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CLINICAL INVESTIGATION

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Bilaterality of idiopathic macular holes

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Abstract ● Background: There has been wide variation in estimates of the incidence of bilateral idiopathic macular holes in the literature. This report of a large series of patients with macular holes provides further information regarding incidence of bilaterality, interval between onset in the first and the second eye, and visual outcome. ● Methods: A retrospective chart review was done of 550 patients with idiopathic macular holes examined at the Bascom Palmer Eye Institute between 1968 and 1994. The incidence of bilaterality was estimated from 365 patients in whom the fellow eye was normal at the initial examination. The rate of onset in the fellow eye was evaluated by survival analysis. Mean follow-up was 31 months (median 17 months). ● Results: Patients with incomplete macular holes (stage 1, aborted stage 1, lamellar) or full-thickness holes had a 19% incidence of bilaterality at 48 months follow-up. In the subset of 32 patients with full-thickness macular holes in the first eye, 13% developed full-thickness holes in the fellow eye within 48 months. The median interval between the onset in the first and in the second eye was 17.5 months. Visual acuity was excellent and stable in eyes with aborted stage 1 and lamellar holes. The visual acuity in the first eye with full-thickness macular hole decreased to 20/200 or worse in 79% of cases within 36 months' follow-up. ● Conclusions: The incidence of bilaterality and poor visual function in the majority of full-thickness idiopathic macular holes by 3 years' duration should be considered when advising patients and planning management.

Introduction

The clinical appearance and staging of idiopathic macular holes have been described by Gass and colleagues [5, 7, 8, 11]. This condition is receiving increasing attention since surgical intervention has been reported to improve vision in a substantial proportion of cases [12]. It is important to establish the potential surgical candidate's risk of bilateral involvement and visual loss due to idiopathic macular holes.

Bedell [3] and Tower [15] originally thought that all fellow eyes would eventually go on to develop macular holes, given enough time. However, more recent studies have estimated involvement of the second eye to be 13–31% [1, 9, 10, 13, 18]. These estimates are probably exessive due to referral bias [1]. Series that have longitudinally observed fellow eyes report a 0–16% incidence of bilaterality [2, 4, 16].

This paper presents the largest reported series of patients with macular holes and provides further information regarding incidence of bilaterality and visual prognosis.

Table 1 Reasons for exclusion

Reason	No. of patients
Retinal detachment	53
Trauma	23
High myopia (>−8.00 D)	20
Diabetic retinopathy	24
Severe glaucoma	6
Vascular occlusion	3
Other conditions (uveitis, media opacities, macular degeneration)	25

Materials and methods

Charts of patients diagnosed with a macular hole between 1968 and 1994 at Bascom Palmer Eye Institute were reviewed. Non-idiopathic macular holes and idiopathic holes associated with other ocular conditions affecting visual acuity were excluded (Table 1).

Of the 550 patients with idiopathic macular holes, 121 had bilateral involvement at the initial visit, 54 had other diseases affecting the vision in the fellow eye, and 10 did not have a sufficiently precise date of onset in the first eye. The remaining 365 patients with a normal fellow eye at the initial examination formed the study cohort.

Follow-up information was obtained from the Bascom Palmer Eye Institute charts and in a few instances from the referring physician. The length of follow-up for the purpose of recording the vision for natural history evaluation was until the last visit or the date of surgery in eyes operated. One hundred and sixty-nine of the 365 initially unilateral cases, and 22 of the 36 cases that became bilateral, had surgery.

The date of macular hole onset was defined by onset of symptoms as reported by the patient, except for two patients who were asymptomatic when a lamellar hole was diagnosed in the second eye. The stage of the macular hole and visual acuity were noted at the initial and follow-up visits. The status of the posterior vitreous in the fellow eye was recorded from notations in the chart. If there was no comment in the chart (n=111), the vitreous was considered to be attached.

For this paper, we defined incomplete macular hole as stage 1, aborted stage 1, or lamellar macular hole, and a full-thickness macular hole as stage 2, 3, or 4 macular hole. Of 365 first eyes, 25 had incomplete macular holes and 340 had full-thickness holes. The incidence of bilaterality was determined from 365 fellow eyes that were normal and asymptomatic at the initial examination. Two groups of patients were evaluated: (1) those with an incomplete or full-thickness macular hole in the first eye who developed an incomplete or full-thickness hole in the second eye (n=36), and (2) the subset of the above group containing only patients with full-thickness macular hole in the first eye who also developed a full-thickness hole in the second eye (n=24). Survival analysis was used to evaluate the incidence of bilaterality and compensate for length of follow-up. The rates were determined for all fellow eyes and for fellow eyes without posterior vitreous detachment.

The weaknesses of this retrospective study include a lack of systematic evaluation of the vitreous in fellow eyes, lack of a standardized refraction and vision charts, and possible referral biases.

