Original Manuscript

ASRS American Society of Retina Specialists

Journal of VitreoRetinal Diseases
2024, Vol. 8(5) 524–532

DOI: 10.1177/24741264241264937
journals.sagepub.com/home/jvrd
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Risk Factors for Progression of Vitreomacular Traction to Macular Hole

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Abstract

Purpose: To evaluate the clinical and optical coherence tomography (OCT) characteristics associated with progression of vitreomacular traction (VMT) to a full-thickness macular hole (FTMH) and lamellar macular hole (LMH). **Methods:** A retrospective cohort study of patients with an OCT-confirmed diagnosis of idiopathic VMT and 6 or more months of follow-up was performed. Clinical data included age, sex, race, systemic comorbidities, hormone replacement therapy, corrected visual acuity (VA), subjective visual symptoms, OCT signs, and the presence of or progression to FTMH or LMH. **Results:** Of the 287 eyes with VMT, 48 (16.7%) progressed to MH. Twelve eyes (4.2%) progressed to LMH, and 36 eyes (12.5%) progressed to FTMH. Female sex ($P = .02$), myopic refractive status in phakic eyes ($P = .02$), subjective decreased VA ($P = .01$), and the presence of an inner segment–outer segment junction disruption on OCT ($P = .003$) were risk factors for progression from VMT to FTMH. Subjective metamorphopsia was a risk factor for progression to FTMH ($P = .001$) and LMH ($P = .01$). In a subgroup analysis, patients who had an FTMH in the fellow eye were significantly more likely to have VMT progress to FTMH in the study eye (24.0% vs 8.7%; $P = .04$). Having an LMH in the fellow eye was not a risk factor for progression to LMH in the study eye ($P = .47$). **Conclusions:** Risk factors were found for the progression of VMT to MH that may be clinically relevant for risk-stratifying patients presenting with VMT.

Keywords

vitreomacular traction syndrome, macular hole, OCT

Introduction

Normal vitreous aging involves progressive gel liquefaction and posterior vitreous cortex separation from the retinal surface, leading to age-related posterior vitreous detachment (PVD).[1–3] An anomalous PVD may occur as a result of an imbalance between the degree of vitreous liquefication and the extent of weakening of vitreoretinal adherence.[4] The development of a PVD involves progression of the vitreoretinal interface through multiple stages of partial vitreous separation from the retina, including vitreomacular adhesion (VMA), in which there remains some perifoveal attachment.[5,6] Adhesions can elicit tractional forces that lead to macular distortion, known as vitreomacular traction (VMT), and result in visual symptoms that include vision loss, blurred vision, and metamorphopsia.[6,7] Persistent traction can result in the development of a macular hole (MH).[6,8] A full-thickness macular hole (FTMH) is an anatomic defect characterized by a focal absence of all neural retinal layers, whereas a lamellar macular hole (LMH) is defined as a partial-thickness retinal defect.[6]

Visual acuity (VA) loss is often most significant once VMT has progressed to an MH.[9,10] Previous studies have shown an association between focal VMT and MH formation and have found that the pharmacologic release of VMT can lead to the development of an LMH or FTMH.[4,11] One study described a classification system for grading VMT based on foveal attachment (grade 1), intraretinal cysts/clefts (grade 2), and foveal detachment (grade 3) that predicted progression to an FTMH.[7] Advances in the resolution of optical coherence tomography (OCT) have allowed for more precise classification of vitreomacular interface pathology, such as VMA, VMT, and MHs.[12,13] However, the epidemiology and natural history of vitreomacular interface abnormalities are limited and few studies have investigated the risk factors for the progression of VMT to MH.[14–20]

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This study evaluated the clinical and OCT characteristics associated with the progression of VMT to MH (FTMH or LMH) in a large cohort evaluated at a tertiary academic center.

Methods

A retrospective single-center observational study was performed from January 2008 to December 2022 and included patients with VMT who had at least 6 months of follow-up at the Duke Eye Center, Durham, NC, USA. Because study inclusion posed no substantial risk to participants and data analysis consisted of de-identified information obtained through retrospective chart review, the requirement of informed consent was waived. Institutional review board (IRB)/ethics committee approval was obtained from the Duke University Health System IRB. This study complied with the US Health Insurance Portability and Accountability Act of 1996 and the tenets of the Declaration of Helsinki.

