instrument contact with optic disc during air-fluid exchange
- To minimize prolonged air flow at high pressure
- To securely close the sclerotomies to minimize air flow through the eye during the air-fluid exchange

- To allow the valved cannulae to leave a puddle of fluid posteriorly until the final aspiration[159]
- To humidify the air[160]
- To use a low-infusion pressure during air-fluid exchange.[161,162]

In addition, it is possible that the air flow through the vitreous cavity is decreased in small-gauge vitrectomy, or by incorporating valved cannulae that decrease air circulation.

Endophthalmitis

Endophthalmitis has been reported in less than 0.05% of vitrectomies, including those performed for macular holes.[144,145]

Gas-Related Complications

Patients who have retinal tamponade achieved by an intravitreal injection of gas bubble must take special precautions for the duration that the gas bubble is in the eye. This includes avoiding air travel and driving or ascending to a higher altitude. Physicians should also discuss the implications of travel to higher altitudes of more than 1000 feet from the site of the operation. For example, driving to or ascending to a higher altitude in some regions may result in gas expansion and increased IOP may result. Bubble expansion at higher altitude causes increased IOP that could risk arterial occlusion, wound dehiscence, gas leakage, or other IOP-related injury.[163] Care must also be taken when traveling to lower elevations because reduction in bubble size may increase the risk of ocular hypotony and postsurgical retinal detachment.[164] Intraocular gas also limits the type of anesthetic agents that can be used. Most surgeons require their patients to wear a wristband warning alert that states that the wearer's eye contains intraocular gas and that anesthetic (e.g., nitrous oxide) should be avoided. The use of nitrous oxide in a patient with intraocular gas may result in a dangerous rise in IOP.[164]

Follow-up Evaluation after Surgery

Patients who have surgery are usually examined the first 1 to 2 days post-operatively and again approximately 1 to 2 weeks following surgery. The frequency and timing of subsequent postoperative visits varies, depending on the outcome of surgery and the patient's symptoms. Components of the follow-up visit should include the following:

- Interval history, including new symptoms
- Visual acuity measurement
- Measurement of IOP

- Slit-lamp biomicroscopy of the anterior chamber and central retina, and indirect binocular ophthalmoscopy of the peripheral retina
- OCT to document the postoperative macular anatomy when indicated

Vitreopharmacolysis

Ocriplasmin

Ocriplasmin is a recombinant protease that was approved by the FDA in 2012 for the management of symptomatic VMA. Ocriplasmin is a recombinant protease that cleaves proteins that compose the vitreoretinal interface. Approval by the FDA was based on the results of a randomized study.[165] The study's inclusion criteria encompassed all eyes with vitreous traction on the macula, including a subset of eyes with stage 2 macular holes. In this subset, the closure rate of macular holes was 40% when the protease was used compared with 10% when the macular holes were injected with an intravitreal saline placebo.[165] In the post-marketing Macula Society Collaborative Study on physician reported outcomes of ocriplasmin use in 208 eyes, VMA release was confirmed in 45% with closure of the FTMH in 40% of eyes without PPV; however, visual acuity decreased in 20%, and adverse events were not infrequent.[166] Additionally, a 2018 post-market analysis revealed a lower macular hole closure success rate (32.2% at months 10-12) compared to the original study.[167 168] In contrast, on average, stage 2 macular holes have a 90% chance of closure when vitrectomy techniques are used.[94,102,103,108] To date, there have been very few head-to-head studies comparing the use of ocriplasmin with PPV. In cases of holes larger than 400 µm, in the absence of evident VMT, or in the presence of epiretinal membrane, vitrectomy is the first choice.[169] Further, there is no data to support the use of ocriplasmin for management of macular hole without VMA, and this would be considered an off-label use of the medication. A 2018 post-market analysis revealed a lower macular hole closure success rate (32.2% at months 10-12) compared with the original study.[167,168]

Complications of Ocriplasmin

Postmarket concerns have been raised about the safety of ocriplasmin. Acute vision loss, electroretinographic abnormalities, macular detachment, and dyschromatopsia have been described.[165]

A 2017 study was published reporting on the use of ocriplasmin in the United Kingdom and concluded that macular hole closure rates were lower than published in the Trial of Microplasmin Intravitreal Injection for Non-surgical Treatment of Focal Vitreomacular Adhesion (MIVI-TRUST) trial data (42.1% vs. 58.3% for small FTMH and 12.7% vs. 36.7% for medium FTMH). The incidence of adverse events was also greater than

previously reported.[168,170] The benefits and risks associated with vitrectomy surgery versus intravitreal ocriplasmin require continued investigation.

The Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion Including Macular Hole (OASIS) trial was designed by the drug manufacturer to evaluate the long-term efficacy and safety profile of ocriplasmin for the treatment of symptomatic VMA/VMT, including FTMH.[171] This trial demonstrated the long-term efficacy and safety of ocriplasmin, providing improved resolution of symptomatic VMA compared with previous phase III trials.

In cases of treatment failure with ocriplasmin, patients may ultimately undergo PPV. The Vitrectomy After Ocriplasmin for Vitreomacular Adhesion or Macular Hole (VAVOOM) study was a multicenter retrospective study of eyes that received intravitreal ocriplasmin between January 2013 and January 2014 for symptomatic VMT, with or without macular hole, and then went on to PPV (ocriplasmin-treated group) for persistent pathology. They were compared with a control group of patients with symptomatic VMT, with or without macular hole, who were offered ocriplasmin injection but proceeded directly to PPV (PPV-only group).[172] Although visual acuity was better at all times in the PPV-only group, the authors concluded that eyes with persistent symptomatic VMT and/or macular hole have similarly high rates of pathology resolution as well as similar visual acuity gains after vitrectomy and regardless of whether they received prior ocriplasmin.

The data from the 2018 American Society of Retinal Specialists Preferences and Trends survey based on VMT with macular hole from 1022 respondents revealed the following: For patients with VMT, small macular hole, and 20/50 vision, the treatment of choice was ocriplasmin; 7.4% US (5.3% international) vitrectomy: 70.4% US (72.4% international) and pneumatic vitreolysis: 9.6% US (10.2% international)

The reported complications associated with ocriplasmin are as follows:

- Retinal tears
- Floaters (usually due to progression of the posterior vitreous detachment)
- Blue-yellow vision, dyschromatopsia or dark vision
- Photopsias
- Visual field abnormalities
- Electroretinography changes
- Weakening of zonular fibers and possible lens subluxation[51]

PROVIDER AND SETTING

Diagnosis and management of macular hole requires expertise, skills, and specialized equipment to detect alterations in the retina and then select, perform, and/or monitor the appropriate treatment regimen. Referral to an ophthalmologist who has expertise and experience in managing this condition is recommended (i.e. a fellowship-trained vitreo-retinal surgeon). The performance of certain diagnostic procedures is often delegated to appropriately trained and supervised personnel. However, the interpretation of the results of the diagnostic procedures, as well as the medical and surgical management of a macular hole, require medical training, clinical judgment, and experience.

