Published in final edited form as:
Ophthalmology. 2004 November ; 111(11): 2027–2032.

Stage 0 Macular Holes: Observations by Optical Coherence Tomography

Annie Chan, BS[1], **Jay S. Duker, MD**[1], **Joel S. Schuman, MD**[2], and **James G. Fujimoto, PhD**[3]

1 *New England Eye Center, Tufts–New England Medical Center, Tufts University School of Medicine, Boston, Massachusetts*

2 *University of Pittsburgh Medical Center Eye Center, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania*

3 *Department of Electrical Engineering and Computer Science, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts*

Abstract

Objective— To introduce the concept of a stage 0 macular hole based on optical coherence tomographic observations of the vitreoretinal interface in fellow eyes of patients with unilateral idiopathic macular holes, and to evaluate the subsequent risk of progression to a full-thickness macular hole.

Design— Retrospective observational case series.

Participants— Ninety-four patients with a unilateral stage 2, 3, or 4 full-thickness macular hole.

Methods— The medical records of patients with a unilateral macular hole diagnosed between 1994 and 2000 at the New England Eye Center were reviewed.

Main Outcome Measure— Development of a full-thickness macular hole in the fellow eye on biomicroscopic fundoscopy or optical coherence tomography (OCT).

Results— In 27 (28.7%) of 94 clinically normal fellow eyes, OCT detected an abnormality of the vitreoretinal interface but normal foveal anatomy. The vitreoretinal abnormalities were further subclassified into severe (4 eyes), moderate (8 eyes), and mild (15 eyes) based on the intensity and morphology of the OCT signal. One of the 4 (25%) severe cases progressed to a full-thickness macular hole, 4 of the 8 (50%) moderate cases became full-thickness macular holes, and no (0%) mild cases progressed to a full-thickness macular hole. Severe and moderate eyes seemed to share characteristic features on OCT that increased their risk of macular hole development (stage 0 macular hole). The macular hole–free survival at 48 months was 94% for stage 0–negative patients, versus 54% for stage 0–positive patients. Univariate analysis revealed that the presence of a stage 0 macular hole was significantly associated with an almost 6-fold increase in the risk of macular hole formation (relative risk: 5.8, 95% confidence interval: 1.16–28.61, $P = 0.03$).

Conclusions— A stage 0 macular hole has a normal biomicroscopic appearance clinically, but has salient features on OCT as a result of oblique vitreous traction. Optical coherence tomographic findings consist of a normal foveal contour and normal retinal thickness and must include the presence of a preretinal, minimally reflective, thin band inserting obliquely on at least one side of the fovea.

Reprint requests to Jay S. Duker, MD, Tufts–New England Medical Center, New England Eye Center, 750 Washington Street, Box #450, Boston, MA 02111-1533. E-mail: jduker@tufts-nemc.org.

Drs Fujimoto and Schuman receive royalties from intellectual property licensed by Massachusetts Institute of Technology, Cambridge, Massachusetts, to Carl Zeiss Meditec, Inc., Dublin, California.

Presented in part as a poster at: Association for Research on Vision and Ophthalmology annual meeting, April, 2004; Fort Lauderdale, Florida. Presented at: American Academy of Ophthalmology annual meeting, October, 2004; New Orleans, Louisiana.

The presence of a stage 0 macular hole in the fellow eye is a significant risk factor for the development of a second macular hole.

Before 1991, idiopathic macular holes were regarded as an untreatable cause of central visual loss. The first reports of surgical success by Kelly and Wendel generated a great deal of interest and spearheaded new research into the prevalence, pathogenesis, and treatment of idiopathic macular holes.[1] For patients contemplating surgery for a unilateral macular hole, knowing the risk of subsequent involvement of the second eye is important. Recent advances in imaging provide additional information concerning the pathogenesis of idiopathic macular holes and may help predict this risk more accurately.