Study Population

The Duke Enterprise Data Unified Content Explorer (Duke University Health System) was used to identify patients with VMA and VMT from Maestro Care, the Duke Health electronic medical record (International Classification of Diseases [ICD]-9 subcode 379.27 and ICD-10 subcodes H43.821, H43.822, H43.823). VMT was defined using the OCT-based anatomic International Vitreomacular Traction Study Group classifications in which VMT is defined by the presence of vitreous traction and distorted foveal morphologic features.[6] All OCT images were obtained using the Spectralis device (Heidelberg Engineering). The first time that VMT was noted on OCT was designated as the baseline examination.

Eyes diagnosed with VMA based on International Vitreomacular Traction Study Group guidelines (vitreous adhesion to the macula with no demonstrable retinal morphologic changes) and eyes in which the vitreomacular interface could not be clearly delineated on the presenting or subsequent OCT images were excluded. Patients with significant macular pathology, including diabetic macular edema, macular neovascularization, intermediate or advanced neovascular age-related macular degeneration (AMD), non-neovascular AMD, retinal artery or vein occlusions; lens dislocation; moderate or severe nonproliferative diabetic retinopathy (DR); proliferative DR; and ocular trauma, including previous ocular surgery with planned or complicated involvement of the posterior segment, were also excluded. In addition, patients who received intravitreal injections for vitreolysis or ocular surgery involving the posterior segment to treat VMT were excluded.

Data Collection

Demographic data included age, sex, and race. Clinical data included details of the ophthalmic examination, active use of hormone replacement therapy (HRT), and a history of systemic diseases, such as hypertension, hyperlipidemia, and diabetes mellitus (DM). The corrected distance VA, axial length, spherical equivalent, lens status (phakic, pseudophakic), refractive status of phakic eyes (myopic, hyperopic), and presence of subjective decreased VA and metamorphopsia in the study eye at baseline examination were recorded.

Spectral-domain OCT measurements, including VMT length (focal VMT defined as 1500 μm or less) and central subfield thickness, were recorded for each eye. Two independent graders documented the presence or absence of OCT signs such as (1) inner retinal disturbance, defined as the presence of disruption of the normal profile of the inner retinal layers, (2) inner segment–outer segment junction layer disruption, defined as any disruption of the inner or outer photoreceptor segment junction, (3) cysts or any cystic changes in the retinal layers, (4) neurosensory elevation, defined as the elevation of the neurosensory retina from the retinal pigment epithelium (RPE) layer, (5) internal limiting membrane (ILM) hyperreflectivity, defined as the presence of a hyperreflective inner retinal signal on the area of VMT, (6) epiretinal membrane (ERM), defined as the presence of ERM on any part of the area of retina encompassed by the OCT, (7) posterior hyaloid hyperreflectivity, defined as a hyperreflective inner retinal signal on any part of the posterior hyaloid encompassed by the OCT, and (8) RPE disturbance, defined as a disruption of the RPE layer (eg, drusen, RPE atrophy). Any disagreements between the 2 graders were resolved through discussion. The stage of the MHs was graded according to the classification of Duker et al.[6]

Progression to an FTMH or LMH in the study eye after the baseline visit was documented by a review of OCT scans from subsequent visits throughout the follow-up. Figure 1 shows representative OCT images of VMT, FTMH, and LMH. Figure 2 shows the defined OCT signs. In patients with unilateral VMT, a history of or concurrent presence of an FTMH or LMH in the fellow eye was also documented.

Statistical Analysis

All data analyses were conducted using open-source software (Python, version 3.7.6, Python Software Foundation, https://www.python.org). The Snellen VA was converted to logMAR notation for analyses.

To account for an intereye correlation, generalized estimating equations (GEEs) were used for analyses in which both eyes of a single patient could be included in the analysis. For GEE analyses involving binary categorical-dependent variables, a binomial distribution was specified. For analyses involving continuous dependent variables, a Gaussian distribution was specified. For analyses at the patient level or in cases in which only 1 eye from each patient was chosen for analysis, continuous variables between 2 groups were compared with a *t* test for comparison of means and categorical variables were analyzed with the Fisher exact test or χ^2 test of independence. To ensure that only the study eye had the condition being analyzed, eyes with unilateral VMT formed the subgroup used for all analyses of the fellow eyes.