COUNSELING AND REFERRAL

Patients should be informed to notify their ophthalmologist promptly when they have new visual symptoms such as an increase in floaters, a loss of visual field, metamorphopsia, or a decrease in visual acuity.[173-175] The goal of vision rehabilitation is to restore functional ability.[176] Patients with function-limiting postoperative visual impairment should be referred for vision rehabilitation and social services.[162,177] More information on vision rehabilitation, including materials for patients, is available at www.aao.org/smart-sight-low-vision.

SOCIOECONOMIC CONSIDERATIONS

The economic considerations related to treatment and management of idiopathic macular hole have not been comprehensively studied. Measures of patient satisfaction after surgery correlate with the visual and anatomic results.[178-180] Vision-related quality of life, assessed by the National Eye Institute Visual Function Questionnaire 25, has been reported to improve following surgery for idiopathic macular hole.[56,178] Research has shown that PPV was the most cost-effective procedure relative to intravitreal injection of either ocriplasmin or saline.[181]

APPENDIX 1. QUALITY OF OPHTHALMIC CARE CORE CRITERIA

Providing quality care
is the physician's foremost ethical obligation, and is
the basis of public trust in physicians.
AMA Board of Trustees, 1986

Quality ophthalmic care is provided in a manner and with the skill that is consistent with the best interests of the patient. The discussion that follows characterizes the core elements of such care.

The ophthalmologist is first and foremost a physician. As such, the ophthalmologist demonstrates compassion and concern for the individual, and utilizes the science and art of medicine to help alleviate patient fear and suffering. The ophthalmologist strives to develop and maintain clinical skills at the highest feasible level, consistent with the needs of patients, through training and continuing education. The ophthalmologist evaluates those skills and medical knowledge in relation to the needs of the patient and responds accordingly. The ophthalmologist also ensures that needy patients receive necessary care directly or through referral to appropriate persons and facilities that will provide such care, and he or she supports activities that promote health and prevent disease and disability.

The ophthalmologist recognizes that disease places patients in a disadvantaged, dependent state. The ophthalmologist respects the dignity and integrity of his or her patients and does not exploit their vulnerability.

Quality ophthalmic care has the following optimal attributes, among others.

- The essence of quality care is a meaningful partnership relationship between patient and physician. The ophthalmologist strives to communicate effectively with his or her patients, listening carefully to their needs and concerns. In turn, the ophthalmologist educates his or her patients about the nature and prognosis of their condition and about proper and appropriate therapeutic modalities. This is to ensure their meaningful participation (appropriate to their unique physical, intellectual, and emotional state) in decisions affecting their management and care, to improve their motivation and compliance with the agreed plan of treatment, and to help alleviate their fears and concerns.
- The ophthalmologist uses his or her best judgment in choosing and timing appropriate diagnostic and therapeutic modalities as well as the frequency of evaluation and follow-up, with due regard to the urgency and nature of the patient's condition and unique needs and desires.
- The ophthalmologist carries out only those procedures for which he or she is adequately trained, experienced, and competent, or, when necessary, is assisted by someone who is, depending on the urgency of the problem and availability and accessibility of alternative providers.
- Patients are assured access to, and continuity of, needed and appropriate ophthalmic care, which can be described as follows.
  - The ophthalmologist treats patients with due regard to timeliness, appropriateness, and his or her own ability to provide such care.
  - The operating ophthalmologist makes adequate provision for appropriate pre- and postoperative patient care.
  - When the ophthalmologist is unavailable for his or her patient, he or she provides appropriate alternate ophthalmic care, with adequate mechanisms for informing patients of the existence of such care and procedures for obtaining it.
  - The ophthalmologist refers patients to other ophthalmologists and eye care providers based on the timeliness and appropriateness of such referral, the patient's needs, the competence and qualifications of the person to whom the referral is made, and access and availability.

- The ophthalmologist seeks appropriate consultation with due regard to the nature of the ocular or other medical or surgical problem. Consultants are suggested for their skill, competence, and accessibility. They receive as complete and accurate an accounting of the problem as necessary to provide efficient and effective advice or intervention, and in turn they respond in an adequate and timely manner. The ophthalmologist maintains complete and accurate medical records.
- On appropriate request, the ophthalmologist provides a full and accurate rendering of the patient's records in his or her possession.
- The ophthalmologist reviews the results of consultations and laboratory tests in a timely and effective manner and takes appropriate actions.
- The ophthalmologist and those who assist in providing care identify themselves and their profession.
- For patients whose conditions fail to respond to treatment and for whom further treatment is unavailable, the ophthalmologist provides proper professional support, counseling, rehabilitative and social services, and referral as appropriate and accessible.

- Prior to therapeutic or invasive diagnostic procedures, the ophthalmologist becomes appropriately conversant with the patient's condition by collecting pertinent historical information and performing relevant preoperative examinations. Additionally, he or she enables the patient to reach a fully informed decision by providing an accurate and truthful explanation of the diagnosis; the nature, purpose, risks, benefits, and probability of success of the proposed treatment and of alternative treatment; and the risks and benefits of no treatment.
- The ophthalmologist adopts new technology (e.g., drugs, devices, surgical techniques) in judicious fashion, appropriate to the cost and potential benefit relative to existing alternatives and to its demonstrated safety and efficacy.
- The ophthalmologist enhances the quality of care he or she provides by periodically reviewing and assessing his or her personal performance in relation to established standards, and by revising or altering his or her practices and techniques appropriately.
- The ophthalmologist improves ophthalmic care by communicating to colleagues, through appropriate professional channels, knowledge gained through clinical research and practice. This includes alerting colleagues of instances of unusual or unexpected rates of complications and problems related to new drugs, devices, or procedures.
- The ophthalmologist provides care in suitably staffed and equipped facilities adequate to deal with potential ocular and systemic complications requiring immediate attention.
- The ophthalmologist also provides ophthalmic care in a manner that is cost effective without unacceptably compromising accepted standards of quality.

Reviewed by: Council
Approved by: Board of Trustees
October 12, 1988

2nd Printing: January 1991
3rd Printing: August 2001
4th Printing: July 2005

LITERATURE SEARCHES FOR THIS PPP

Literature searches of the PubMed and Cochrane databases were conducted in April 2018; the search strategies are provided at www.aao.org/ppp. Specific limited update searches were conducted after June 2019.

