Vitreous Structure and Visual Function in Myopic Vitreopathy Causing Vision-Degrading Myodesopsia

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• PURPOSE: Myopic vitreopathy features precocious fibrous vitreous liquefaction and early posterior vitreous detachment (PVD). It is unclear whether visual function is affected by myopic vitreopathy and PVD. This study assessed the relationships among axial length, structural vitreous density, PVD, and visual function.

• DESIGN: Retrospective case-control study.

• METHODS: Ultrasonography measurements were made of axial length, logMAR VA, contrast sensitivity function (CSF [Freiburg acuity contrast test]), and quantitative B-scan ultrasonography.

• RESULTS: Seventy-nine subjects (45 men and 34 women; mean age: 49 ± 14 years) were analyzed. Axial lengths ranged from 22 to 29.2 mm (mean: 24.9 ± 1.8 mm; myopic eyes: 26.35 ± 1.35 mm; and nonmyopic eyes: 23.45 ± 0.75 mm; $P < .001$). With increasing axial length there was greater vitreous echodensity (R: 0.573; $P < .01$) and degradation in CSF (R: 0.611; $P < .01$). Subgroup analyses found that myopic eyes (> -3 diopters) had 37% more vitreous echodensity than nonmyopic eyes (762 ± 198 arbitrary units [AU] vs. 557 ± 171 AU, respectively; $P < .001$) and that CSF was 53% worse in myopic eyes (3.30 ± 1.24 Weber index [%W]) than in nonmyopic eyes (2.16 ± .59 %W; $P < .001$). Myopic eyes with PVD had 33% greater vitreous echodensity (815 ± 217 AU; $P < .001$) and 62% degradation in CSF (3.63 ± 2.99 %W) compared to nonmyopic eyes with PVD (613 ± 159 AU; 2.24 ± 0.69 %W; $P < .001$, each). Limited vitrectomy was performed in 11 of 40 cases (27.5%), normalizing vitreous echodensity and CSF in each case.

• CONCLUSIONS: Axial myopia is associated with increased fibrous vitreous liquefaction and echodensity, as well as profound degradation of CSF. PVD in myopic eyes is associated with even more structural and functional abnormalities, normalized by limited vitrectomy. These findings may explain some common complaints of myopic patients with respect to vision and quality of life. (Am J Ophthalmol 2021;224:246–253. © 2020 Elsevier Inc. All rights reserved.)

MYOPIA IS A LEADING CAUSE OF VISUAL IMPAIRment,[1] predicted to attain epidemic proportions in coming years.[2] The prevalence of myopia in the United States increased from 25% to 44% between 1972 and 2004.[3] In East Asia, the prevalence of myopia is significantly higher, approximating 80%-90% among young adults,[4] and 84% in children.[5] It is estimated that by 2050 there will be 5 billion myopic people in the world.[2] Although the optical effects of myopia can be corrected with eyewear or surgery, consequences of ocular pathology represent a risk factor for cataract, glaucoma, retinal detachment, and myopic maculopathy.[6] An important aspect of myopia that has largely been ignored is the effect on vitreous.

Myopia is commonly associated with increased ocular axial length. Years ago, however, Spencer[7] identified that, in addition to axial elongation, a myopic eye is also enlarged vertically and horizontally. Thus, the vitreous body in a myopic eye is volumetrically larger than in emmetropia, a structural difference that likely increases with increasing severity of axial myopia. The term "myopic vitreopathy" refers to the internal structural abnormalities of vitreous associated with axial myopia, primarily fibrous vitreous liquefaction,[8] which is likely the consequence of both inherited and degenerative processes. Myopic vitreopathy is also often associated with early onset posterior vitreous detachment (PVD), resulting in further effects upon vision,[9–11] as well as rhegmatogenous retinal events.[12,13]

Previous studies have shown that quantitative ultrasonography is a useful way to evaluate vitreous structure in various clinical settings.[14–16] Considering the fibrous vitreous liquefaction that characterizes myopic vitreopathy and the increased prevalence of PVD in myopic eyes, it is hypothesized that vitreous echodensity will be increased

Accepted for publication Sep 10, 2020.