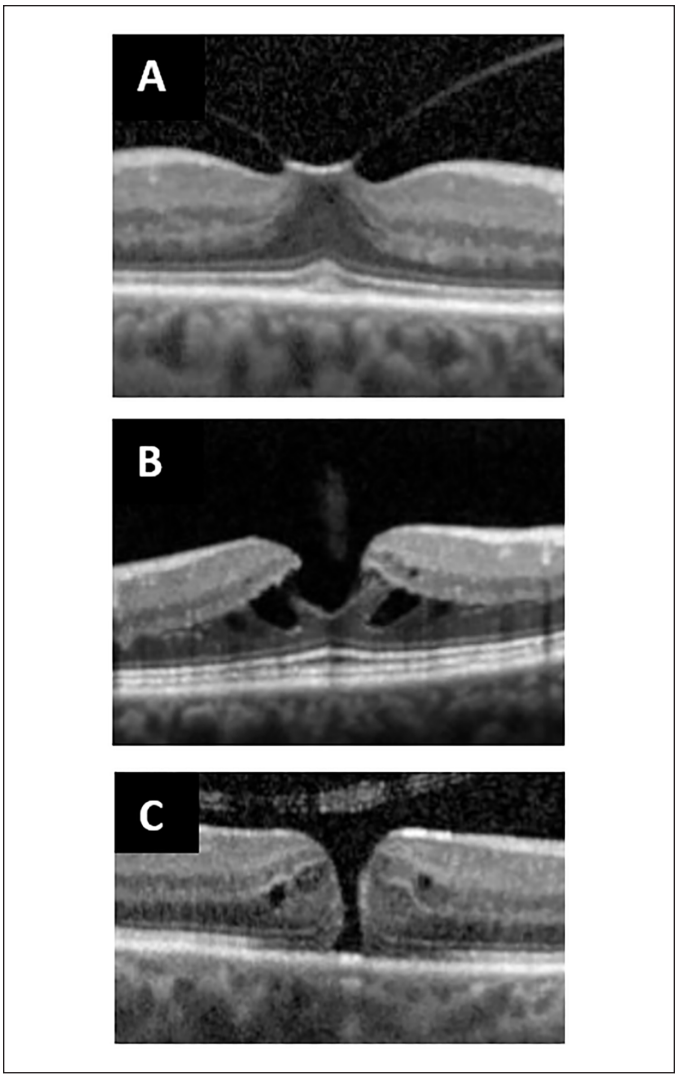

Figure 1. Representative optical coherence tomography images of (A) vitreomacular traction, (B) lamellar macular hole, and (C) full-thickness macular hole.

All means are ±SD. An α value of 0.05 was used to establish statistical significance for all analyses.

Results

After exclusion of 2 eyes for poor-quality OCT images, 287 eyes from 225 patients were evaluated over a mean follow-up of 5 years. The mean age was 69 ± 8 years. Of the patients, 66.7% were women and the majority identified as White (67.5%).

Table 1 shows the patients' demographic and clinical characteristics. The mean corrected VA at the baseline examination was 0.3 ± 0.8 logMAR. Of the eyes, 53.5% had documented subjective reduced VA and 18.5% had subjective metamorphopsia. Eyes were predominately phakic (65.2%) and hyperopic (58.5%). The VMT was predominantly focal (89.9%), with a mean length of 751 ± 952 μm.

Of the 287 eyes, 48 (16.7%) progressed from VMT to MH over a mean follow-up of 5 years, with 36 eyes (12.5%) progressing to FTMH and 12 eyes (4.2%) progressing to LMH. Among eyes that progressed to FTMH, 26 (72.2%) were classified as stage 2 MHs and 10 (27.8%) as stage 3 or 4 MHs. The mean follow-up time for progression from VMT to FTMH was significantly less than that for LMH (8 ± 12 months vs 31 ± 24 months; $P < .001$).