(Retinal Perforations/epidemiology[mh]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (Risk Factors[mh]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (Cost-Benefit Analysis[mh]) OR (Cost of Illness[mh]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (Quality of Life[mh]) AND (macular hole*[tiab])

(Retinal Perforations/surgery[mh] OR Retinal Perforations/therapy[mh]) AND (macular hole*[tiab])

(Retinal Perforations/etiology[MAJR]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (macular hole*[tiab])

(macular hole*[tiab]) AND ((review*[tiab] AND (literature[tiab] OR systematic[tiab] OR search*[tiab])) OR meta-analysis[tiab])

(Retinal Perforations/diagnosis[MAJR]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (Treatment Outcome[mh]) AND (macular hole*[tiab])

(Retinal Perforations[mh]) AND (Postoperative Complications[mh]) AND (macular hole*[tiab])

(Retinal Perforations/surgery[mh] OR Retinal Perforations/therapy[mh]) AND (macular hole*[tiab]

RELATED ACADEMY MATERIALS

Basic and Clinical Science Course
Retina and Vitreous (Section 12, 2019–2020)

Focal Points
Diagnosis and Management of Macular Holes (2015)

Ophthalmic Technology Assessment –
Published in *Ophthalmology*, which is distributed free to Academy members; links to full text available at www.aao.org/ota.
Laser Scanning and Imaging for Macular Disease OTA (2007)
Surgical Management of Macular Holes (2001; reviewed for currency 2012)

Patient Education
Face-Down Recovery After Retinal Surgery Brochure (2014)
Macular Hole Brochure (2014)
Retina Informed Consent Video Collection (2013)

Preferred Practice Pattern® Guidelines – Free download available at www.aao.org/ppp.
Comprehensive Adult Medical Eye Evaluation (2015)

To order any of these products, except for the free materials, please contact the Academy's Customer Service at 866.561.8558 (U.S. only) or 415.561.8540 or www.aao.org/store.

REFERENCES

1. Shinoda K, Hirakata A, Hida T, et al. Ultrastructural and immunohistochemical findings in five patients with vitreomacular traction syndrome. *Retina.* 2000;20(3):289-293.
2. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924-926.
3. Shiono A, Kogo J, Klose G, et al. Photoreceptor outer segment length: a prognostic factor for idiopathic epiretinal membrane surgery. *Ophthalmology.* 2013;120(4):788-794.
4. Colucciello M. Evaluation and Management of Macular Holes. Focal Points: Clinical Modules for Ophthalmologists. Module 1. San Francisco, CA: American Academy of Ophthalmology; 2003.
5. Benson WE, Cruickshanks KC, Fong DS, et al. Surgical management of macular holes: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2001;108(7):1328-1335.
6. Aaberg TM, Blair CJ, Gass JD. Macular holes. *Am J Ophthalmol.* 1970;69(4):555-562.
7. Kuhn F, Morris R, Mester V, Witherspoon CD. Internal limiting membrane removal for traumatic macular holes. *Ophthalmic Surg Lasers.* 2001;32(4):308-315.
8. Wang S, Xu L, Jonas JB. Prevalence of full-thickness macular holes in urban and rural adult Chinese: the Beijing Eye Study. *Am J Ophthalmol.* 2006;141(3):589-591.
9. Nangia V, Jonas JB, Khare A, Lambat S. Prevalence of macular holes in rural central India. The Central India Eye and Medical Study. *Graefes Arch Clin Exp Ophthalmol.* 2012;250(7):1105-1107.
10. McCannel CA, Ensminger JL, Diehl NN, Hodge DN. Population-based incidence of macular holes. *Ophthalmology.* 2009;116(7):1366-1369.
11. Eye Disease Case-Control Study Group. Risk factors for idiopathic macular holes. *Am J Ophthalmol.* 1994;118(6):754-761.
12. Ezra E, Wells JA, Gray RH, et al. Incidence of idiopathic full-thickness macular holes in fellow eyes. A 5-year prospective natural history study. *Ophthalmology.* 1998;105(2):353-359.
13. Niwa H, Terasaki H, Ito Y, Miyake Y. Macular hole development in fellow eyes of patients with unilateral macular hole. *Am J Ophthalmol.* 2005;140(3):370-375.
14. Lewis ML, Cohen SM, Smiddy WE, Gass JD. Bilaterality of idiopathic macular holes. *Graefes Arch Clin Exp Ophthalmol.* 1996;234(4):241-245.
15. Fisher YL, Slakter JS, Yannuzzi LA, Guyer DR. A prospective natural history study and kinetic ultrasound evaluation of idiopathic macular holes. *Ophthalmology.* 1994;101(1):5-11.
16. Guyer DR, de Bustros S, Diener-West M, Fine SL. Observations on patients with idiopathic macular holes and cysts. *Arch Ophthalmol.* 1992;110(9):1264-1268.
17. Chew EY, Sperduto RD, Hiller R, et al. Clinical course of macular holes: the Eye Disease Case-Control Study. *Arch Ophthalmol.* 1999;117(2):242-246.
18. Kumagai K, Ogino N, Hangai M, Larson E. Percentage of fellow eyes that develop full-thickness macular hole in patients with unilateral macular hole. *Arch Ophthalmol.* 2012;130(3):393-394.
19. Gass JD. Idiopathic senile macular hole. Its early stages and pathogenesis. *Arch Ophthalmol.* 1988;106(5):629-639.
20. Gass JD. Reappraisal of biomicroscopic classification of stages of development of a macular hole. *Am J Ophthalmol.* 1995;119(6):752-759.
21. Gaudric A, Haouchine B, Massin P, Paques M, Blain P, Erginay A. Macular hole formation: new data provided by optical coherence tomography. *Arch Ophthalmol.* 1999;117(6):744-751.
22. Haouchine B, Massin P, Gaudric A. Foveal pseudocyst as the first step in macular hole formation: a prospective study by optical coherence tomography. *Ophthalmology.* 2001;108(1):15-22.
23. Azzolini C, Patelli F, Brancato R. Correlation between optical coherence tomography data and biomicroscopic interpretation of idiopathic macular hole. *Am J Ophthalmol.* 2001;132(3):348-355.
24. Casuso LA, Scott IU, Flynn HW, Jr., et al. Long-term follow-up of unoperated macular holes. *Ophthalmology.* 2001;108(6):1150-1155.
25. Blain P, Paques M, Massin P, et al. Epiretinal membranes surrounding idiopathic macular holes. *Retina.* 1998;18(4):316-321.
26. Hee MR, Puliafito CA, Wong C, et al. Optical coherence tomography of macular holes. *Ophthalmology.* 1995;102(5):748-756.
27. Ansari H, Rodriguez-Coleman H, Langton K, Chang S. Spontaneous resolution of bilateral stage 1 macular holes documented by optical coherence tomography. *Am J Ophthalmol.* 2002;134(3):447-449.