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0002-9394/$36.00
https://doi.org/10.1016/j.ajo.2020.09.017

with increasing ocular axial length. It is further hypothesized that, in myopia, there will be degradation in contrast sensitivity function (CSF) that correlates with increased axial length and the presence of PVD, as has been previously shown in the general population.[10,11]

METHODS

• **SUBJECTS:** This retrospective, case-controlled study adhered to tenets of the Declaration of Helsinki ethical principles. Each of 79 subjects (45 men and 34 women; mean age: 49 ± 14 years) provided informed consent as approved by the institutional review board of St. Joseph Hospital (Orange, California) and were evaluated at the VMR Institute for Vitreous Macula Retina (Huntington Beach, California). All patients with the diagnosis of myopia or myopia and floaters evaluated between 2014 and 2019 were included if they underwent specialized testing with B-scan quantitative ultrasonography (QUS) (see "Vitreous Structure" section below), US measurement of axial length, and measurement of CSF (see "Visual Function" section below). Exclusion criteria were a history of vitreoretinal pathology (eg, retinal detachment, vitreous hemorrhage, diabetic retinopathy, any maculopathy, and so forth), or previous intraocular surgery, except for laser in situ keratomileusis (LASIK) or uncomplicated cataract surgery, performed at least 12 months prior to study entry. Specifically, no eyes with vitreoschisis, premacular membranes, macular pucker, macular atrophy, lacquer cracks, foveoschisis, or choroidal neovascularization were included. One eye per subject was randomly selected for study inclusion. Controls were age- and sex-matched to this group.

Subjects were identified as "myopic" if the refractive error was ≥ −3 diopters (D) (spherical equivalent). With this definition, there were 40 myopic eyes and 39 nonmyopic eyes. Only 11 of 40 myopic eyes (27.5%) had undergone LASIK surgery, and 2 eyes (5%) had photorefractive keratectomy. Only 6 of 40 myopic eyes (15%) and 4 of 39 nonmyopic eyes (10.3%; $P = .72$) had cataract surgery previously, all receiving a monofocal posterior chamber intraocular lens (IOL) (multi-focal IOLs were excluded to avoid any possible effects on CSF). All phakic eyes had ≤1+ nuclear sclerosis and cortical opacification, consistent with their relatively young ages and Snellen best-corrected VA (BCVA) ≥ 20/25.

Macular status was mild retinal pigment epithelium attenuation in only 10 of 40 myopic cases (25%) and 4 of 39 nonmyopic cases (10%), as well as small focal retinal pigment epithelium defects in only 8 of 40 myopic cases (20%) and 3 of 39 nonmyopic cases (7.7%). The absence of vitreoschisis, premacular membranes, macular pucker, macular atrophy, lacquer cracks, foveoschisis, and choroidal neovascularization was confirmed by fluorescein angiography (Topcon, Tokyo, Japan) and spectral domain optical coherence tomography (SD-OCT; Optos, Marlborough, Massachusetts), results of which helped to rule out defects in the inner segment/outer segment junction in all cases.

• **VITREOUS STRUCTURE:** Ultrasonography was performed using vector A/B-scan biometry (Aviso; Quantel Medical, Clermont-Ferrand, France) to measure axial length[17,18] and to diagnose PVD, defined as a thin, hyper-reflective line anterior to the fundus.[19] SD-OCT was also performed in each case to confirm PVD when the posterior vitreous cortex was close enough to the fundus to be visualized and to rule out macular pathology.[19] Axial lengths were measured by US, as previously described.[17,18,20,21] QUS was used to assess vitreous structure by using a customized probe (15- MHz; 20-mm focal length; 7-mm aperture) to obtain on-globe (temporal) longitudinal scans through the premacular vitreous in nasal gaze.[14,15] As previously described in detail,[14,16] 3 parameters were measured using the same system settings: 1) the sum of the square of the acoustic values within the central/posterior vitreous divided by the area of measurement (energy [E]); 2) the percentage of the central/posterior vitreous filled by echogenic clusters greater than 50 pixels (P50) or 0.069 mm; and 3) the mean of the acoustic values divided by the area of the central/posterior measurement area (mean [M]). A combination of these parameters was calculated as the QUS composite index = (½E + [M × 10] + [P50 × 100]) arbitrary units (AU), as previously described.[16] P50 and the composite index were used in this analysis to enable comparison with previous studies.[16]