Table 2 shows the demographic and clinical risk factors for progression to MH. Female sex was associated with increased progression of VMT to FTMH (16.1% of women vs 5.3% of men; $P = .02$) but not LMH (4.7% of women vs 3.2% of men; $P = .56$). There were no differences in progression of VMT to MH based on race or ethnicity. The use of HRT and a diagnosis of hypertension, hyperlipidemia, or DM were not associated with progression to MH (all $P > .05$). In addition, there was no difference in progression to FTMH or LMH in women older than 50 years of age taking HRT compared with those who were not ($P > .05$).

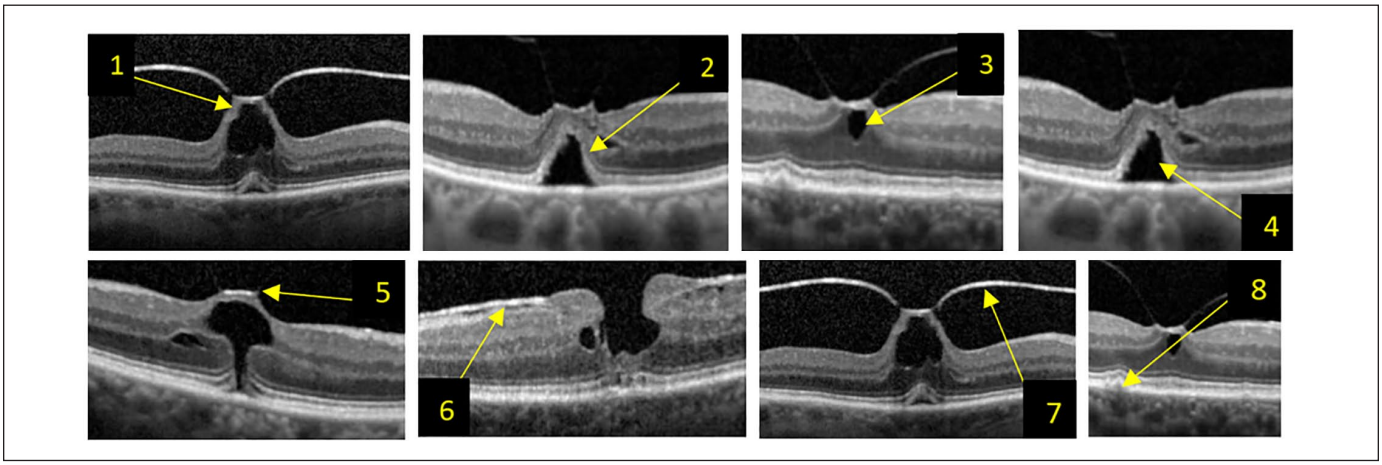

Figure 2. Representative optical coherence tomography images show (1) inner retinal disturbance, (2) inner segment–outer segment junction layer disruption, (3) cystic changes, (4) neurosensory elevation, (5) internal limiting membrane hyperreflectivity, (6) epiretinal membrane, (7) posterior hyaloid hyperreflectivity, and (8) retinal pigment epithelium disturbance.

Table 1. Baseline Demographics, Clinical, and OCT Characteristics of Patients With VMT.

Variable	VMT
Mean age (y) ± SD	69.4 ± 8.4
Female sex, n (%)	150/225 (66.7)
Race, n (%)	
White	152/225 (67.5)
Black or African American	62/225 (27.6)
Asian	7/225 (3.1)
Multiracial	1/225 (0.4)
Other	3/225 (1.3)
On HRT, n (%)	8/225 (3.6)
Systemic disease, n (%)	
Hypertension	127/225 (56.4)
Hyperlipidemia	106/225 (47.1)
Diabetes mellitus	61/225 (27.1)
Mean logMAR VA ± SD	0.3 ± 0.8
Mean Snellen equivalent ±SD	20/40 ± 20/125
Subjective visual symptoms, n (%)	
Decreased VA	153/287 (53.3)
Metamorphopsia	53/287 (18.5)
Lens status, n (%)	
Phakia	186/285 (65.2)
Pseudophakia	99/285 (34.7)
Mean axial length (mm) ± SD	23.7 ± 1.2
Mean SE (D) ± SD	−0.20 ± 1.9
Refractive status, n (%)	
Hyperopic	137/234 (58.5)
Myopic	81/234 (34.6)
Plano	16/234 (6.8)
Mean CST ± SD (μm)	323.0 ± 97.3
Mean VMT length ± SD (μm)	751.4 ± 952.4
VMT length type, n (%)	
Focal	248/276 (89.9)
Broad	28/276 (10.1)