28. Stalmans P, Spileers W, Dralands L. The use of optical coherence tomography in macular diseases. *Bull Soc Belge Ophtalmol.* 1999;272:15-30.
29. Spaide RF, Wong D, Fisher Y, Goldbaum M. Correlation of vitreous attachment and foveal deformation in early macular hole states. *Am J Ophthalmol.* 2002;133(2):226-229.
30. Folk JC, Boldt HC, Keenum DG. Foveal cysts: a premacular hole condition associated with vitreous traction. *Arch Ophthalmol.* 1998;116(9):1177-1183.
31. Kishi S, Kamei Y, Shimizu K. Tractional elevation of Henle's fiber layer in idiopathic macular holes. *Am J Ophthalmol.* 1995;120(4):486-496.
32. Kishi S, Hagimura N, Shimizu K. The role of the premacular liquefied pocket and premacular vitreous cortex in idiopathic macular hole development. *Am J Ophthalmol.* 1996;122(5):622-628.
33. Johnson MW, Van Newkirk MR, Meyer KA. Perifoveal vitreous detachment is the primary pathogenic event in idiopathic macular hole formation. *Arch Ophthalmol.* 2001;119(2):215-222.
34. de Bustros S. Vitrectomy for Prevention of Macular Hole Study Group. Vitrectomy for prevention of macular holes. Results of a randomized multicenter clinical trial. *Ophthalmology.* 1994;101(6):1055-1059; discussion 1060.
35. Johnson RN, Gass JD. Idiopathic macular holes. Observations, stages of formation, and implications for surgical intervention. *Ophthalmology.* 1988;95(7):917-924.
36. Hikichi T, Yoshida A, Akiba J, Trempe CL. Natural outcomes of stage 1, 2, 3, and 4 idiopathic macular holes. *Br J Ophthalmol.* 1995;79(6):517-520.
37. Hikichi T, Yoshida A, Akiba J, Konno S, Trempe CL. Prognosis of stage 2 macular holes. *Am J Ophthalmol.* 1995;119(5):571-575.
38. Kim JW, Freeman WR, el-Haig W, Maguire AM, Arevalo JF, Azen SP. Vitrectomy for Macular Hole Study Group. Baseline characteristics, natural history, and risk factors to progression in eyes with stage 2 macular holes. Results from a prospective randomized clinical trial. *Ophthalmology.* 1995;102(12):1818-1829.
39. Kim JW, Freeman WR, Azen SP, el-Haig W, Klein DJ, Bailey IL. Vitrectomy for Macular Hole Study Group. Prospective randomized trial of vitrectomy or observation for stage 2 macular holes. *Am J Ophthalmol.* 1996;121(6):605-614.
40. Hikichi T, Trempe CL. Risk of decreased visual acuity in full-thickness idiopathic macular holes. *Am J Ophthalmol.* 1993;116(6):708-712.
41. Morgan CM, Schatz H. Idiopathic macular holes. *Am J Ophthalmol.* 1985;99(4):437-444.
42. Hikichi T, Akiba J, Trempe CL. Effect of the vitreous on the prognosis of full-thickness idiopathic macular hole. *Am J Ophthalmol.* 1993;116(3):273-278.
43. Freeman WR, Azen SP, Kim JW, el-Haig W, Mishell DR, 3rd, Bailey I. The Vitrectomy for Treatment of Macular Hole Study Group. Vitrectomy for the treatment of full-thickness stage 3 or 4 macular holes: results of a multicentered randomized clinical trial. *Arch Ophthalmol.* 1997;115(1):11-21.
44. Ezra E, Gregor ZJ. Moorfields Macular Hole Study Group. Surgery for idiopathic full-thickness macular hole: two-year results of a randomized clinical trial comparing natural history, vitrectomy, and vitrectomy plus autologous serum: Moorfields Macular Hole Study Group report number 1. *Arch Ophthalmol.* 2004;122(2):224-236.
45. Feder RS, Olsen TW, Prum BE, Jr., et al. Comprehensive adult medical eye evaluation Preferred Practice Pattern® Guidelines. *Ophthalmology.* 2016;123(1):P209-236.
46. Ho AC, Guyer DR, Fine SL. Macular hole. *Surv Ophthalmol.* 1998;42(5):393-416.
47. Gass JD, Joondeph BC. Observations concerning patients with suspected impending macular holes. *Am J Ophthalmol.* 1990;109(6):638-646.
48. Smiddy WE, Gass JD. Masquerades of macular holes. *Ophthalmic Surg.* 1995;26(1):16-24.
49. McDonald HR, Williams GA, Scott IU, Haller JA, Maguire AM, Marcus DM. Laser scanning imaging for macular disease: a report by the American Academy of Ophthalmology. *Ophthalmology.* 2007;114(6):1221-1228.
50. Duker JS, Kaiser PK, Binder S, et al. The International Vitreomacular Traction Study Group classification of vitreomacular adhesion, traction, and macular hole. *Ophthalmology.* 2013;120(12):2611-2619.
51. Folk JC, Adelman RA, Flaxel CJ, Hyman L, Pulido JS, Olsen TW. Idiopathic Epiretinal Membrane and Vitreomacular Traction Preferred Practice Pattern((R)) Guidelines. *Ophthalmology.* 2016;123(1):P152-181.
52. Brockmann T, Steger C, Weger M, Wedrich A, Haas A. Risk assessment of idiopathic macular holes undergoing vitrectomy with dye-assisted internal limiting membrane peeling. *Retina.* 2013;33(6):1132-1136.