• **VISUAL FUNCTION:** VA was reported in logarithm of minimal angle of resolution (logMAR). All patients were refracted to a BCVA of logMAR 0.097 (Snellen equivalent: 20/25) or better prior to visual function testing. Subjects were then taken to another room to dark adapt for 10 minutes before CSF was measured using the Freiburg Acuity Contrast Test (FrACT), using automated software and the same light-emitting diode monitor. Mesopic lighting conditions were simulated with the luminance of the light-emitting diode monitor set to maximum brightness. At least 1 meter of viewing distance is recommended by the test developers, so 2.9 meters was used for each subject in this and all previous studies at this institute. Screen resolution (pixels/mm) was manually measured using a ruler and calculated by the software for determining visual angle.[22-24] The FrACT uses a monochromatic, tumbling Landolt-C optotype (3.3-degree diameter; 20/200) where the gap of the C randomly rotates to 1 of 8 orientations to be identified by the subject, with sequential testing that automatically adjusts the difficulty of the trials according to the subject's test performance. At various contrast levels and a spatial frequency of 5 cycles per degree, FrACT uses psychometric methods combined with anti-aliasing and dithering to provide an automated, paced, accurate measurement of CSF,[25] providing the contrast threshold between the minimum and maximum luminance levels, defined as the Weber index (%W), in

TABLE. Demographics and Subject Data

	Nonmyopic Eyes		Myopic Eyes	
	Without PVD	With PVD	Without PVD	With PVD
No. of subjects	22	17	20	20
Mean ± SD age, y	42.1 ± 14.9[a]	57.8 ± 7.0[a]	39.9 ± 12.7[a]	57.7 ± 6.8[a]
Lens status	1/22 IOL	3/17 IOL	1/20 IOL	5/20 IOL
Mean ± SD mean visual acuity, logMAR	0.040 ± 0.06	0.083 ± 0.11	0.061 ± 0.06	0.096 ± 0.11
Mean ± SD axial length, mm	23.3 ± 0.8[b]	23.6 ± 0.7[b]	26.3 ± 1.4[b]	26.4 ± 1.3[b]
Vitreous echodensity, AU	513 ± 170[c]	613 ± 159[c]	709 ± 164[c]	815 ± 217[c]
Mean ± SD contrast sensitivity function, %W	2.05 ± 0.42	2.24 ± 0.69[d]	2.97 ± 1.30[d]	3.63 ± 1.10[d]

%W = Weber index (see Methods); AU = arbitrary units (see Methods); IOL = (monofocal) intraocular lens, PVD = posterior vitreous detachment.

[a] $P < .001$, comparing eyes with PVD to eyes without PVD, within respective groups (myopic vs. nonmyopic).

[b] $P < .001$, comparing all myopic eyes to all nonmyopic eyes.

[c] $P < .05$, comparing all groups in incremental steps (ie, nonmyopic without PVD, to nonmyopic with PVD, to myopic with PVD, to myopic without PVD).

[d] $P < .05$, comparing nonmyopic with PVD to myopic without PVD and myopic without PVD to myopic with PVD.

which %W: 100% × ([luminance$_{max}$ − luminance$_{min}$]/[luminance$_{max}$]) where the higher the Weber index, the worse the CSF (more degradation).

This method has been used in previous studies, that established high reproducibility,[26] a finding that was confirmed in the investigators' institution where initial studies found reproducibility of 92%,[27] and subsequent studies established repeatability of 89.2% in controls and 94.4% in subjects with vision-degrading myodesopsia.[28] This CSF testing paradigm was also used previously to evaluate the effects of PVD,[9] aging vitreous,[15] Nd:YAG laser vitreolysis,[16] limited vitrectomy for vision-degrading myodesopsia,[27,28] and surgery for macular pucker.[29]

• **STATISTICS:** Student *t*-tests were used to analyze the statistical significance of differences between VA (logMAR), CSF, QUS, and axial lengths in myopic eyes (defined as axial length greater than 24.74 mm, consistent with previous studies[20,21]) versus those in nonmyopic eyes, with or without PVD. Correlations between vitreous echodensity and CSF with respect to axial lengths were evaluated by linear regression and Pearson correlation coefficients. Mediation modeling was performed using Stata software (Stata, College Station, Texas).