Abbreviations: CST, central subfield thickness; HRT, hormone replacement therapy; OCT, optical coherence tomography; SE, spherical equivalent; VA, visual acuity; VMT, vitreomacular traction.

There were no significant differences in the baseline VA in patients who progressed to an FTMH ($P=.64$) or LMH ($P=.50$) compared with those who did not. The presence of subjective decreased VA at baseline was associated with progression to an FTMH ($P=.01$), while the presence of metamorphopsia at baseline was associated with progression to both FTMH ($P=.001$) and LMH ($P=.01$). A subjective decreased VA was associated with progression to FTMH only when there was inner segment–outer segment disturbance on OCT ($P=.04$), while metamorphopsia was a risk factor independent of inner segment–outer segment disturbance ($P=.02$). Patient lens status, axial length, and spherical equivalent were not associated with progression to MH. Among phakic patients, significantly more myopic patients than hyperopic patients progressed to FTMH ($P=.04$) but not LMH ($P=.13$).

Table 3 shows the OCT risk factors for progression to MH. There was no association between VMT length at baseline and the subsequent development of MH ($P>.05$). The presence of inner retinal disturbance, cysts, ILM hyperreflectivity, ERM, and RPE disturbance was not associated with progression to MH (all $P>.05$). The presence of inner segment–outer segment disruption was associated with progression to FTMH ($P=.003$) but not to LMH ($P=.96$), and the presence of posterior hyaloid hyperreflectivity was negatively associated with progression to FTMH ($P=.02$) but not to LMH ($P=.51$). The presence of neurosensory elevation was negatively associated with progression to LMH ($P<.001$) but not to FTMH ($P=.27$).

In a subset analysis of 174 patients with unilateral VMT in the study eye, 25 eyes (14.4%) were diagnosed with an FTMH in the fellow eye and 13 eyes (7.5%) were diagnosed with an LMH in the fellow eye. Patients with an FTMH in the fellow eye were significantly more likely to have VMT progress to FTMH in the study eye (24.0% vs 8.7%; $P=.04$). However, LMH in the fellow eye was not a risk factor for progression to LMH in the study eye (7.7% vs 4.3%; $P=.47$) (Table 4).

Conclusions

This retrospective study assessed the factors influencing the progression of VMT to FTMH and LMH in one of the largest cohorts of eyes with VMT in the literature. Two hundred eighty-seven eyes with VMT found on OCT were included; 36 eyes (12.5%) developed an FTMH and 12 eyes (4.2%) developed an LMH over a mean follow-up of 5 years. This is consistent with previously published studies of the incidence of MH development in eyes with VMT.[8,10,20,21]

Women had a significantly greater risk for progression from VMT to FTMH, consistent with findings in previous studies.[1,22–24] One reason for this finding may be the fluctuation of estrogen levels in perimenopausal and postmenopausal women, which affects vitreous liquefaction.[22,24] Previous studies have shown a higher risk for PVD in women during menopause, suggesting that hormonal changes may translate into changes in the vitreoretinal interface[25]; however, case-control studies of the association between indicators of estrogen exposure and MH have reported mixed results.[22,25,26] In our study, no significant differences were found in the progression to MH between women older than 50 years taking HRT and those who were not. The degree and rate of estrogen depletion are 2 of the most important factors in the development of menopausal changes (vasomotor symptoms, urogenital atrophy, osteoporosis, changes in lipid metabolism) during the postmenopausal years.[27] As such, it is possible that women with a greater degree or rate of estrogen depletion are more likely to be prescribed HRT, which may counterbalance its protective effects. Studies with larger cohorts are needed to assess the influence of estrogen and progesterone on MH pathogenesis. In addition, studies to evaluate the role of sex differences in the risk for progression to MH are needed.