53. Parravano M, Giansanti F, Eandi CM, Yap YC, Rizzo S, Virgili G. Vitrectomy for idiopathic macular hole. *The Cochrane database of systematic reviews.* 2015(5):CD009080.
54. Chan CK, Mein CE, Crosson JN. Pneumatic Vitreolysis for Management of Symptomatic Focal Vitreomacular Traction. *J Ophthalmic Vis Res.* 2017;12(4):419-423.
55. Madi HA, Masri I, Steel DH. Optimal management of idiopathic macular holes. *Clin Ophthalmol.* 2016;10:97-116.
56. Lois N, Burr J, Norrie J, et al. Internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole: a pragmatic randomized controlled trial. *Investigative ophthalmology & visual science.* 2011;52(3):1586-1592.
57. American Academy of Ophthalmology. Preoperative assessment: responsibilities of the ophthalmologist. 2012; https://www.aao.org/about/policies. Accessed August 1, 2018.
58. American Academy of Ophthalmology. An ophthalmologist's duties concerning postoperative care - 2012. 2012; https://www.aao.org/clinical-statement/ophthalmologists-duties-concerning-postoperative-c. Accessed August 1, 2018.
59. Chung SE, Kim KH, Kang SW. Retinal breaks associated with the induction of posterior vitreous detachment. *Am J Ophthalmol.* 2009;147(6):1012-1016.
60. Eckardt C, Eckardt U, Groos S, Luciano L, Reale E. Removal of the internal limiting membrane in macular holes. Clinical and morphological findings. *Ophthalmologe.* 1997;94(8):545-551.
61. Christensen UC, Kroyer K, Sander B, et al. Value of internal limiting membrane peeling in surgery for idiopathic macular hole stage 2 and 3: a randomised clinical trial. *Br J Ophthalmol.* 2009;93(8):1005-1015.
62. Pilli S, Zawadzki RJ, Werner JS, Park SS. Visual outcome correlates with inner macular volume in eyes with surgically closed macular hole. *Retina.* 2012;32(10):2085-2095.
63. Rahimy E, McCannel CA. IMPACT OF INTERNAL LIMITING MEMBRANE PEELING ON MACULAR HOLE REOPENING: A Systematic Review and Meta-Analysis. *Retina.* 2016;36(4):679-687.
64. Margherio RR, Margherio AR, Williams GA, Chow DR, Banach MJ. Effect of perifoveal tissue dissection in the management of acute idiopathic full-thickness macular holes. *Arch Ophthalmol.* 2000;118(4):495-498.
65. Tognetto D, Grandin R, Sanguinetti G, et al. Internal limiting membrane removal during macular hole surgery: results of a multicenter retrospective study. *Ophthalmology.* 2006;113(8):1401-1410.
66. Brooks HL, Jr. Macular hole surgery with and without internal limiting membrane peeling. *Ophthalmology.* 2000;107(10):1939-1948; discussion 1948-1939.
67. Kwok AK, Lai TY, Wong VW. Idiopathic macular hole surgery in Chinese patients: a randomised study to compare indocyanine green-assisted internal limiting membrane peeling with no internal limiting membrane peeling. *Hong Kong Med J.* 2005;11(4):259-266.
68. Spiteri Cornish K, Lois N, Scott N, et al. Vitrectomy with internal limiting membrane (ILM) peeling versus vitrectomy with no peeling for idiopathic full-thickness macular hole (FTMH). *The Cochrane database of systematic reviews.* 2013(6):CD009306.
69. Spiteri Cornish K, Lois N, Scott NW, et al. Vitrectomy with internal limiting membrane peeling versus no peeling for idiopathic full-thickness macular hole. *Ophthalmology.* 2014;121(3):649-655.
70. Bae K, Kang SW, Kim JH, Kim SJ, Kim JM, Yoon JM. Extent of internal limiting membrane peeling and its impact on macular hole surgery outcomes: a randomized trial. *Am J Ophthalmol.* 2016;169:179-188.
71. Michalewska Z, Michalewski J, Adelman RA, Nawrocki J. Inverted internal limiting membrane flap technique for large macular holes. *Ophthalmology.* 2010;117(10):2018-2025.
72. Michalewska Z, Michalewski J, Dulczewska-Cichecka K, Adelman RA, Nawrocki J. TEMPORAL INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE VERSUS CLASSIC INVERTED INTERNAL LIMITING MEMBRANE FLAP TECHNIQUE: A Comparative Study. *Retina.* 2015;35(9):1844-1850.
73. Rizzo S, Tartaro R, Barca F, Caporossi T, Bacherini D, Giansanti F. Internal Limiting Membrane Peeling Versus Inverted Flap Technique for Treatment of Full-Thickness Macular Holes: A Comparative Study in a Large Series of Patients. *Retina.* 2018;38 Suppl 1:S73-S78.
74. Chatziralli IP, Theodossiadis PG, Steel DHW. Internal Limiting Membrane Peeling in Macular Hole Surgery; Why, When, and How? *Retina.* 2018;38(5):870-882.
75. Ternent L, Vale L, Boachie C, Burr JM, Lois N. Full-Thickness Macular Hole and Internal Limiting Membrane Peeling Study (FILMS) Group. Cost-effectiveness of internal limiting membrane peeling versus no peeling for patients with an idiopathic full-thickness macular hole: results from a randomised controlled trial. *The British journal of ophthalmology.* 2012;96(3):438-443.

76. Tognetto D, Zenoni S, Sanguinetti G, Haritoglou C, Ravalico G. Staining of the internal limiting membrane with intravitreal triamcinolone acetonide. *Retina.* 2005;25(4):462-467.
77. Da Mata AP, Burk SE, Foster RE, et al. Long-term follow-up of indocyanine green-assisted peeling of the retinal internal limiting membrane during vitrectomy surgery for idiopathic macular hole repair. *Ophthalmology.* 2004;111(12):2246-2253.
78. Beutel J, Dahmen G, Ziegler A, Hoerauf H. Internal limiting membrane peeling with indocyanine green or trypan blue in macular hole surgery: a randomized trial. *Arch Ophthalmol.* 2007;125(3):326-332.
79. Kwok AK, Li WW, Pang CP, et al. Indocyanine green staining and removal of internal limiting membrane in macular hole surgery: histology and outcome. *Am J Ophthalmol.* 2001;132(2):178-183.
80. Shah GK, Rosenblatt BJ, Blinder KJ, Grand MG, Smith M. Triamcinolone-assisted internal limiting membrane peeling. *Retina.* 2005;25(8):972-975.
81. Haritoglou C, Gandorfer A, Gass CA, Schaumberger M, Ulbig MW, Kampik A. Indocyanine green-assisted peeling of the internal limiting membrane in macular hole surgery affects visual outcome: a clinicopathologic correlation. *Am J Ophthalmol.* 2002;134(6):836-841.
82. Engelbrecht NE, Freeman J, Sternberg P, Jr., et al. Retinal pigment epithelial changes after macular hole surgery with indocyanine green-assisted internal limiting membrane peeling. *Am J Ophthalmol.* 2002;133(1):89-94.
83. Tsipursky MS, Heller MA, De Souza SA, et al. Comparative evaluation of no dye assistance, indocyanine green and triamcinolone acetonide for internal limiting membrane peeling during macular hole surgery. *Retina.* 2013;33(6):1123-1131.
84. Bellerive C, Cinq-Mars B, Louis M, et al. Retinal function assessment of trypan blue versus indocyanine green assisted internal limiting membrane peeling during macular hole surgery. *Can J Ophthalmol.* 2013;48(2):104-109.
85. Horio N, Horiguchi M. Effect on visual outcome after macular hole surgery when staining the internal limiting membrane with indocyanine green dye. *Arch Ophthalmol.* 2004;122(7):992-996.
86. Baba T, Hagiwara A, Sato E, Arai M, Oshitari T, Yamamoto S. Comparison of vitrectomy with brilliant blue G or indocyanine green on retinal microstructure and function of eyes with macular hole. *Ophthalmology.* 2012;119(12):2609-2615.
87. Shiono A, Kogo J, Klose G, Ueno S, Takagi H. Effects of indocyanine green staining on the recovery of visual acuity and macular morphology after macular hole surgery. *Ophthalmologica Journal international d'ophtalmologie International journal of ophthalmology Zeitschrift fur Augenheilkunde.* 2013;230(3):138-143.
88. Machida S, Toba Y, Nishimura T, Ohzeki T, Murai K, Kurosaka D. Comparisons of cone electroretinograms after indocyanine green-, brilliant blue G-, or triamcinolone acetonide-assisted macular hole surgery. *Graefes Arch Clin Exp Ophthalmol.* 2014;252(9):1423-1433.
89. Williamson TH, Lee E. Idiopathic macular hole: analysis of visual outcomes and the use of indocyanine green or brilliant blue for internal limiting membrane peel. *Graefes Arch Clin Exp Ophthalmol.* 2014;252(3):395-400.
90. Machida S, Nishimura T, Ohzeki T, Murai KI, Kurosaka D. Comparisons of focal macular electroretinograms after indocyanine green-, brilliant blue G-, or triamcinolone acetonide-assisted macular hole surgery. *Graefes Arch Clin Exp Ophthalmol.* 2017;255(3):485-492.
91. Thompson JT, Smiddy WE, Glaser BM, Sjaarda RN, Flynn HW, Jr. Intraocular tamponade duration and success of macular hole surgery. *Retina.* 1996;16(5):373-382.
92. Thompson JT, Glaser BM, Sjaarda RN, Murphy RP, Hanham A. Effects of intraocular bubble duration in the treatment of macular holes by vitrectomy and transforming growth factor-beta 2. *Ophthalmology.* 1994;101(7):1195-1200.
93. Mulhern MG, Cullinane A, Cleary PE. Visual and anatomical success with short-term macular tamponade and autologous platelet concentrate. *Graefes Arch Clin Exp Ophthalmol.* 2000;238(7):577-583.
94. Almeida DR, Wong J, Belliveau M, Rayat J, Gale J. Anatomical and visual outcomes of macular hole surgery with short-duration 3-day face-down positioning. *Retina.* 2012;32(3):506-510.
95. Forsaa VA, Krohn J. Air Tamponade Combined with Nonsupine Positioning in Macular Hole Surgery for Pseudophakic Eyes. *Retina.* 2017;37(9):1750-1756.
96. Goldbaum MH, McCuen BW, Hanneken AM, Burgess SK, Chen HH. Silicone oil tamponade to seal macular holes without position restrictions. *Ophthalmology.* 1998;105(11):2140-2148.
97. Pertile G, Claes C. Silicone oil vs. gas for the treatment of full-thickness macular hole. *Bull Soc Belge Ophtalmol.* 1999;274:31-36.