• **RESULTS:** The Table presents subject demographics and test results. Axial lengths ranged from 22.0 to 29.2 mm (mean: 24.9 ± 1.8 mm). There were no statistically significant differences between axial lengths in men and women ($P = .136$). Similarly, there were no differences in axial lengths between nonmyopic eyes without PVD (23.3 ± 0.8 mm) and those with PVD (23.6 ± 0.7 mm), as well as myopic eyes without PVD (26.3 ± 1.4 mm) and those with PVD (26.4 ± 1.3 mm).

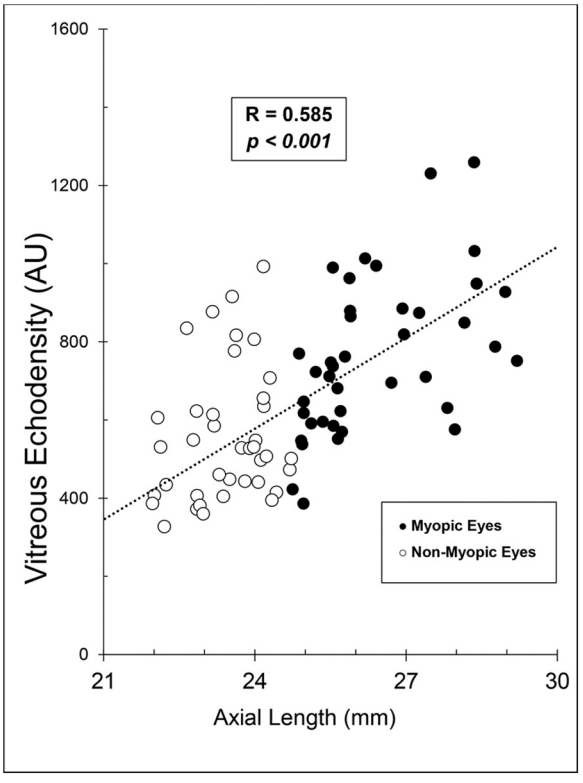

FIGURE 1. Axial length and vitreous echodensity. With increasing axial length there is increasing vitreous density, as determined by quantitative ultrasonography. R = 0.585; $P < .001$. AU = arbitrary units.

There was a positive correlation between axial length and vitreous echodensity (R = 0.585; $P < .001$) (Figure 1). Myopic eyes had 37% more vitreous echodensity than

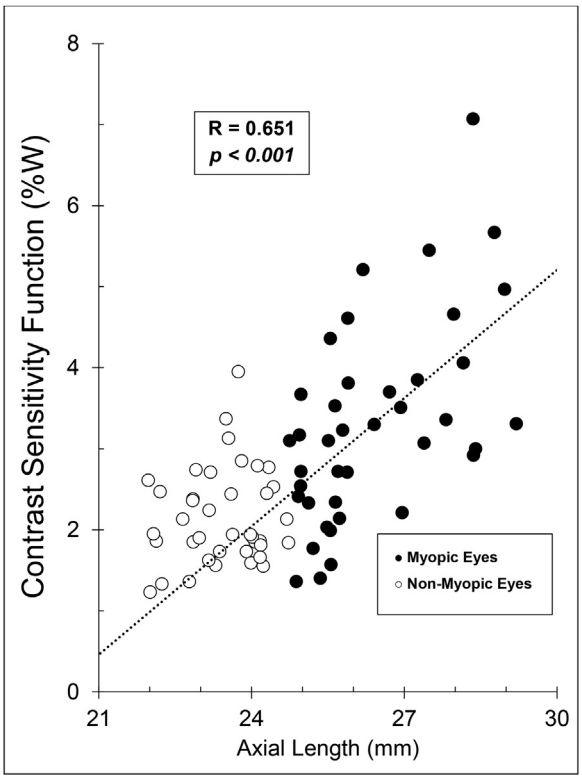

FIGURE 2. Axial length and contrast sensitivity function. Contrast sensitivity function worsens (higher Weber index [% W]) with increasing axial length. R = 0.651; $P < .001$.