This study was reviewed and approved by the University of Miami Human Subjects Research Committee.

Results

Baseline characteristics

Of 550 patients, 707 eyes were affected: 51% of these were right eyes and 49% left eyes. Macular holes were diagnosed at the Bascom Palmer Eye Institute with increased frequency as the study period progressed. Eleven macular holes were diagnosed between 1968 and 1977 (1.1/year), 160 from 1978 to 1987 (16/year), and 378 between 1988 and 1994 (54/year). The sex distribution was 71% female, 29% male, and the mean age at onset was 67 years. The age and sex distribution were similar in unilateral and bilateral cases. The distribution of refractive errors in all eyes with macular holes was −6.00 to −8.00 D in 2%, less than −6.00 D in 90%, aphakic in 0.7%, pseudophakic in 7%, and unknown in 0.3% of eyes.

The median follow-up interval was 15 months for the 329 patients remaining unilateral (mean=28 months, range 1–220 months) and 17.5 months for the 36 patients who were observed to develop a macular hole in the fellow eye (mean=30 months, range=1–200 months). These differences were not statistically significant.

Posterior vitreous

The status of the posterior vitreous was described in 254 of the fellow eyes (70%); 63% were attached and 36% were detached. The charts from 111 patients contained no comment on the status of the vitreous, and for evaluation of incidence of bilaterality these eyes were included with those that had attached vitreous. Only two eyes (0.3% of all fellow eyes, 2% of those with detached vitreous) in this series had posterior vitreous detachment (PVD) noted before a macular hole developed.

Stages of macular hole in the 36 patients with observed onset in the second eye

Stage 1 (impending macular holes) was diagnosed with increasing frequency during the study. One impending hole was diagnosed between 1968 and 1977, the remainder between 1978 and 1994: Tables 2 and 3 show the stages of macular holes at onset and at final visit or prior to surgery in the first eyes and second eyes respectively. At initial examination of the first eye, one eye had aborted the hole with a pseudo-operculum, and three had formed a lamellar hole with operculum. No patient had an incomplete macular hole in both eyes at final follow-up. Twenty-four eyes (first and second eyes) had stage 1 macular holes at initial diagnosis. Three were operated at stage 1, five aborted or formed a lamellar hole, and 16

Table 2 Stages of macular holes: first eye (n=36)

	Onset	Final	No. operated
Abort/lamellar	2	3	
Stage 1	6	1	1
Stage 2	6	0	
Stage 3	19	18	5
Stage 4	3	14	2

Table 3 Stages of macular holes: second eye (n=36)

	Onset	Final	No. operated
Abort/lamellar	2	6	
Stage 1	18	2	2
Stage 2	11	6	4
Stage 3	5	15	6
Stage 4	0	7	2

(67%) progressed to full-thickness holes. Seventeen eyes had stage 2 macular holes; four were operated, two remained stable, and 11 progressed to stage 3 or 4 (85% of non-operated eyes). Of 24 stage 3 eyes, 11 were operated, two remained stable, 10 progressed to stage 4 (77% of non-operated eyes) and one spontaneously sealed. At the initial visit only three eyes were stage 4, but by the final or presurgery visit 18 more eyes had progressed to stage 4, and four were operated.

Visual outcome of 36 patients with observed onset in the second eye

Visual acuity was recorded in all eyes except one fellow eye, and best refracted visual acuity was documented in 80% of eyes at the initial visit, 51% of eyes at the final visit, and 90% prior to surgery. Of the eyes in which vision deteriorated to 20/200, 68% were refracted at the time of visual loss, but often not thereafter. One patient had significant recovery of vision in the first eye, with a lamellar hole (20/100 to 20/40), after the second eye was affected with a full-thickness macular hole. Visual acuity was 20/40 or better in all aborted stage 1 and lamellar macular holes. One stage 3 hole spontaneously resolved, with improvement of vision from 20/100 to 20/60. The distribution of final visual acuity versus final stage of macular hole is seen in Table 4. Only five eyes with full-thickness macular holes had vision worse than 20/200.

All stage 2 eyes had vision better than 20/200. A survival analysis for eyes with stage 3 and 4 holes decreasing to 20/200 vision is seen in Fig. 1. Visual acuity in 79% of the first eyes deteriorated to 20/200 or worse within 36 months' follow-up. There was a gradual increase in the proportion of second eyes that dropped to 20/200 or worse vision (Fig. 1), although shorter follow-up prevented precise estimation of the rate of visual decline.