98. Lai JC, Stinnett SS, McCuen BW. Comparison of silicone oil versus gas tamponade in the treatment of idiopathic full-thickness macular hole. *Ophthalmology.* 2003;110(6):1170-1174.
99. Ciulla TA, Frederick AR, Jr., Kelly C, Amrein R. Postvitrectomy positioning complicated by ulnar nerve palsy. *Am J Ophthalmol.* 1996;122(5):739-740.
100. Rabon RJ, Zakov ZN, Meyers SM, Wilbourn AJ. Ulnar nerve mononeuropathies after face-down positioning. *Am J Ophthalmol.* 1986;102(1):125.
101. Treister G, Wygnanski T. Pressure sore in a patient who underwent repair of a retinal tear with gas injection. *Graefes Arch Clin Exp Ophthalmol.* 1996;234(10):657-658.
102. Mittra RA, Kim JE, Han DP, Pollack JS. Sustained postoperative face-down positioning is unnecessary for successful macular hole surgery. *Br J Ophthalmol.* 2009;93(5):664-666.
103. Dhawahir-Scala FE, Maino A, Saha K, Mokashi AA, McLauchlan R, Charles S. To posture or not to posture after macular hole surgery. *Retina.* 2008;28(1):60-65.
104. Tornambe PE, Poliner LS, Grote K. Macular hole surgery without face-down positioning. A pilot study. *Retina.* 1997;17(3):179-185.
105. Tranos PG, Peter NM, Nath R, et al. Macular hole surgery without prone positioning. *Eye.* 2007;21(6):802-806.
106. Isomae T, Sato Y, Shimada H. Shortening the duration of prone positioning after macular hole surgery- comparison between 1-week and 1-day prone positioning. *Jpn J Ophthalmol.* 2002;46(1):84-88.
107. Simcock PR, Scalia S. Phacovitrectomy without prone posture for full thickness macular holes. *Br J Ophthalmol.* 2001;85(11):1316-1319.
108. Guillaubey A, Malvitte L, Lafontaine PO, et al. Comparison of face-down and seated position after idiopathic macular hole surgery: a randomized clinical trial. *Am J Ophthalmol.* 2008;146(1):128-134.
109. Carvounis PE, Kopel AC, Kuhl DP, Heffez J, Pepple K, Holz ER. 25-gauge vitrectomy using sulfur hexafluoride and no prone positioning for repair of macular holes. *Retina.* 2008;28(9):1188-1192.
110. Tadayoni R, Vicaut E, Devin F, et al. A randomized controlled trial of alleviated positioning after small macular hole surgery. *Ophthalmology.* 2011;118(1):150-155.
111. Alberti M, la Cour M. Nonsupine positioning in macular hole surgery: a noninferiority randomized clinical trial. *Retina.* 2016;36(11):2072-2079.
112. Elborgy ES, Starr MR, Kotowski JG, Chehade JEA, Iezzi R. No Face-down Positioning Surgery for the Repair of Chronic Idiopathic Macular Holes. *Retina.* 2018.
113. Couvillion SS, Smiddy WE, Flynn HW, Jr., Eifrig CW, Gregori G. Outcomes of surgery for idiopathic macular hole: a case-control study comparing silicone oil with gas tamponade. *Ophthalmic surgery, lasers & imaging : the official journal of the International Society for Imaging in the Eye.* 2005;36(5):365-371.
114. Rizzo S, Genovesi-Ebert F, Vento A, Cresti F, Miniaci S, Romagnoli MC. Heavy silicone oil (Densiron-68) for the treatment of persistent macular holes: Densiron-68 endotamponade for persistent macular holes. *Graefes Arch Clin Exp Ophthalmol.* 2009;247(11):1471-1476.
115. Li DQ, Choudhry N. Swept-Source OCT Visualization of Macular Hole Closure in Gas-Filled Eyes. *Ophthalmic Surg Lasers Imaging Retina.* 2017;48(5):392-398.
116. Masuyama K, Yamakiri K, Arimura N, Sonoda Y, Doi N, Sakamoto T. Posturing time after macular hole surgery modified by optical coherence tomography images: a pilot study. *Am J Ophthalmol.* 2009;147(3):481-488 e482.
117. Sano M, Inoue M, Itoh Y, et al. Duration of Prone Positioning after Macular Hole Surgery Determined by Swept-Source Optical Coherence Tomography. *Retina.* 2017;37(8):1483-1491.
118. Hu Z, Xie P, Ding Y, Zheng X, Yuan D, Liu Q. Face-down or no face-down posturing following macular hole surgery: a meta-analysis. *Acta Ophthalmol.* 2016;94(4):326-333.
119. Haritoglou C, Reiniger IW, Schaumberger M, Gass CA, Priglinger SG, Kampik A. Five-year follow-up of macular hole surgery with peeling of the internal limiting membrane: update of a prospective study. *Retina.* 2006;26(6):618-622.
120. Jaycock PD, Bunce C, Xing W, et al. Outcomes of macular hole surgery: implications for surgical management and clinical governance. *Eye.* 2005;19(8):879-884.
121. Hirneiss C, Neubauer AS, Gass CA, et al. Visual quality of life after macular hole surgery: outcome and predictive factors. *Br J Ophthalmol.* 2007;91(4):481-484.
122. Thompson JT, Sjaarda RN, Lansing MB. The results of vitreous surgery for chronic macular holes. *Retina.* 1997;17(6):493-501.
123. Kang HK, Chang AA, Beaumont PE. The macular hole: report of an Australian surgical series and meta-analysis of the literature. *Clin Experiment Ophthalmol.* 2000;28(4):298-308.