The currently accepted classification scheme for staging macular holes is based on biomicroscopic observations and interpretations by Gass,[2–4] not clinicopathologic considerations. Gass's theory of tangential vitreous traction was initially widely accepted, but several anatomic features of macular holes were inadequately explained by this theory. There is general agreement that abnormal vitreofoveal traction is intimately involved in macular hole formation, but the precise mechanism has been controversial. One of the main reasons for this controversy is that the posterior hyaloid itself is typically invisible on clinical examination and, until recently, difficult to detect with most imaging modalities. The high-resolution cross-sectional imaging of the retina achieved by optical coherence tomography (OCT) has enabled clinicians to study the vitreofoveal pathoanatomy more easily.[5–7]

The sequence of events leading to a full-thickness macular hole has been well documented by OCT.[7–10] Using OCT imaging, investigators have reported the presence of a localized separation of the posterior vitreous with persistent adherence of the vitreous at the fovea in eyes with stage 1 and stage 2 macular holes, as well as in fellow eyes that were biomicroscopically normal.[7–12] This has been described as a perifoveal posterior vitreous detachment (PVD). It is hypothesized that anteroposterior forces are exerted at the site of persistent attachment. These tractional forces cause intraretinal splitting in stage 1 macular holes, leading to a pseudocyst or, more rarely, a foveolar detachment as hypothesized by Gass.[2,3] The roof of the pseudocyst eventually opens, with concomitant elevation of the foveal floor. The retinal layers become disrupted as this progresses to a full-thickness dehiscence.

We have observed a distinct pattern on OCT that appears in some eyes before stage 1 macular hole formation. In this article, we describe this phenomenon and introduce the concept of a stage 0 macular hole, based on information obtained from OCT images of fellow eyes of idiopathic macular holes. To our knowledge, this is the first such study to classify these findings as a stage 0 macular hole and, more importantly, the first to determine the relative risk of a stage 0 hole in macular hole formation.

Patients and Methods

Studies were performed on the prototype OCT system based on a slit-lamp biomicroscope. The prototype instrument had ~10-mm axial image resolution and acquired 100 A-scans per OCT image. A total of 182 patients with a diagnosis of a macular hole were identified from a computer database containing all patients examined with the prototype OCT system between September 1994 and August 2000 at the New England Eye Center. Patients with bilateral involvement at the initial visit or with no follow-up after the initial visit were excluded. Patients were also excluded due to predisposing factors, including intraocular inflammatory disease, ocular surgery, trauma, and retinal detachment. Only patients diagnosed with a stage 2, 3, or 4 full-thickness macular hole were included in this study. All patients engaged in an informed consent process and signed a written consent document before being examined and imaged by

the prototype OCT for both eyes. The study was reviewed and approved by the Tufts–New England Medical Center Institutional Review Board committee.

Patients received a complete ophthalmic examination of both eyes, including best-corrected visual acuities (VAs), Amsler grid testing, indirect and contact lens slit-lamp biomicroscopy, fundus photography, fluorescein angiography, and OCT. An experienced operator performed all OCT examinations through a dilated pupil. At least 6 radial scans of 6 mm in length, centered through the fovea, were obtained for each eye. A PVD was considered to be present only if a complete or partial ring of glial tissue (a Weiss ring) was seen on biomicroscopic examination. Fellow eyes with a clinically documented PVD were excluded.

Each macular hole was graded clinically according to the criteria established by Gass. In addition, with respect to the clinically normal fellow eyes, vitreoretinal anatomic alterations were classified as mild, moderate, and severe cases based solely on the intensity and morphology of the OCT preretinal signal in the perifoveal region. Severe cases were defined by the presence of a thin, minimally reflective, preretinal band (posterior hyaloid) located on both sides of the fovea seen clearly inserting into the perifoveal region (Fig 1, top). Moderate cases were defined by the presence of a thin, minimally reflective, preretinal band seen clearly inserting on only one side of the perifoveal region (Fig 1, middle). In mild cases, a preretinal band was visible, but no distinct point of insertion could be seen (Fig 1, bottom).

Follow-up information was obtained from New England Eye Center charts and, in one instance, from the referring physician.

The principal outcome measure in this study was the development of a macular hole in the fellow eye. Due to the overall limited number of events in this study, the Kaplan–Meier method was used for descriptive purposes only. Univariate analysis based on the Cox proportional hazards model was performed to calculate hazard ratios with 95% confidence intervals (CIs). Statistical analysis was performed with SAS,[13] and the graphs were produced using S-Plus.[14]

Results

Ninety-four patients with a diagnosis of an idiopathic stage 2, 3, or 4 full-thickness macular hole in one eye and a biomicroscopically normal fellow eye at the initial examination formed the study cohort. There were 67 (71.3%) women and 27 (28.7%) men. The mean patient age was 65 years (range, 31–84). The average length of follow-up was 41 months (range, 2–142).