Table 2. Demographic and Clinical Risk Factors for Progression From VMT to MH.

	Progression to FTMH		Progression to LMH	
Variable	Variable Value	*P* Value	Variable Value	*P* Value
Age (y), n/N (%)		.97		.97
<65	9/73 (12.3)		3/73 (4.1)	
≥65	27/214 (12.6)		9/214 (4.2)	
Sex, n/N (%)		.02[a]		.56
Female	31/193 (16.1)		9/193 (4.7)	
Male	5/94 (5.3)		3/94 (3.2)	
Race/ethnicity, n/N (%)		.40		.74
Black	13/84 (15.5)		3/84 (3.6)	
Non-Black	23/203 (11.3)		9/203 (4.4)	
HRT, n/N (%)		.85		.39
Yes	1/11 (9.1)		1/11 (9.1)	
No	35/276 (12.7)		11/276 (4.0)	
Hypertension, n/N (%)		.62		.10
Yes	22/163 (13.5)		4/163 (2.5)	
No	14/124 (11.3)		8/124 (6.5)	
Hyperlipidemia, n/N (%)		.77		.68
Yes	18/136 (13.2)		5/136 (3.7)	
No	18/151 (11.9)		7/151 (4.6)	
Diabetes, n/N (%)		.50		.91
Yes	8/76 (10.5)		3/76 (3.9)	
No	28/211 (13.3)		9/211 (4.3)	
Mean VA ± SD		.64		.50
Progressed	20/40 ± 20/40		20/32 ± 20/25	
Did not progress	20/40 ± 20/160		20/40 ± 20/160	
Subjective decrease in VA, n/N (%)		.01[a]		.73
Yes	26/153 (17.0)		7/153 (4.6)	
No	10/133 (7.5)		5/133 (3.8)	
Subjective metamorphopsia, n/N (%)		.001[a]		.01[a]
Yes	14/53 (26.4)		6/53 (11.3)	
No	22/234 (9.4)		6/234 (2.6)	
Mean SE (D) ± SD		.07		.35
Progressed	−0.69 ± 2.22		−0.54 ± 1.37	
Did not progress	−0.14 ± 1.82		−0.19 ± 1.90	
Mean axial length (mm) ± SD		.80		.72
Progressed	23.7 ± 1.21		23.5 ± 0.83	
Did not progress	23.7 ± 1.20		23.7 ± 1.21	
Refractive status, n/N (%)		.04[a]		.13
Hyperopia	8/85 (9.4)		1/85 (1.2)	
Myopia	13/65 (20.0)		4/65 (6.2)	
Lens status, n/N (%)		.70		.60
Phakia	24/186 (12.9)		7/186 (3.8)	
Pseudophakia	11/99 (11.1)		5/99 (5.1)	

Abbreviations: FTMH, full-thickness macular hole; HRT, hormone replacement therapy; LMH, lamellar macular hole; MH, macular hole; SE, spherical equivalent; VA, visual acuity; VMT, vitreomacular traction.
[a]Statistically significant ($P \leq .05$).

The presence of subjective metamorphopsia at baseline was associated with progression of VMT to MH, although the baseline VA was not. In addition, a subjective decrease in the baseline VA was associated with progression to FTMH but not to LMH. Of note, metamorphopsia is an independent predictor of progression to FTMH, while decreased VA is a predictor only when there is inner segment–outer segment disruption on OCT. Previous studies have described the clinical symptoms of VMT, including decreased vision, photopsia, micropsia, and metamorphopsia, as slowly progressive and

Table 3. OCT Risk Factors for Progression From VMT to MH.