Table 4 Visual acuity vs stage of macular hole (at final visit or surgery)

	20/20–40	20/50–70	20/80–160	≤20/200
Abort/lamellar	9	0	0	0
Stage 1	2	1	0	0
Stage 2	1	5	0	0
Stage 3	1	7	6	18
Stage 4	0	2	9	10

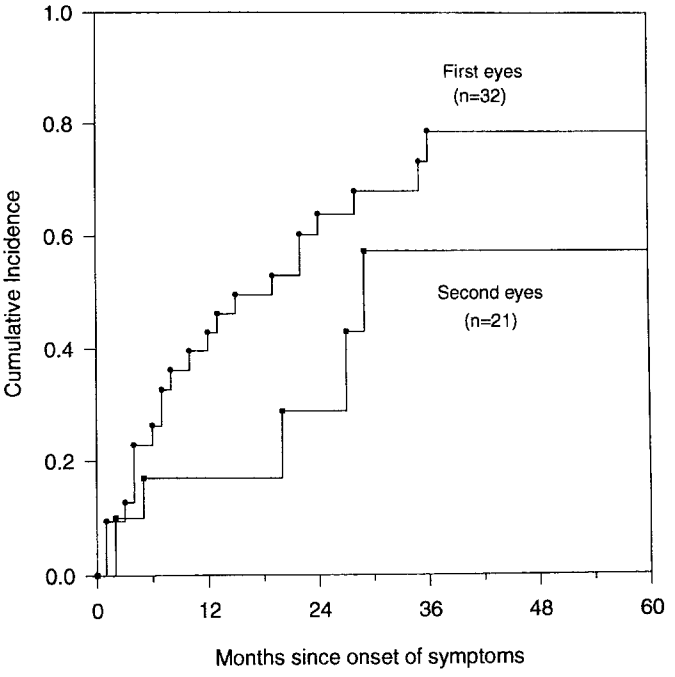

Fig. 1 Proportion of eyes of bilateral cases with visual acuity of 20/200 or worse. *Lines* indicate the rates (calculated with Kaplan-Meier analysis) at which vision deteriorates to of 20/200 or worse. Visual loss is shown separately for the first and second eyes of these patients. Only eyes with stage 3 and 4 macular holes are included in the analysis, as no eye with stage 1 or 2 hole dropped to 20/200 vision. At 36 months after the patients noticed symptoms in their first eyes, 79% of these eyes had lost vision to 20/200. At 36 months after patients noticed symptoms in their second eye, 57% of these eyes had lost vision to 20/200

Incidence of bilaterality

Survival analysis (Fig. 2) shows the rate of onset of bilateral incomplete and/or full-thickness macular holes and the subset of only bilateral full-thickness macular holes. The median interval between the onset in the first and in the second eye was 17.5 months (mean 30 months, range 1–200 months). The age of onset was not correlated with the interval between onset in the first and the second eye (P=0.09). The incidence of bilaterality of all stages of macular holes was 19% within 4 years in fellow eyes regardless of the status of the posterior vitreous, and 22% in eyes with attached vitreous.