All 94 fellow eyes had a normal macula and no PVD on fundus biomicroscopy and a normal foveal contour and macular thickness on OCT at the initial visit. Optical coherence tomography detected an abnormality of the vitreoretinal interface in 27 (28.7%) fellow eyes at the initial visit or during the follow-up period. From this group, 1 of the 4 severe cases progressed to a full-thickness macular hole (25%), 4 of the 8 moderate cases became full-thickness macular holes (50%), and no mild cases (0%) progressed to a full-thickness macular hole. The mean interval between the onset of a macular hole in the first and second eye in these patients was 29 months (range, 6–47). Of the 67 fellow eyes without any evidence of an abnormal vitreoretinal interface, 3 (4.3%) developed full-thickness macular holes. The mean interval between the onset of a macular hole in the first and second eyes in these patients was 16 months (range, 6–21).

Only fellow eyes with definite signs of oblique traction (≥1 posterior hyaloid insertion points on OCT) were considered true stage 0 macular holes. A stage 0 macular hole is defined as a clinically normal eye with a normal foveal contour and normal retinal thickness on OCT, but must also have a preretinal, minimally reflective, thin band (posterior hyaloid) inserting on at

least one side of the fovea as a result of oblique traction. The severe and moderate cases in this study met the definition of a stage 0 macular hole. The rate of macular hole formation in these eyes is 5/12 (42%).

Cumulative survival curves were generated according to the Kaplan–Meier method and are shown in Figure 2. The macular hole–free survival of fellow eyes at 48 months was 94% for stage 0–negative patients, versus 54% for stage 0–positive patients. The predictive value of a stage 0 hole in macular hole formation was evaluated by univariate analysis based on the Cox proportional hazards regression model and expressed as a relative risk. The results revealed that the presence of a stage 0 hole was associated with an almost 6-fold increase in risk of macular hole formation (relative risk: 5.8, 95% CI: 1.16–28.61, $P = 0.03$).

Case Report

A 59-year-old woman was referred for surgery for a stage 3 full-thickness macular hole in her right eye. In the left eye, VA was 20/20, no PVD was found, and the macula appeared normal on biomicroscopy. Optical coherence tomography revealed a normal macular profile and a partial separation of the posterior hyaloid with persistent adherence at the foveolar center. Six months later, VA had decreased to 20/80 in the left eye, and OCT revealed a new disruption in the inner layer of the retina indicating an eccentric stage 2 macular hole. This patient subsequently underwent successful pars plana vitrectomy of her left eye. Two months after surgery, VA improved to 20/20 in the left eye. Biomicroscopic examination showed closure of the macular hole. Postoperative OCT confirmed successful reapproximation of the edges of the macular hole (Fig 3).

Discussion

The vitreous was implicated in the development of macular holes as early as 1924.[15] Since then, different theories regarding the role of vitreous traction have been proposed to explain the underlying mechanism.[2–4,16–21] Several authors postulated that the initial stages of macular holes were the result of a PVD secondary to anteroposterior traction. This theory was replaced in 1988 when Gass described a clinical classification scheme for staging macular holes and introduced the concept of tangential vitreous traction.[2] The pre-foveal opacity seen in some macular holes was thought to contain neural tissue, but this could not explain the reports of excellent visual improvement after surgery. Gass later reappraised his theory to suggest that no foveal tissue was lost from the macula, but rather that the hole was caused by centrifugal displacement of photoreceptors after a central dehiscence at the umbo.[4]

Until recently, attempts at directly visualizing the vitreo-retinal interface were challenging. The availability of OCT has allowed clinicians to witness the earliest stages of macular hole formation and establish the sequence of events leading from vitreous traction to a full-thickness hole. Optical coherence tomography has elucidated that the traction in the early stages of macular hole development is actually oblique. In many cases of early macular holes and biomicroscopically normal fellow eyes, there seems to be a separation of the hyaloid face with focal attachments at the fovea and optic disc. This phenomenon was first described by Hee et al.[8] Further OCT studies by Gaudric et al illustrated the natural progression of these initial findings into a full-thickness macular hole.[9] In addition, Johnson et al provided evidence from B-scan ultrasonography and surgery suggesting that a perifoveal vitreous detachment, as the initial stage of age-related PVD, is the primary pathogenic event in idiopathic macular hole development.[22] However, the present study is the first to classify these findings as a stage 0 macular hole and, more importantly, the first to evaluate the risk of progression to a full-thickness macular hole in clinically normal fellow eyes that exhibited these features on OCT.