	Progression to FTMH		Progression to LMH	
Variable	Variable Value	*P* Value	Variable Value	*P* Value
VMT		1.00		1.00
Focal	33/248 (13.3)		11/248 (4.4)	
Broad	1/28 (3.6)		0/28	
Inner retinal disturbance		.06		.92
Yes	29/187 (15.5)		8/187 (4.3)	
No	7/99 (7.1)		4/99 (4.0)	
IS–OS disruption		.003[a]		.96
Yes	19/81 (23.5)		6/81 (7.4)	
No	17/205 (8.3)		6/205 (2.9)	
Cyst		.14		.64
Yes	23/148 (15.5)		7/148 (4.7)	
No	13/138 (9.4)		5/138 (3.6)	
Neurosensory elevation		.27		<.001[a]
Yes	5/24 (20.8)		0/24	
No	30/261 (11.5)		12/261 (4.6)	
ILM hyperreflectivity		.06		.15
Yes	17/176 (9.7)		5/176 (2.8)	
No	18/109 (16.5)		7/109 (6.4)	
ERM		.16		.92
Yes	10/115 (8.7)		5/115 (4.3)	
No	26/171 (15.2)		7/171 (4.1)	
Posterior hyaloid hyperreflectivity		.02[a]		.51
Yes	3/71 (4.2)		71 (2.8)	
No	32/214 (15.0)		2/10/214 (4.7)	
RPE disturbance		.12		.72
Yes	4/17 (23.5)		1/17 (5.9)	
No	31/268 (11.6)		11/268 (4.1)	

Abbreviations: ERM, epiretinal membrane; FTMH, full-thickness macular hole; ILM, internal limiting membrane; IS–OS, inner segment–outer segment junction; LMH, lamellar macular hole; MH, macular hole; RPE, retinal pigment epithelium; VMT, vitreomacular traction.
[a]Statistically significant ($P \leq .05$).

Table 4. Fellow Eye MH Status As a Risk Factor for Progression of VMT to MH.

	Progression to FTMH in Study Eye		Progression to LMH in Study Eye	
Fellow-Eye Status	n/N (%)	*P* Value	n/N (%)	*P* Value
FTMH		.04[a]		.60
Yes	6/25 (24.0)		0/25	
No	13/149 (8.7)		8/149 (5.3)	
LMH		.64		.47
Yes	2/13 (15.4)		1/13 (7.7)	
No	17/161 (10.6)		7/161 (4.3)	

Abbreviations: FTMH, full-thickness macular hole; LMH, lamellar macular hole; MH, macular hole; VMT, vitreomacular traction.
[a]Statistically significant ($P \leq .05$).

have reported that discrepancies between symptoms and clinical findings are quite common, with patients often presenting with excellent VA despite extensive macular traction.[1,11] Given that metamorphopsia is thought to be caused by changes at the photoreceptor level as well as inner retinal thickening over time, it is possible that acute traction, such as rapid progression of VMT, is more likely to result in subjective decreased VA and metamorphopsia as well as progression to a full-thickness hole.[28] Thus, metamorphopsia in conjunction with OCT findings may be a sensitive and clinically useful risk factor for predicting progression of VMT to MH.

Our study found that refractive status at baseline was a risk factor for progression to FTMH, with myopic eyes progressing to FTMH more frequently than hyperopic eyes. This is consistent with a previous study of the development of VMA-related consequences on OCT (defined as VMT, MH, and macular pucker) that found an association between myopia and VMA with complications.[29] Of note, the difference was not significant in eyes that progressed to LMH. We did not find a significant difference in lens status in eyes that progressed to MH compared with those that did not. Previous studies have found phakia to be associated with a greater tendency for VMT release

with the injection of ocriplasmin for enzymatic vitreolysis compared with pseudophakia.[30–32] This was thought to be the result of potential selection bias for more resistant or adherent cases of VMT in pseudophakic eyes given that these eyes had cataract surgery without vitreous detachment.[30,31] Further research is warranted to evaluate the effect of refractive status and cataract surgery on vitreous liquefaction.[32]