124. Wendel RT, Patel AC, Kelly NE, Salzano TC, Wells JW, Novack GD. Vitreous surgery for macular holes. *Ophthalmology.* 1993;100(11):1671-1676.
125. Willis AW, Garcia-Cosio JF. Macular hole surgery. Comparison of longstanding versus recent macular holes. *Ophthalmology.* 1996;103(11):1811-1814.
126. Tilanus MA, Cuypers MH, Bemelmans NA, Pinckers AJ, Deutman AF. Predictive value of pattern VEP, pattern ERG and hole size in macular hole surgery. *Graefes Arch Clin Exp Ophthalmol.* 1999;237(8):629-635.
127. Scott RA, Ezra E, West JF, Gregor ZJ. Visual and anatomical results of surgery for long standing macular holes. *Br J Ophthalmol.* 2000;84(2):150-153.
128. Cheng L, Azen SP, El-Bradey MH, et al. Effects of preoperative and postoperative epiretinal membranes on macular hole closure and visual restoration. *Ophthalmology.* 2002;109(8):1514-1520.
129. Kobayashi H, Kobayashi K. Correlation of quantitative three-dimensional measurements of macular hole size with visual acuity after vitrectomy. *Graefes Arch Clin Exp Ophthalmol.* 1999;237(4):283-288.
130. Ullrich S, Haritoglou C, Gass C, Schaumberger M, Ulbig MW, Kampik A. Macular hole size as a prognostic factor in macular hole surgery. *Br J Ophthalmol.* 2002;86(4):390-393.
131. Byhr E, Lindblom B. Preoperative measurements of macular hole with scanning laser ophthalmoscopy. Correlation with functional outcome. *Acta Ophthalmol Scand.* 1998;76(5):579-583.
132. Ip MS, Baker BJ, Duker JS, et al. Anatomical outcomes of surgery for idiopathic macular hole as determined by optical coherence tomography. *Arch Ophthalmol.* 2002;120(1):29-35.
133. Valldeperas X, Wong D. Is it worth reoperating on macular holes? *Ophthalmology.* 2008;115(1):158-163.
134. Hillenkamp J, Kraus J, Framme C, et al. Retreatment of full-thickness macular hole: predictive value of optical coherence tomography. *Br J Ophthalmol.* 2007;91(11):1445-1449.
135. Haritoglou C, Gass CA, Schaumberger M, Gandorfer A, Ulbig MW, Kampik A. Long-term follow-up after macular hole surgery with internal limiting membrane peeling. *Am J Ophthalmol.* 2002;134:661-666f.
136. Passemard M, Yakoubi Y, Muselier A, et al. Long-term outcome of idiopathic macular hole surgery. *Am J Ophthalmol.* 2010;149(1):120-126.
137. Scott IU, Moraczewski AL, Smiddy WE, Flynn HW, Jr., Feuer WJ. Long-term anatomic and visual acuity outcomes after initial anatomic success with macular hole surgery. *Am J Ophthalmol.* 2003;135(5):633-640.
138. Bhatnagar P, Kaiser PK, Smith SD, Meisler DM, Lewis H, Sears JE. Reopening of previously closed macular holes after cataract extraction. *Am J Ophthalmol.* 2007;144(2):252-259.
139. Simcock PR, Scalia S. Phaco-vitrectomy for full-thickness macular holes. *Acta Ophthalmol Scand.* 2000;78(6):684-686.
140. Lahey JM, Francis RR, Fong DS, Kearney JJ, Tanaka S. Combining phacoemulsification with vitrectomy for treatment of macular holes. *Br J Ophthalmol.* 2002;86(8):876-878.
141. Paques M, Massin P, Blain P, Duquesnoy AS, Gaudric A. Long-term incidence of reopening of macular holes. *Ophthalmology.* 2000;107(4):760-766.
142. Christmas NJ, Smiddy WE, Flynn HW, Jr. Reopening of macular holes after initially successful repair. *Ophthalmology.* 1998;105(10):1835-1838.
143. Duker JS, Wendel R, Patel AC, Puliafito CA. Late re-opening of macular holes after initially successful treatment with vitreous surgery. *Ophthalmology.* 1994;101(8):1373-1378.
144. Banker AS, Freeman WR, Kim JW, Munguia D, Azen SP. Vitrectomy for Macular Hole Study Group. Vision-threatening complications of surgery for full-thickness macular holes. *Ophthalmology.* 1997;104(9):1442-1452; discussion 1452-1443.
145. Park SS, Marcus DM, Duker JS, et al. Posterior segment complications after vitrectomy for macular hole. *Ophthalmology.* 1995;102(5):775-781.
146. Meng Q, Zhang S, Ling Y, Cui D, Jin Y. Long-term anatomic and visual outcomes of initially closed macular holes. *Am J Ophthalmol.* 2011;151(5):896-900.
147. Paques M, Chastang C, Mathis A, et al. Platelets in Macular Hole Surgery Group. Effect of autologous platelet concentrate in surgery for idiopathic macular hole: results of a multicenter, double-masked, randomized trial. *Ophthalmology.* 1999;106(5):932-938.
148. Sjaarda RN, Glaser BM, Thompson JT, Murphy RP, Hanham A. Distribution of iatrogenic retinal breaks in macular hole surgery. *Ophthalmology.* 1995;102(9):1387-1392.