Based on our observations of OCT images of clinically normal fellow eyes, we have identified a set of salient findings. We propose a modification to the current Gass clinical criteria by classifying these findings on OCT as a stage 0 macular hole. In stage 0 macular holes, the fibers of the posterior hyaloid seem to insert on the fovea obliquely, then flatten and extend to the periphery, and finally reinsert onto the retinal surface outside the foveal area. The difference in signal may be due to the location of the macular hole. The oblique vitreous forces may be distributed unevenly in eccentric holes. The vitreous changes in most patients with idiopathic macular holes are unlike the marked changes seen in vitreomacular traction syndromes. Furthermore, OCT may be more accurate than conventional methods for staging macular holes and potentially may serve as the basis for a new classification scheme.

In terms of management, surgery is not warranted for most stage 1 macular holes because there is a 40% to 50% chance of spontaneous vitreofoveal separation with resolution of associated signs and symptoms.[23] However, counseling patients with unilateral macular holes can be difficult when addressing the risk of bilateral involvement. A recent prospective study by Chew et al reported that, in fellow unaffected eyes, the rate of development of new macular holes during follow-up was 4.3% at ≤3 years, 6.5% at 4 to 5 years, and 7.1% at ≥6 years.[24] Patients may feel reassured that their risk for bilateral involvement is low, but should be aware that a stage 0 macular hole in the fellow eye may put them at a higher risk for macular hole development in that eye. Based on our study, we estimate that there is an almost 6-fold increase in risk for patients with stage 0 macular holes in their fellow eyes. Of course, a prospective study would be important for confirming the estimated risk of a stage 0 macular hole.

In the case of both an absent biomicroscopically visible PVD and an absent perifoveal posterior hyaloid insertion on OCT (67 patients), there are 2 possibilities. First, perhaps the process of vitreomacular separation has not been initiated and thus these eyes are still at risk for developing a macular hole—this would account for the 4.3% in this group who eventually developed a second macular hole. Another possible explanation is that the scans were not long enough to detect a missed PVD.

We observed that no so-called mild cases developed into a full-thickness macular hole. It is conceivable that these mild cases were actually complete PVDs that were not detected by biomicroscopic examination or by OCT and were thus conferred theoretical immunity to macular hole development. In these mild eyes, there was no clear point of insertion of the posterior hyaloid into the perifoveal area and, thus, no evidence of oblique traction. In the current study, all fellow eyes that eventually progressed to full-thickness macular holes exhibited at least one prominent point of insertion of the posterior hyaloid at the perifoveal region on OCT. Therefore, a clear point of insertion of the posterior hyaloid on at least one side of the fovea is necessary for a diagnosis of a true stage 0 macular hole on OCT.

Uchino et al described a similar configuration on OCT in healthy eyes of normal patients, as a precursor to age-related PVD.[25] In these eyes, he showed that the initial separation occurred in the superior quadrant and continued slowly to involve all quadrants until a complete PVD occurred. The moderate eyes in our study are similar to his stage 1 PVD, whereas the severe eyes are similar to his stage 2 PVD, with respect to the presence of a perifoveal posterior hyaloid insertion. It is indeed difficult to distinguish between an early macular hole and an early age-related PVD on OCT. However, it is important to note that Uchino et al looked at a population of patients very different from that of our study. Their study cohort was composed of all healthy patients with healthy eyes, whereas our cohort is composed of patients who have already developed a full-thickness idiopathic macular hole and are likely to be at a higher risk for developing a second full-thickness macular hole. We attempted to estimate this risk by evaluating OCT images of fellow eyes. In our study, 3 of 67 (4.5%) fellow eyes without this

OCT configuration developed a full-thickness macular hole, as opposed to 5 of 12 patients with a stage 0 macular hole (42%).