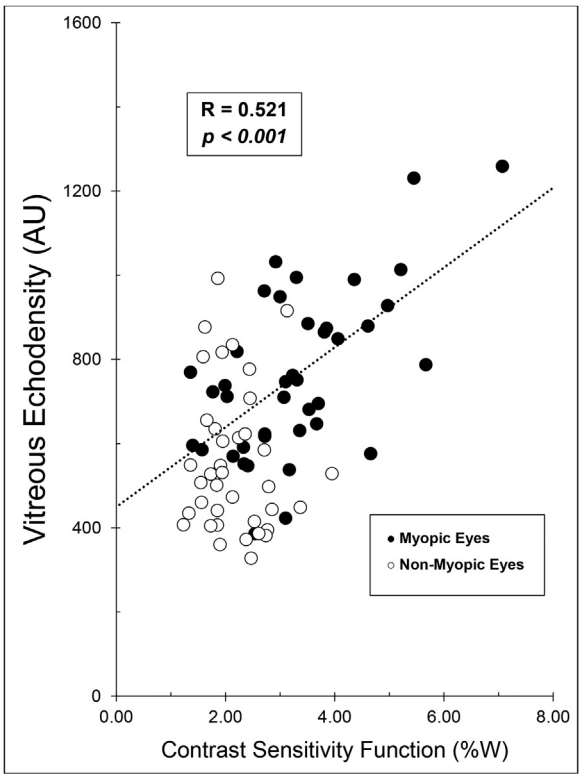

FIGURE 3. Correlation of vitreous echodensity with contrast sensitivity function. There is a positive correlation between vitreous density, as measured by quantitative ultrasonography, and contrast sensitivity function, suggesting that with increasing vitreous density there is worsening of contrast sensitivity function. R = 0.521; $P < .001$. AU = arbitrary units.

nonmyopic eyes (762 ± 198 AU vs. 557 ± 171 AU, respectively; $P < .001$) (Table).

BCVA was no different in myopic eyes than in nonmyopic eyes, ranging from logMAR 0 to 0.09 (Snellen equivalent: 20/20-20/25; $P = .244$). However, CSF was increasingly degraded with greater axial length (R = 0.651; $P < .001$) (Figure 2). CSF degradation correlated with increasing vitreous echodensity (R = 0.521; $P < .001$) (Figure 3), as previously reported in the general population.[9-11,14,15,27,28] In the present study, CSF was 53% worse in myopic eyes (3.30 ± 1.24 %W) than in nonmyopic eyes (2.16 ± 0.59 %W; $P < .001$).

B-scan US results confirmed the presence of PVD in 37 of 79 eyes (47%). This was associated with age, as the average age of subjects with PVD was 57.7 ± 6.8 years, whereas subjects without PVD were 41.0 ± 13.8 years old ($P < .001$). The presence of PVD was associated with greater vitreous echodensity in nonmyopic eyes (613 ± 159 vs. 513 ± 170 AU, respectively; $P < .05$), as well as in myopic eyes (815 ± 217 vs. 709 ± 164 AU, respectively; $P < .05$) (Figure 4), consistent with previous reports.[9,15] Interestingly, myopic eyes without PVD had greater vitreous echodensity (709 ± 164 AU) than nonmyopic eyes with PVD (613 ± 159; $P < .05$) (Figure 4). This was also true of CSF, which was worse in myopic eyes without PVD (2.97 ± 1.30 %W) than in nonmyopic eyes with PVD (2.24 ± 0.69 %W; $P < .03$) (Figure 5). The worst CSF was detected in myopic eyes with PVD (3.63 ± 1.10 %W), which was 22% worse than in myopic eyes without PVD (2.97 ± 1.30 %W; $P < .05$) (Figure 5) and 62% worse than in nonmyopic eyes with PVD (2.24 ± 0.69 %W; $P < .03$) (Figure 5).

Mediation modeling confirmed causal relationships among axial length, vitreous density, and CSF. The proportion of the effect of axial length on contrast sensitivity (direct) was 62%, and the proportion mediated by vitreous echodensity (indirect) was 38%. Using the equation-level goodness of fit (R^2), 37% of the variability in CSF was explained by a relationship between vitreous echodensity and axial length and their relationship with CSF. These findings support the hypothesis that there is increased vitreous echodensity with increasing axial length (Figure 1) associated with proportionate degradation of CSF (Figure 3).

