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Prevalence and Surgical Outcomes of Macular Hole in Eyes with Age-Related Macular Degeneration

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Purpose: To report the prevalence and surgical outcomes of macular holes (MHs) in eyes with age-related macular degeneration (AMD).

Design: Interventional, retrospective, consecutive case series.

Participants: Patients with MH and concurrent non-neovascular (NNV) or neovascular (NV) AMD.

Methods: The records of 27 912 patients diagnosed with AMD between 2009 and 2014 at Associated Retinal Consultants were reviewed. Demographic data, visual acuity (VA), funduscopic examination, and optical coherence tomography were reviewed in those with a concurrent diagnosis of MH.

Main Outcome Measures: The VA and MH closure status.

Results: A total of 15 196 patients with NNV and 12 716 patients with NV AMD were identified. A total of 199 eyes (0.7%) had MHs (160 NNV [1.1%]; 39 NV [0.3%]). Mean time to diagnosis of MH after the initial visit was 11.2 months (7.1 NNV; 24.8 NV). A total of 127 eyes underwent surgical repair (106 NNV; 21 NV). The final closure rate in those who underwent vitrectomy was 89.8% (91.5% NNV; 81.0% NV) and 25.0% in those who were observed (18.5% NNV, $P < 0.0001$; 44.4% NV, $P = 0.02$). Preoperative logarithm of the minimum angle of resolution VAs in NNV and NV AMD was 0.8±0.4 and 0.8±0.5, respectively, and final VA was 0.6±0.5 ($P < 0.001$) and 0.9±0.6 ($P = 0.52$), respectively. Mean follow-up time was 5.0 years.

Conclusions: The prevalence of MH was higher in eyes with NNV AMD than in those with NV AMD. The surgical closure rate was comparable in both groups, but VA improvement reached statistical significance only in the NNV AMD group. *Ophthalmology Retina 2016;■:1–7 © 2016 by the American Academy of Ophthalmology*

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries and has an estimated worldwide prevalence of 8.7%.[1] Complications include geographic atrophy (GA), choroidal neovascularization, hemorrhage, exudation, retinal pigment epithelial (RPE) detachment or tear, and fibrosis with profound central vision loss.[2] Non-neovascular (NNV) AMD currently is managed with vitamin supplementation if certain characteristics are met.[3] Neovascular (NV) AMD is treated with intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents.[4]

Macular hole (MH) also is a prevalent macular pathology. Full-thickness macular holes (FTMHs) are visually significant disruptions of foveal anatomy with an estimated incidence of 0.02% to 0.8% in those aged >40 years.[5,6] Originally described by Gass in 1988, the pathophysiologic mechanism of MH formation involves posterior hyaloid contraction, perifoveal vitreous detachment, and anterior-posterior vitreoretinal forces.[7,8] Current treatment options include observation, pharmacologic vitreolysis, and vitrectomy with or without internal limiting membrane (ILM) peeling.[9,10] Lamellar MHs are partial-thickness defects in the neurosensory retina, which are generally less visually significant.[11]

Our understanding and treatment of AMD and MH as individual entities have significantly improved over the years. However, little is known regarding eyes that harbor both AMD and MH.[12–14] Many questions remain unanswered, such as the prevalence, treatment response, and visual outcomes. The purpose of this study was to determine the prevalence of MHs in both NV and NNV AMD and to present the long-term surgical outcomes.

Methods

This was a single-center, interventional, consecutive, comparative, retrospective review of all medical records that contained diagnostic codes of a "macular hole" and "age-related macular degeneration" from January 1, 2009, to November 30, 2014, at the Associated Retinal Consultants. Institutional review board approval was granted. The study complied with the Health Insurance Portability and Accountability Act of 1996 and conformed to the tenets of the Declaration of Helsinki.

Eligibility

Inclusion criteria included a diagnosis of an MH and concurrent AMD. Exclusion criteria were: patients who (1) developed AMD after MH diagnosis, (2) underwent MH surgery at an outside facility, (3) had prior vitreoretinal surgery for another pathology before or concurrently with the MH diagnosis, (4) had other concurrent macular or vaso-occlusive pathology that may confound the

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visual acuities, and (5) were missing clinical information from the visits that required data collection, as noted next.

Data Collection

Demographic characteristics at first visit included age, gender, laterality, and concurrent ocular disease. Use of Age-Related Eye Disease Study supplementation and smoking status were obtained through self-reported patient questionnaires. Ocular characteristics extracted from the clinical examination records included best-corrected visual acuity (VA), lens status, posterior vitreous detachment (PVD) status, and number of intravitreal anti-VEGF injections and photodynamic therapy sessions. Additional characteristics, including vitreomacular traction (VMT), epiretinal membrane (ERM), GA, and intraretinal or subretinal fluid were determined by the clinical examination, color fundus photography, and optical coherence tomography (OCT) as noted by the authors' interpretation.