There are several limitations in this study. The data were limited by the overall number of events and therefore should be interpreted with caution. With longer and better follow-up, we might detect more macular holes. It is possible that patients who developed a macular hole in the fellow eye may be more likely to come back and be ascertained preferentially. However, this would not explain the discrepancy between the different rates of bilateral macular hole formation in the 2 groups of patients: those without a stage 0 macular hole and those with a stage 0 macular hole on OCT. A larger number of patients need to be studied in order to assess the risk of stage 0 macular holes more rigorously.

In conclusion, a stage 0 macular hole has a normal biomicroscopic appearance clinically but has salient features on OCT as a result of oblique vitreous traction. Findings include a normal foveal contour and normal retinal thickness, and must include the presence of a preretinal, minimally reflective band inserting obliquely on at least one side of the fovea on OCT. A patient with a stage 0 macular hole in the fellow eye is estimated to be approximately 6 times more likely to develop a macular hole in that eye than a patient without a stage 0 macular hole. These new findings may be helpful in counseling patients regarding surgical management.

Acknowledgements

The authors thank Lori Lyn Price from the Institute for Clinical Research and Health Policy Studies at Tufts–New England Medical Center for assistance with the data analysis.

References

1. Kelly NE, Wendel RT. Vitreous surgery for idiopathic macular holes: results of a pilot study. Arch Ophthalmol 1991;109:654–9. [PubMed: 2025167]
2. Gass JDM. Idiopathic senile macular hole: its early stages and pathogenesis. Arch Ophthalmol 1988;106:629–39. [PubMed: 3358729]
3. Johnson RN, Gass JD. Idiopathic macular holes. Observations, stages of formation, and implications for surgical intervention. Ophthalmology 1988;95:917–24. [PubMed: 3174041]
4. Gass JD. Reappraisal of biomicroscopic classification of stages of development of a macular hole. Am J Ophthalmol 1995;119:752–9. [PubMed: 7785690]
5. Huang D, Swanson EA, Lin CP, et al. Optical coherence tomography. Science 1991;254:1178–81. [PubMed: 1957169]
6. Hee MR, Izatt JA, Swanson EA, et al. Optical coherence tomography of the human retina. Arch Ophthalmol 1995;113:325–32. [PubMed: 7887846]
7. Puliafito CA, Hee MR, Lin CP, et al. Imaging of macular diseases with optical coherence tomography. Ophthalmology 1995;102:217–29. [PubMed: 7862410]
8. Hee MR, Puliafito CA, Wong C, et al. Optical coherence tomography of macular holes. Ophthalmology 1995;102:748–56. [PubMed: 7777274]
9. Gaudric A, Haouchine B, Massin P, et al. Macular hole formation: new data provided by optical coherence tomography. Arch Ophthalmol 1999;117:744–51. [PubMed: 10369584]
10. 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;108:15–22. [PubMed: 11150257]
11. Tanner V, Chauhan DS, Jackson TL, Williamson TH. Optical coherence tomography of the vitreoretinal interface in macular hole formation. Br J Ophthalmol 2001;85:1092–7. [PubMed: 11520763]
12. Chauhan DS, Antcliff RJ, Rai PA, et al. Papillofoveal traction in macular hole formation: the role of optical coherence tomography. Arch Ophthalmol 2000;118:32–8. [PubMed: 10636411]
13. SAS [computer program]. Version 8.2. Cary, NC: SAS Institute; 2001.