To further test the hypothesis that vitreous density was a major contributor to degradation of CSF in myopia, the myopic patients who chose to undergo vitrectomy (n =

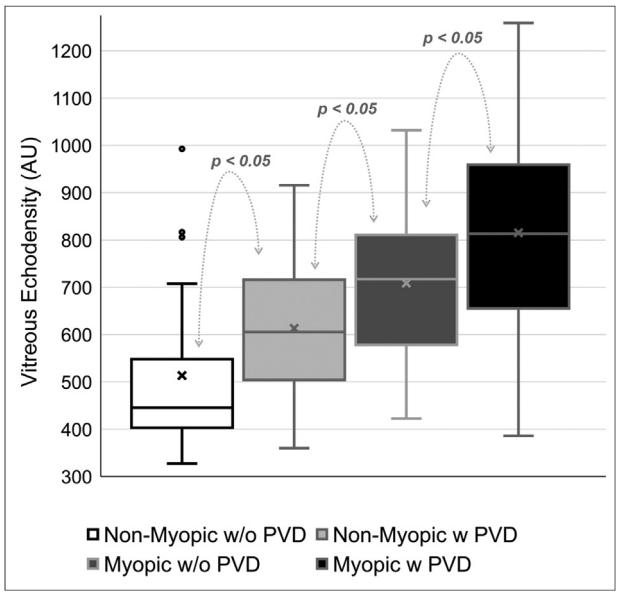

FIGURE 4. Vitreous echodensity in myopic and nonmyopic eyes with and without PVD. Vitreous echodensity in nonmyopic eyes with PVD was 20% greater than in nonmyopic eyes without PVD ($P < .05$). Vitreous echodensity in myopic eyes without PVD was 16% greater than in nonmyopic eyes with PVD ($P < .05$). Vitreous echodensity in myopic eyes with PVD was the worst of all, fully 60% worse than nonmyopic eyes without PVD and 15% worse than myopic eyes without PVD ($P < .05$). (Myopia was defined as ≥ -3D). The presence or absence of PVD was determined by B-scan ultrasonography.) AU = arbitrary units; D = diopters; PVD = posterior vitreous detachment.

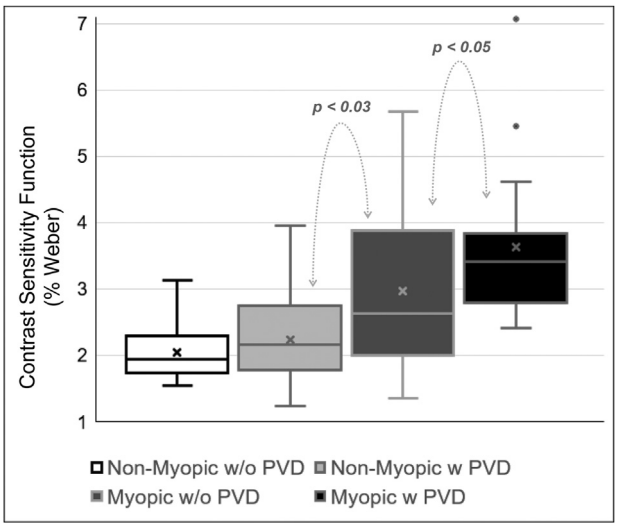

FIGURE 5. CSF in myopic and nonmyopic eyes with and without PVD. CSF in myopic eyes without PVD was 45% worse than in nonmyopic eyes without PVD and 30% worse than nonmyopic eyes with PVD ($P < 0.03$). CSF in myopic eyes with PVD was 55% worse than nonmyopic eyes without PVD and 22% worse than myopic eyes without PVD. $P < .05$). CSF = Contrast sensitivity function; PVD = posterior vitreous detachment; %Weber = Weber index.