149. Minihan M, Cleary PE. Autologous platelet concentrate in the surgical management of macular holes. *Dev Ophthalmol.* 1997;29:36-43.
150. Heier JS, Topping TM, Frederick AR, Jr., Morley MG, Millay R, Pesavento RD. Visual and surgical outcomes of retinal detachment following macular hole repair. *Retina.* 1999;19(2):110-115.
151. Fajgenbaum MAP, Neffendorf JE, Wong RS, Laidlaw DAH, Williamson TH. INTRAOPERATIVE AND POSTOPERATIVE COMPLICATIONS IN PHACOVITRECTOMY FOR EPIRETINAL MEMBRANE AND MACULAR HOLE: A Clinical Audit of 1,000 Consecutive Eyes. *Retina.* 2018;38(9):1865-1872.
152. Parke DW, 3rd, Lum F. Return to the Operating Room after Macular Surgery: IRIS Registry Analysis. *Ophthalmology.* 2018;125(8):1273-1278.
153. Pendergast SD, McCuen BW, II. Visual field loss after macular hole surgery. *Ophthalmology.* 1996;103(7):1069-1077.
154. Paques M, Massin P, Santiago PY, Spielmann AC, Gaudric A. Visual field loss after vitrectomy for full-thickness macular holes. *Am J Ophthalmol.* 1997;124(1):88-94.
155. Arima T, Uemura A, Otsuka S, Doi N, Nakao K. Macular hole surgery-associated peripheral visual field loss. *Jpn J Ophthalmol.* 1998;42(6):476-483.
156. Boldt HC, Munden PM, Folk JC, Mehaffey MG. Visual field defects after macular hole surgery. *Am J Ophthalmol.* 1996;122(3):371-381.
157. Bopp S, Lucke K, Hille U. Peripheral visual field loss after vitreous surgery for macular holes. *Graefes Arch Clin Exp Ophthalmol.* 1997;235(6):362-371.
158. Welch JC. Dehydration injury as a possible cause of visual field defect after pars plana vitrectomy for macular hole. *Am J Ophthalmol.* 1997;124(5):698-699.
159. Welch JC. Prevention of visual field defect after macular hole surgery by passing air used for fluid-air exchange through water. *Am J Ophthalmol.* 1999;128(3):396-397.
160. Ohji M, Nao IN, Saito Y, Hayashi A, Tano Y. Prevention of visual field defect after macular hole surgery by passing air used for fluid-air exchange through water. *Am J Ophthalmol.* 1999;127(1):62-66.
161. Gass CA, Haritoglou C, Messmer EM, Schaumberger M, Kampik A. Peripheral visual field defects after macular hole surgery: a complication with decreasing incidence. *Br J Ophthalmol.* 2001;85(5):549-551.
162. Hirata A, Yonemura N, Hasumura T, Murata Y, Negi A. Effect of infusion air pressure on visual field defects after macular hole surgery. *Am J Ophthalmol.* 2000;130(5):611-616.
163. Levasseur SD, Rahhal FM. Travel to high mountain elevations following vitrectomy with intraocular gas. *Retina.* 2013;33(7):1456-1461.
164. Gsellman L, Amini R. Patients With Intravitreal Gas Bubbles at Risk of High Intraocular Pressure Without Exceeding Elevation of Surgery: Theoretical Analysis. *Investigative ophthalmology & visual science.* 2016;57(7):3340-3347.
165. Stalmans P, Benz MS, Gandorfer A, et al. MIVI-TRUST Study Group. Enzymatic vitreolysis with ocriplasmin for vitreomacular traction and macular holes. *The New England journal of medicine.* 2012;367(7):606-615.
166. Lim JI, Glassman AR, Aiello LP, et al. Macula society collaborative retrospective study of ocriplasmin for symptomatic vitreomacular adhesion. *Opthalmology Retina.* 2017;1(5):413-420.
167. Dugel PU, Regillo C, Eliott D. Characterization of anatomic and visual function outcomes in patients with full-thickness macular hole in ocriplasmin phase 3 trials. *Am J Ophthalmol.* 2015;160(1):94-99 e91.
168. Khanani AM, Duker JS, Heier JS, et al. Ocriplasmin Treatment Leads to Symptomatic Vitreomacular Adhesion/Vitreomacular Traction Resolution in the Real-World Setting: The Phase IV Orbit Study. *Ophthalmology Retina.* 2018.
169. Maier M, Abraham S, Frank C, Lohmann CP, Feucht N. [Pharmaological vitreolysis with ocriplasmin as a treatment option for symptomatic focal vitreomacular traction with or without macular holes (</=400 mum) compared to tranconjunctival vitrectomy]. *Ophthalmologe.* 2017;114(2):148-154.
170. Haynes RJ, Yorston D, Laidlaw DA, Keller J, Steel DH. Real world outcomes of ocriplasmin use by members of the British and Eire Association of Vitreoretinal Surgeons. *Eye (Lond).* 2017;31(1):107-112.
171. Dugel PU, Tolentino M, Feiner L, Kozma P, Leroy A. Results of the 2-year Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion Including Macular Hole (OASIS) randomized trial. *Ophthalmology.* 2016;123(10):2232-2247.

172. Greven MA, Garg S, Chiu B, et al. Vitrectomy After ocriplasmin for VitreOmacular adhesion Or Macular hole (VAVOOM) study. *Br J Ophthalmol.* 2016;100(9):1211-1215.
173. Dayan MR, Jayamanne DG, Andrews RM, Griffiths PG. Flashes and floaters as predictors of vitreoretinal pathology: is follow-up necessary for posterior vitreous detachment? *Eye.* 1996;10:456-458.
174. Byer NE. Natural history of posterior vitreous detachment with early management as the premier line of defense against retinal detachment. *Ophthalmology.* 1994;101(9):1503-1514.
175. Smiddy WE, Michels RG, de Bustros S, de la Cruz Z, Green WR. Histopathology of tissue removed during vitrectomy for impending idiopathic macular holes. *Am J Ophthalmol.* 1989;108(4):360-364.
176. Stelmack JA, Tang XC, Reda DJ, Rinne S, Mancil RM, Massof RW. LOVIT Study Group. Outcomes of the Veterans Affairs Low Vision Intervention Trial (LOVIT). *Arch Ophthalmol.* 2008;126(5):608-617.
177. Fontenot JL, Bona MD, Kaleem MA, et al. Vision Rehabilitation Preferred Practice Pattern®. *Ophthalmology.* 2018;125(1):P228-P278.
178. Pearce IA, Branley M, Groenewald C, McGalliard J, Wong D. Visual function and patient satisfaction after macular hole surgery. *Eye.* 1998;12 (Pt 4):651-658.
179. Polk TD, Smiddy WE, Flynn HW, Jr. Bilateral visual function after macular hole surgery. *Ophthalmology.* 1996;103(3):422-426.
180. Hikichi T, Onodera A, Ishiko S, Fujio N, Mori F, Yoshida A. Stereo acuity in patients with unilateral macular hole and after unilateral macular hole surgery. *Graefes Arch Clin Exp Ophthalmol.* 2001;239(2):128-132.
181. Chang JS, Smiddy WE. Cost evaluation of surgical and pharmaceutical options in treatment for vitreomacular adhesions and macular holes. *Ophthalmology.* 2014;121(9):1720-1726.