14. S-Plus [computer program]. Version 6.1. Seattle: Insightful Corp; 2002.
15. Lister W. Holes in the retina and their clinical significance. Br J Ophthalmol 1924;8:1–20.
16. Reese AB, Jones IS, Cooper WC. Macular changes secondary to vitreous traction. Am J Ophthalmol 1967;64(suppl):544–9. [PubMed: 6039077]
17. Tolentino, FI.; Schepens, CL.; Freeman, HM. Vitreoretinal Disorders: Diagnosis and Management. Philadelphia: WB Saunders; 1976. p. 400-12.
18. McDonnell PJ, Fine SL, Hillis AI. Clinical features of idiopathic macular cysts and holes. Am J Ophthalmol 1982;93:777–86. [PubMed: 7091263]
19. Morgan CM, Schatz H. Involutional macular thinning: a pre-macular hole condition. Ophthalmology 1986;93:153–61. [PubMed: 3951821]
20. Akiba J, Quiroz MA, Trempe CL. Role of posterior vitreous detachment in idiopathic macular holes. Ophthalmology 1990;97:1610–3. [PubMed: 2087292]
21. Avila MP, Jalkh AE, Murakami K, et al. Biomicroscopic study of the vitreous in macular breaks. Ophthalmology 1983;90:1277–83. [PubMed: 6664666]
22. Johnson MW, Van Newkirk MR, Meyer KA. Perifoveal vitreous detachment is the primary pathogenic event in idiopathic macular hole formation. Arch Ophthalmol 2001;119:215–22. [PubMed: 11176982]
23. 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;101:1055–9. [PubMed: 8008347]discussion 1060
24. Chew EY, Sperducto RD, Hiller R, et al. Clinical course of macular holes: the Eye Disease Case-Control Study. Arch Ophthalmol 1999;117:242–6. [PubMed: 10037571]
25. Uchino E, Uemura A, Ohba N. Initial stages of posterior vitreous detachments in healthy eyes of older persons evaluated by optical coherence tomography. Arch Ophthalmol 2001;119:1475–9. [PubMed: 11594947]

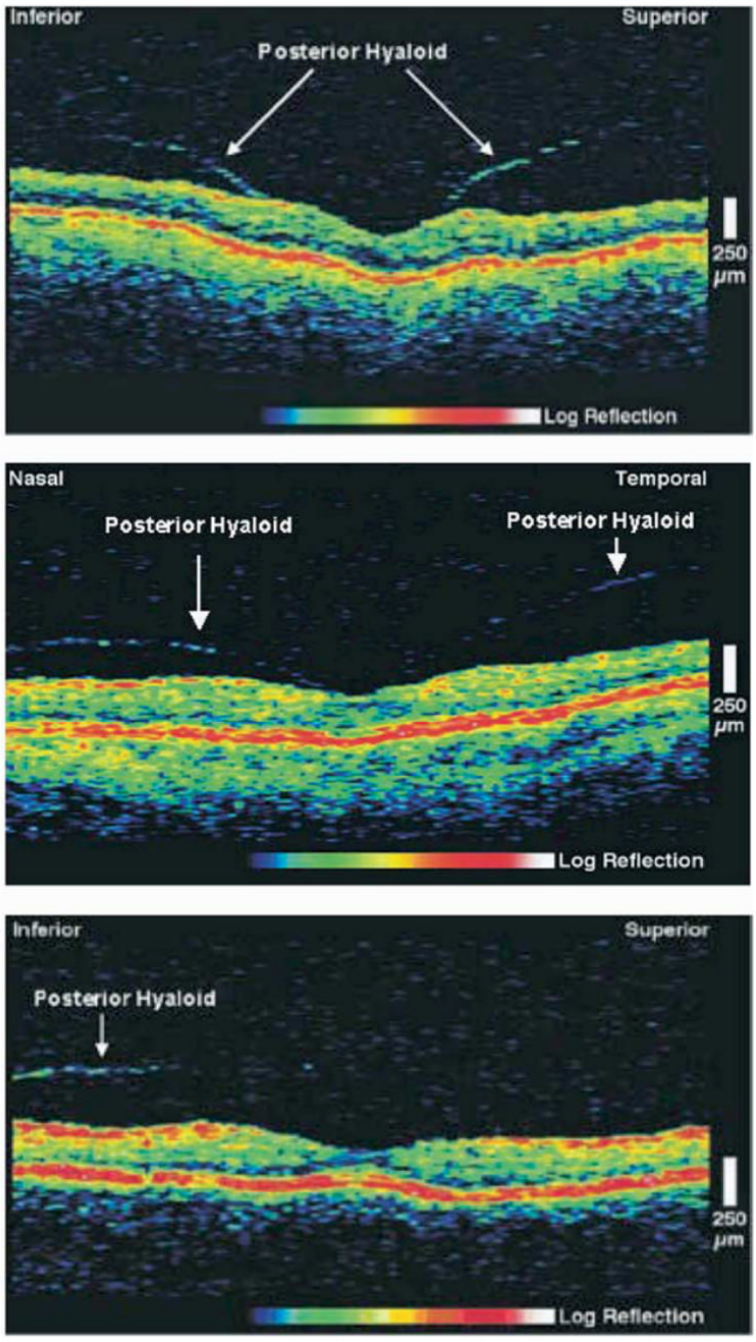

Figure 1.