11) were compared with those who chose observation alone (n = 29). Preoperatively, vitreous echodensity was greater in those who chose vitrectomy than in myopic cases with floaters who chose observation (782 ± 198 AU vs. 702 ± 161 AU, respectively; $P = .10$), and similarly, CSF was worse in those who chose vitrectomy (3.75 ± 0.88 %W vs. 3.30 ± 1.42 %W, respectively; $P = .12$). These strong trends did not attain statistical significance due to small sample sizes. However, postoperative QUS results decreased, and CSF improved in every case. Vitreous echodensity (composite index [see above]) decreased by 40% (from 782 ± 198 to 425 ± 78 AU, respectively; $P = .0002$), and CSF improved by 36% (3.75 %W to 2.05 %W, respectively; $P = .00004$). For a comparison to previous studies,[28] the QUS P50 index (percentage of the central and posterior vitreous filled by echogenic structures >50 pixels or 0.069 mm) was assessed as previously described.[14] Postoperatively, the P50 index decreased by 90.7% (preoperative: 9.164 ± 1.934 AU; postoperative: 0.832 ± 0.411 AU; $P < .0001$). This is consistent with the 94.1% reduction previously reported in 75 cases of limited vitrectomy.[28] These findings are highly suggestive (if not strong evidence) that vitreous opacification was a major cause of subjective vision disturbance, objective degradation in CSF, and overall patient unhappiness.

DISCUSSION

DONDERS[30] CREDITED VON GRAEFE AS THE FIRST TO ASSERT that the cause of myopia was to be found in the "vitreous humor." However, the International Myopia Institute recently defined myopia with no mention of vitreous or myopic vitreopathy.[31] Previous studies have identified that myopia and associated changes in vitreous are a leading cause of vitreous floaters, at times resulting in the disease of vision-degrading myodesopsia from clinically significant vitreous opacities.[10,32] The present study found that myopic eyes had 37% greater vitreous echodensity (QUS) and 53% worse CSF than age-matched controls. Myopic eyes with PVD had 33% greater vitreous echodensity, 62% worse degradation in CSF than nonmyopic eyes with PVD ($P < .001$), and 77% CSF degradation compared to nonmyopic eyes without PVD ($P < .001$), accompanied by 59% increased vitreous echodensity ($P < .001$). These findings represent important new data regarding myopic vitreopathy.

Myopic vitreopathy likely degrades CSF through increased internal vitreous collagen aggregation, as

reflected by increased vitreous echodensity, even in the absence of PVD. Posterior vitreous separation from the retina induces even greater premacular vitreous density (as determined by US) that further lowers CSF, probably due to light scattering by the detached posterior vitreous cortex, which contains a high density of collagen fibrils[9,14,15,33,34] and a nonspherical, irregular surface with folds.[32,34] However, the molecular events underlying these structural phenomena are not well understood.

Early studies found reduced protein concentration, collagen content, and hyaluronate concentrations in myopic vitreous compared to controls.[35] More recent studies in mouse models found lower levels of vitreous potassium, sodium, and chloride, as well as proteins involved in ocular tissue homeostasis and repair, whereas proteins of the inflammatory response class were overexpressed.[36] Another pathogenic mechanism could be upregulation of oxidative stress and lipid metabolism pathways,[37] which could promote vitreous gel liquefaction. In a study of vitrectomy specimens from 44 nonmyopic eyes, 42 eyes with low-to-moderate myopia, and 51 eyes with pathologic myopia, Peng and associates[38] recently reported a strongly positive correlation ($\beta = 0.714$; $P < .0001$) between axial length and vitreous levels of Dickkopf-1 (DKK1), a natural antagonist of the canonical Wnt/β-catenin signaling pathway.

The structural hallmark of myopic vitreopathy is fibrous vitreous liquefaction.[39,40] Itakura and associates recently used swept-source OCT imaging to detect a two-fold enlargement of the bursa premacularis of Worst,[41] presumably the result of gel liquefaction. The finding of 50% higher levels of matrix metalloproteinases in vitreous of myopic eyes compared to that in controls suggests that liquid vitreous in myopia may arise from enzymatic breakdown of existing gel vitreous.[42] Alternatively, others have suggested that, in myopia, there is an increase in the synthesis of liquid vitreous, which may be more important than an increase in liquefaction of existing gel.[43,44] The mechanism of myopic fibrous vitreous liquefaction has important relevance not only to the formation of light-scattering structures within the vitreous body but also to the predisposition to PVD proffered by liquefaction. PVD not only worsens patient complaints of vitreous floaters and further degrades CSF, as observed in the present study, but also introduces the risks of anomalous PVD with attendant risks for rhegmatogenous and tractional effects upon the retina and optic disc.[45-48]