Diagnosis of MH was determined by fundoscopy or OCT. The OCT devices included spectral domain (Heidelberg Engineering, Carlsbad, CA, and Cirrus, Carl Zeiss Meditec, Dublin, CA) or time domain (Stratus, Carl Zeiss Meditec). The MH diagnosis (full-thickness or lamellar) and staging were based on both OCT findings and the caliper-based function on spectral domain imaging as determined by the authors.[15] For time domain images, we used the caliper-available images as a rough estimation to determine MH size.

Data were recorded for the following visits: the first visit, date of MH diagnosis, and final visit. For patients who underwent surgical repair of the MH, postoperative visit month 1 and year 1 also were included. Intraoperative characteristics of patients undergoing vitrectomy for MH treatment were documented, including gauge, ILM peeling, and use of indocyanine green (ICG).

Data Analysis

Statistical analysis was performed using STATA Version 13.1 (StataCorp LP, College Station, TX). Snellen best-corrected VA was converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis. Baseline, intraoperative, and follow-up characteristics of patients with NV and NNV AMD were compared using the Fisher exact t test (categoric variables) and Mann−Whitney U test (continuous variables). The MH closure rates, initial VA, and final VA were then compared between operative and nonoperative eyes by the type of AMD with the Mann−Whitney U test as outlined earlier. Statistical significance was defined as $P < 0.05$. All tests were 2 tailed.

Results

A total of 27 912 patients with AMD were identified during the study period. Of 15 196 patients with NNV AMD and 12 716 patients with NV AMD, 199 eyes with MHs from 185 patients were identified with a prevalence of 0.7% (1.0% NNV AMD; 0.3% NV AMD; $P < 0.0001$). Of the eyes with MHs, 158 (79.4%) were FTMH and 44 (22.1%) were lamellar MHs. The overall FTMH prevalence rate was 0.5% (0.8% NNV AMD; 0.2% NV AMD). Of note, 115 of 160 eyes with NV AMD (71.9%) and 15 of 39 eyes with NNV AMD (38.5%) had MHs on initial presentation. Thus, the estimated incidence rate of MH formation was 0.3% (45 eyes) in NV AMD and 0.2% (24 eyes) in NNV AMD.

There were no statistical differences in baseline characteristics between the NV and NNV groups with respect to age, gender, laterality, smoking status, lens status, PVD, and number of ocriplasmin injections (Table 1). There were also no differences in the presence of concurrent eye pathology between the 2 groups,

Table 1. Baseline Characteristics of Eyes with Concurrent Macular Hole and Age-Related Macular Degeneration

	Total	NNV AMD	NV AMD	P Value
Demographics				
Eyes, n	199	160	39	
Age at first visit, mean (range, yrs)	74 (52−96)	74.1 (52−96)	74 (56−90)	0.90
Gender				
Male, n (%)	58 (29.1)	45 (77.5)	13 (22.4)	0.56
Female, n (%)	141 (70.8)	115 (81.5)	26 (18.5)	
Current smoker				
Yes, n (%)	28 (14.1)	22 (78.6)	6 (21.4)	0.80
No, n (%)	171 (85.6)	138 (80.8)	33 (19.3)	
AREDS formula				
Yes, n (%)	59 (29.6)	51 (86.4)	8 (13.6)	0.18
No, n (%)	140 (70.4)	109 (77.8)	31 (22.1)	
Ocular Characteristics				
Laterality, n (%)				
Right	97 (48.7)	80 (82.5)	17 (17.5)	0.48
Left	102 (51.2)	80 (78.4)	22 (21.5)	
Lens status				
Phakic	97 (48.7)	77 (79.4)	20 (20.6)	0.86
Pseudophakic	102 (51.2)	83 (81.4)	19 (18.6)	
PVD				
Yes	57 (28.6)	47 (82.4)	10 (17.5)	0.70
No	142 (71.4)	113 (79.6)	29 (20.4)	
Ocriplasmin used, n (%)	8 (100.0)	5 (62.5)	3 (37.5)	0.14
Average follow up, yrs (mean, range)	5.0 (0.1−18.1)	4.6 (0.1−18.1)	6.2 (0.2−17.0)	0.046

AMD = age-related macular degeneration; AREDS = Age-Related Eye Disease Study; NNV = non-neovascular; NV = neovascular; PVD = posterior vitreous detachment.