Optical coherence tomography of fellow eyes with abnormalities at the vitreoretinal interface, classified according to the morphology and severity of the signal from the visible posterior hyaloid. **Top**, Severe case: prominent insertion of posterior hyaloid on both sides (superiorly and inferiorly) of the perifoveal region. **Middle**, Moderate case: prominent insertion of posterior hyaloid on only one side (nasal) of the perifoveal region. There is no distinct point of insertion on the other side (temporal). **Bottom**, Mild case: a preretinal signal corresponding to the posterior hyaloid is visible inferiorly, but there is no clear point of insertion. No posterior vitreous detachment was found on clinical examination.

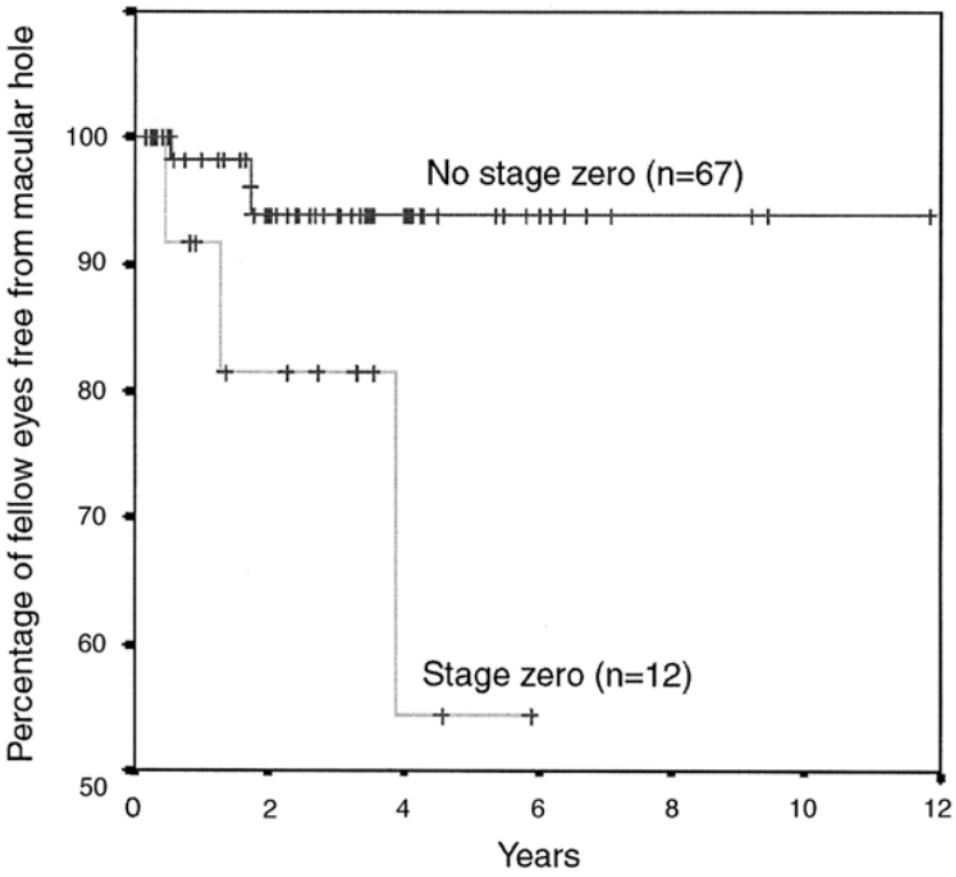

Figure 2.
Kaplan–Meier survival curve. A comparison of the proportion free from a macular hole in biomicroscopically normal fellow eyes between patients with a stage 0 macular hole and those without.