Early studies found PVD more frequently in moderate or high myopia than in emmetropia.[49] Akiba[50] used preset lens biomicroscopy in 224 myopic (>−6 D) and 222 emmetropic eyes, and found that, in emmetropia, no patients younger than 39 years of age had PVD. In contrast, patients with high myopia had PVD in the fourth decade (23%), with increasing prevalence up to 100% prevalence in those 70 years or older. Akiba concluded that PVD develops nearly 10 years earlier in highly myopic than in emmetropic eyes and is more prevalent throughout life. Yonemoto and associates[51] determined that, in the general population, the average age of PVD onset was 61 years for emmetropia, with a younger age of onset at increasing levels of myopia. From these data, they determined that, for each diopter of myopic refractive error, 0.91 years could be subtracted from the average age of PVD onset in emmetropic eyes. This was confirmed by Itakura and associates[41] who used swept source OCT and found that highly myopic subjects with partial and complete PVD were younger than controls ($P < .0001$). It should be pointed out, however, that OCT is not an accurate way to diagnose PVD, as comparisons to intraoperative findings determined a predictive value of only 53%, leading the authors to recommend ultrasonography be used to diagnose PVD.[52] The present study found ultrasonography was also useful for quantifying vitreous density in myopic patients, as was the case in other circumstances.[14-16,28,53] Future studies with advanced real-time in vivo QUS methods could provide detailed analysis of the microstructural features that cause ultrasound scattering by vitreous,[53] data that should provide new insights to better understand the molecular mechanism(s) of myopic vitreopathy as well as gauge disease severity, follow evolution, and monitor the response to future therapeutic modalities.

Although currently the most effective way to cure vision-degrading myodesopsia from myopic vitreopathy is by limited vitrectomy,[10,11,27,28,32] that was not the focus of this investigation, despite the observed elimination of the problem and restoration of normal CSF following limited vitrectomy in this cohort. Indeed, the magnitude of the burgeoning global epidemic of myopia makes a surgical approach untenable on a broad scale. Thus, an enhanced understanding of the pathophysiology of myopic vitreopathy is needed in order to develop less costly curative interventions applicable to the enormity of the problem.

The strengths of this study are the restriction to myopic patients without confounding factors such as lens opacification and maculopathy, the use of axial length rather than refractive error for quantitative analyses, and the use of objective, quantitative assessments of the association between axial length and both vitreous structure (QUS) and visual function (CSF), using a testing paradigm that has been in development for several years and has proven utility in a variety of settings.[9,14-16,27-29,32] The limitations of the study relate to the relatively small size of some subgroups, resulting in strong trends but not attaining statistical significance for the comparisons between the subjects who chose vitrectomy versus the subjects who chose observation, and the exclusion criteria that did not allow the evaluation of vitreoschisis, foveoschisis, and myopic maculopathy. However, these exclusions were necessary in order to isolate and evaluate the effects of vitreous, the main objective of this research.

Finally, although the current investigation tried to isolate and study the effects of vitreous, there were other

factors that might have influenced CSF in myopic patients. One previous study found reduced sensitivity to contrast in comparison to emmetropia, which worsened with increasing degrees of myopia.[54] Unfortunately, myopia was defined only as spherical equivalent refractive error and not axial length, so the results may not be comparable to the findings described herein. Furthermore, that study did not characterize any aspect of ocular status, such as lens or vitreous opacification, presence or absence of PVD, and macular status. Because all patients in that study were younger than 31 years of age, the likelihood of cataract and PVD was quite low. It may well be, however, that the explanation for their findings relates to increasing amounts of vitreous opacification with progressive myopic vitreopathy. The results reported herein would suggest that this is the case.

In summary, the findings reported herein detected increased vitreous echodensity and degraded CSF that were directly proportional to increasing axial length in myopic eyes. Each finding was worsened by PVD, consistent with previous reports.[9,15] Mediation modeling suggested a causal relationship, but the normalization of both vitreous structure and visual function following limited vitrectomy strongly argues for vitreous opacification as the cause of vision loss and unhappiness in myopic patients, which is apparently worse with increasing axial length. It is important to note that these changes are on a relatively macroscopic and clinical scale and do not identify the underlying molecular mechanisms which need to be elucidated before effective countermeasures can be developed, perhaps even to prevent myopic vitreopathy.

ALL AUTHORS HAVE COMPLETED AND SUBMITTED THE ICMJE FORM FOR DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST and none were reported. Research analyses and the publication of this article were supported by VMR Research Foundation. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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