On OCT analyses, we found that the presence of inner segment–outer segment disruption was a risk factor for progression of VMT to FTMH, while posterior hyaloid hyperreflectivity was negatively associated with progression to FTMH and neurosensory elevation was negatively associated with progression to LMH. We did not find a significant difference in VMT length or the presence of ERM between eyes that progressed to FTMH or LMH and those that did not. Previous publications have shown a greater tendency for VMT release with ocriplasmin injection in eyes with focal VMT and those without ERM. This may be related to the mechanism of ocriplasmin-induced release of VMT, with a maximum impact on small adhesions and an inability of the ocriplasmin to dissolve ERMs.[30,31] We did find a significant association between the presence of inner segment–outer segment disruption at baseline and progression to FTMH. This OCT sign is characterized by greater disruption of retinal anatomy and photoreceptor architecture and may reflect greater traction on the macula at baseline, contributing to FTMH formation within the follow-up period.[33] The presence of hyperreflectivity on the detached posterior hyaloid was negatively associated with progression of VMT to FTMH, which may reflect stronger adhesion between the vitreous and the ERM than between the ERM and ILM and may reduce the risk for FTMH formation in these eyes.[34]

Our understanding of LMH pathophysiology is limited, and the classification of LMH has undergone several iterations[6]; however, more recent OCT-based definitions have differentiated LMHs from ERM foveoschisis (classically "tractional" LMH, defined by contractile ERM) and macular pseudohole (foveal center–sparing ERM).[35] It is possible that neurosensory elevation is associated with stronger tractional forces within the inner retina, which may decrease the incidence of release and LMH formation.[36] Given the smaller sample of eyes that developed LMH, additional studies with larger cohorts of patients with LMH over a longer follow-up period are indicated to further evaluate OCT signs that may be predictive of progression to LMH.

In a subgroup analysis, we found that an FTMH in the fellow eye increased the likelihood that VMT in the study eye would progress to FTMH, with 24.0% of eyes with an FTMH in the fellow eye progressing to an FTMH over the study period. Previous studies have estimated that up to 25% of patients with a unilateral MH eventually develop bilateral involvement[22,37]; however, we did not find a correlation between an LMH in the fellow eye and progression of the study eye to an LMH or to FTMH. A previous study of 35 patients over 4.6 years similarly suggested that the presence of an LMH in 1 eye does not significantly increase the risk for developing an LMH in the fellow eye.[38] Nava et al[38] theorized that the evolution of an LMH may require a longer time span than was investigated in their study. Given that LMH development is usually characterized as progressing more slowly, it is possible that a longer follow-up would eventually show a higher incidence of bilateral involvement.[6,39,40] In our cohort, the time to development of an LMH was significantly longer than the time to development of an FTMH, which may support Nava et al's theory. Thus, future studies with a longer follow-up of patients with an FTMH or LMH may be helpful to further characterize trends in the development of MHs in fellow eyes.

Our study has several inherent limitations. As a retrospective study, certain variables were not possible to control, such as the uniformity of follow-up visits and charting practices. Patients were enrolled from a single tertiary-care center, which may not be representative of the general population. In addition, specific subgroups in our study comprised relatively smaller samples, including eyes that progressed to LMH (n = 12 [4.2%]) and eyes of patients taking HRT (n = 11 [3.8%]). As such, it is possible this group was not sufficiently representative of the population as a whole. Additional studies with larger subgroups are warranted to better show the risk for progression of VMT to MH in these subgroups. Furthermore, patients who had cataract surgery during the follow-up period were not excluded. Previous studies have reported that cataract surgery may change the vitreomacular interface status in eyes with preexisting VMT.[41] Further studies are warranted to evaluate the effects of cataract surgery on vitreous liquefaction and the vitreomacular interface.

In conclusion, this retrospective study found that female sex, decreased subjective VA, and the presence of inner segment–outer segment disruption on OCT are risk factors for progression of VMT to FTMH and the presence of baseline metamorphopsia is a risk factor for progression to FTMH and to LMH. An FTMH in the fellow eye predicts progression to an FTMH in the study eye. These findings may be clinically relevant for risk-stratifying patients presenting with VMT.

Authors' Note

Presented at the annual meeting of the Association for Research in Vision and Ophthalmology, April 23–27, 2023, New Orleans, LA, USA.

Ethical Approval

Ethical approval for this study was obtained from the Duke University Health System IRB (Pro00106397). This study complied with the US Health Insurance Portability and Accountability Act of 1996 and the tenets of the Declaration of Helsinki.

Statement of Informed Consent

Informed consent was waived for the present study because inclusion in the study posed no substantial risk to participants and data analysis consisted of de-identified data obtained through retrospective chart review.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

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