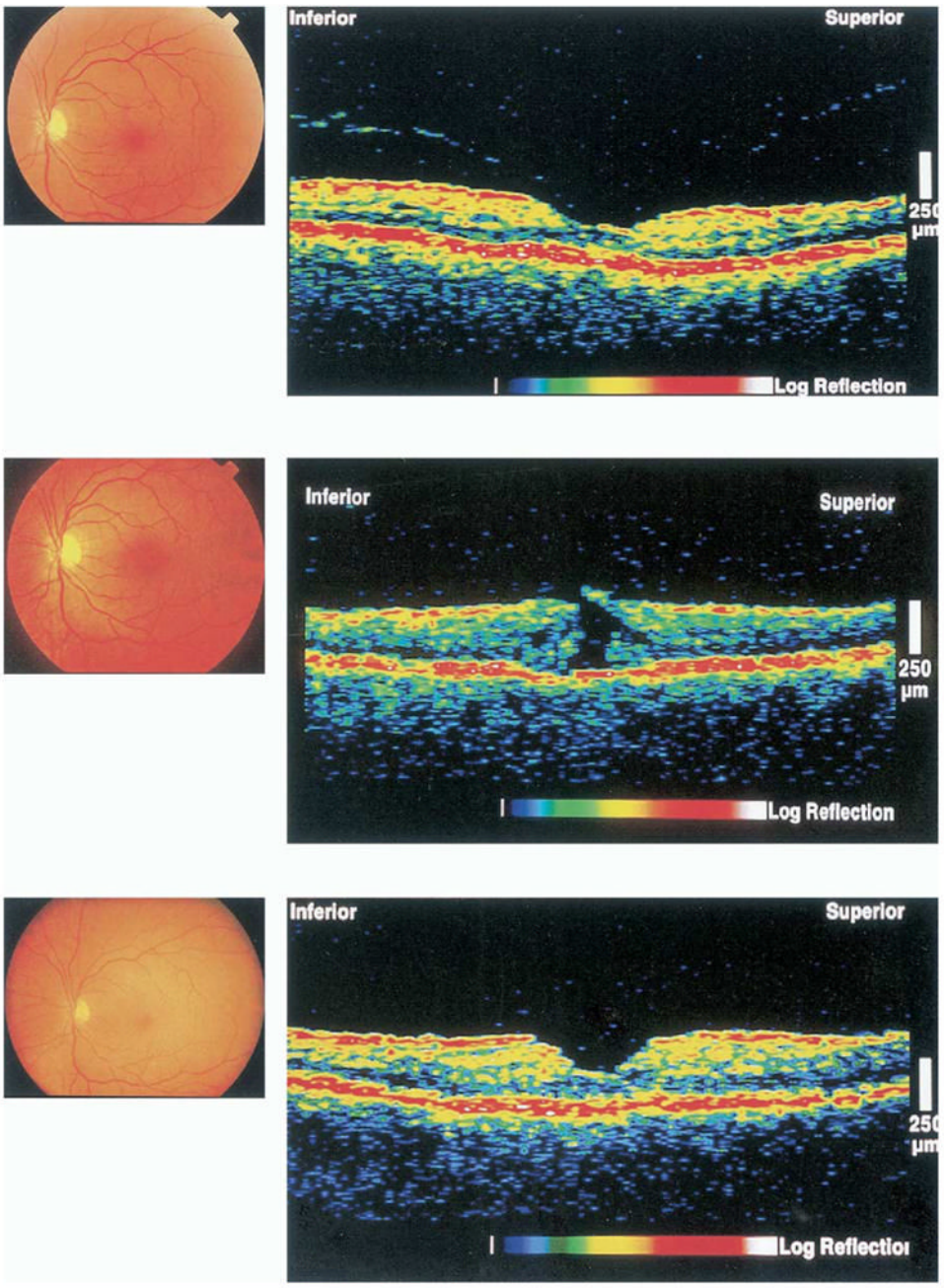

Figure 3.

Evolution of a stage 0 macular hole to a stage 2 macular hole and subsequent surgical repair (case report). **Top**, Normal color photograph. Optical coherence tomography (OCT) showing normal foveal contour and thickness, a partially separated posterior hyaloid with persistent adherence at the fovea. **Middle**, Six months later, a color photograph reveals an eccentric full-thickness defect. Optical coherence tomography shows a new disruption in the inner layer of the retina, constituting a stage 2 macular hole. **Bottom**, Two months after macular hole surgery, a color photograph reveals resolution of the macular hole. The postoperative OCT image demonstrates reapproximation of the edges of the macular hole.