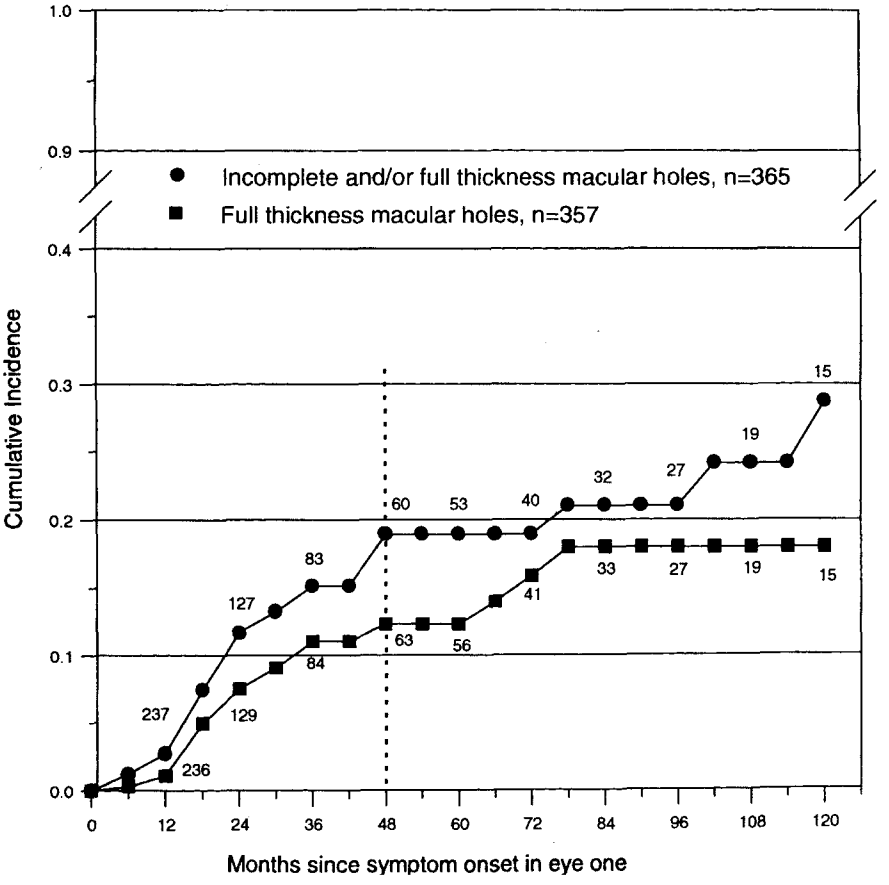

Fig. 2 Incidence of second eye involvement among patients with initially unilateral idiopathic macular holes. *Lines* indicate the cumulative incidence (by life table analysis) of incomplete and/or full-thickness holes (*circles*) and bilateral full-thickness holes (*squares*). *Numbers* next to the incidence lines show the remaining sample sizes. The incidence at 48 months is 19% for incomplete and/or full-thickness holes and 13% for bilateral full-thickness holes. After 54 months, decreasing sample sizes and increasing standard errors make these estimates less precise

In patients with a full-thickness macular hole in the first eye, the incidence of onset of full-thickness macular hole in the second eye within 4 years was 13% of all fellow eyes and 14% of eyes with attached vitreous at initial visit. Two eyes (2% of those with detached vitreous) had PVD described prior to the onset of the macular hole. We place less importance on the rate estimates after 54 months due to decreasing sample sizes.

Discussion

The prevalence of bilaterality of macular holes has been reported as 13–31% [1, 9, 13]. In our series the prevalence of bilaterality of incomplete and full-thickness macular holes was 28%. This and previous series are subject to referral bias, but the bias is lessened by examining follow-up features of initially normal fellow eyes [2, 4, 16]. Such studies describe an incidence of macular hole formation of 0–17% over a mean follow-up of 36–47 months [2, 4, 16]. In our series of 365 normal fellow eyes, the incidence of bilateral incomplete and/or full-thickness macular hole was 19% (22% in eyes with attached vitreous). The incidence of bilateral full-thickness macular holes was 13% (14% in eyes with attached vitreous). Although a few patients had long intervals between the onset in the first eye and that in the second eye (up to 16 years), more than one half of the onsets in the second eye occurred within 18 months of the onset in the first eye. There was no significant correlation between the age of onset and the time that elapsed between onset the first and in the second eye.

The rate of occurrence in eyes with initially attached posterior vitreous has been reported to be higher, up to 29% [16]. In some reports, none of the eyes with detached vitreous have been observed to develop a macular hole [2, 16]. In the current study, the second eye developed a full-thickness macular hole in 14% of eyes without PVD and only 2% of eyes with PVD at baseline, suggesting that PVD is generally protective against development of a macular hole [2, 5, 6, 16]. However, it should be noted that only 25% of fellow eyes in this series had PVD at baseline.

The classification system for stages of idiopathic macular holes was developed by Dr. Gass at Bascom Palmer Eye Institute, and many clinical cases were classified, including stage 1 (impending) macular holes, before his publication in 1988 [5]. A 67% incidence of progression of stage 1 holes to full-thickness holes was observed in the present study, similar to Gass's rate of

57% [5]. Progression to full-thickness macular holes occurred in 85% of eyes with stage 2 holes and 77% of eyes with stage 3 holes at initial diagnosis, similar to rates noted previously [9]. We noted spontaneous resolution of a stage 3 hole in one eye (<1%), a lower incidence than the 5–6% reported by Guyer et al. [9] and Yuzawa et al. [19].

The visual acuities in aborted stage 1 and lamellar macular holes in this series were excellent and stable (20/40 or better), as in previous studies [2, 5, 7, 14, 17]. The visual acuities in full-thickness macular holes tended to decline until stabilizing at 20/200 [1, 11, 13, 14]. Visual acuity in 79% of first eyes with stage 3 and 4 holes at initial diagnosis had deteriorated to the 20/200 level within 36 months of onset. Vision was worse than 20/200 in only five eyes. The gradual increase in proportion of second eyes that dropped to visions of 20/200 or worse as the study progressed probably indicates that with longer follow-up, vision in the second eyes will deteriorate to the same levels as the first eyes.

Although the incidence of bilateral involvement is not high, it must be considered in the counseling and management of patients with idiopathic macular holes. Careful clinical examination of the vitreous and macula in the fellow eye in patients with idiopathic macular hole is important in predicting the risk of involvement in the fellow eye. If the macula is normal and a PVD is present, the risk of involvement is low, but if the vitreous is attached, the eye is at a higher risk of developing a macular hole. Eyes with full-thickness macular holes have a poor prognosis for maintaining good central vision.

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