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Relationship between Full-Thickness Macular Hole Onset and Posterior Vitreous Detachment

A Temporal Onset Theory

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Purpose: To evaluate the relationship between full-thickness macular hole (FTMH) onset and perifoveal posterior vitreous detachment using OCT data.

Design: Retrospective study.

Participants: A total of 742 patients with FTMH or impending macular hole (MH) in $\geq$ 1 eye, as determined by ophthalmoscopy and OCT.

Methods: Macular holes were staged using OCT results. Patients with the posterior vitreous membrane clearly detected in the OCT images and vitreoretinal adhesion size $\leq$ 1500 μm—eyes with MH stages 1−3—were included in the study. The contralateral eyes were also included in the analyses if they showed the focal type of vitreomacular adhesion (VMA) (i.e., vitreoretinal adhesion $\leq$ 1500 μm). The distance between the posterior vitreous membrane and the surface of the retina was defined as the posterior vitreous separation height (PVSH). Using the OCT images, PVSHs of each eye in 4 directions (nasal, temporal, superior, and inferior) at 1 mm from the center of the MH or fovea were calculated.

Main Outcome Measures: The main outcome measures were PVSHs according to the MH stage and VMA, the relationship of the foveal inner tear with PVSH, and the likelihood of a foveal inner tear based on the direction.

Results: The PVSH trends in each of the 4 directions were as follows: VMA < MH stage 1 = MH stage 2 < MH stage 3. Initial MH stage 2 (onset of FTMH) was defined as the presence of a gap in only 1 of the 4 directions from the center of the MH. With increased PVSH, the likelihood of a gap increased ($P = 0.002$), and a temporal gap was more likely to occur than a nasal gap ($P = 0.002$).

Conclusions: At FTMH onset, a foveal inner tear likely appears on the temporal side or the side showing a high PVSH value.

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Tangential traction due to the contraction of the vitreous cortex in the parafovea[1,2] or anteroposterior traction with parafoveal vitreous detachment[3–5] may be involved in the onset and development of a macular hole (MH). In particular, analyses of the detailed structure of the retina and the state of the retinal vitreous interface have become possible since the development of OCT. Using OCT-based findings, the International Vitreomacular Traction Study Group[6] considered parafoveal vitreous detachment an important factor involved in the development of MH, and based on the state of parafoveal vitreous detachment and changes in the foveal structure, they classified MH progression as vitreomacular adhesion (VMA), vitreomacular traction, and full-thickness macular hole (FTMH). According to this classification, VMA is the prestage of MH, and vitreomacular traction and FTMH correspond to MH stage 1 and MH stages 2−4, respectively, in the Gass classification.

The anatomic difference between MH stage 1 and MH stages 2−4 is the absence or presence of a full-thickness gap in the entire layer of the foveal retina from the inner limiting membrane to the photoreceptor layer. This difference has a significant effect on the spontaneous remission of MH. Thus, MH stage 1 is likely to resolve spontaneously and usually does not require surgery.[1,7–12] Conversely, MH stages 2−4 are less likely to resolve spontaneously[1,7–12] and are indications for surgery. Thus, understanding the progression of MH and differentiating between MH stages 1 and 2 is extremely important when deciding whether surgery is required. However, the mechanism of disease progression is unknown. Understanding this mechanism will help develop strategies to prevent disease progression or help elucidate the factors that should be noted during follow-up at the VMA and MH stage 1 and during surgery. To the

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best of our knowledge, no previous studies have examined the involvement of the vitreous cortex and the changes in the macular shape during the progression from MH stage 1 to MH stage 2 (FTMH) in detail. In this study, we analyzed the relationships of MH stage 1 and FTMH with perifoveal vitreous detachment. Moreover, we examined the involvement of posterior vitreous detachment in the progression from MH stage 1 to FTMH.

Methods

Patients and OCT Examination

This study was performed in accordance with the tenets of the Declaration of Helsinki. The institutional review board of Osaka University Hospital approved the study protocol. Due to the retrospective nature of the study, patient consent was not obtained. We reviewed the medical records of 742 patients with FTMH or impending MH in ≥ 1 eye, as determined by ophthalmoscopy and OCT performed in the Department of Ophthalmology at Osaka University Hospital between January 2008 and June 2015. An OCT-based classification system was used for MH staging.[3] Patients with traumatic or secondary MH, such as from macular edema or high myopia (high myopia ≥ −6 D or axial length ≥ 26.0 mm); patients who underwent intraocular lens insertion (to exclude the influence of vitreous changes due to cataract surgery[13]); and patients who did not undergo OCT using Cirrus™ HD-OCT (Carl Zeiss Meditec AG) with the 512 × 128 cube scan mode (6 mm × 6 mm) were excluded from this study.

Among the remaining patients, we selected patients whose posterior vitreous membrane was clearly observed on the OCT images and whose vitreoretinal adhesion size was ≤ 1500 μm. According to Wu et al.,[14] the difference between the OCT images of MH stage 3 and stage 4 is that the presence of the posterior vitreous membrane can be confirmed on the OCT image in MH stage 3 but not MH stage 4. Therefore, we did not include patients with MH stage 4 in this study. The contralateral eyes of the included patients were also analyzed if they showed the focal type of VMA. According to the classification by Duker et al.,[6] VMA and vitreomacular traction are categorized into focal (≤ 1500 μm) and broad (> 1500 μm) types based on the vitreoretinal adhesion size. As we aimed to examine the influence of perifoveal vitreous detachment on MH development, we included eyes with VMA of the focal type or MH in which perifoveal vitreous detachment can be confirmed in the OCT image.

Both eyes were included in the study if MH was detected in both eyes. If the MH stage progressed after the initial diagnosis, the data at the time of initial diagnosis were included in the analysis. The OCT scan that provided the first measurable image was used if MH was evaluated multiple times using OCT. Macular hole staging and VMA evaluations were performed by 2 retina specialists (H.S. and A.S., each with > 5 years of experience as a retina specialist), and if these evaluations differed, a third retina specialist (K.N., with > 5 years of experience as a retina specialist) performed the final evaluation.

Height of Posterior Vitreous Separation

The posterior vitreous separation height (PVSH), which is the distance between the retinal surface and the posterior vitreous membrane, was evaluated using OCT images. The PVSH values were measured at 1 mm in the nasal, temporal, superior, and inferior directions from the fovea center in the VMA group and from the MH center in the MH group (Fig 1A−C). The PVSH values were determined by 2 retina specialists (H.S. and A.S.), and the mean values were used in further analyses.

Foveal Inner Tear in MH Stage 2

A foveal inner tear can be observed in MH stage 2. The range of the tear is between 0° to 360° when viewed from the fovea. The foveal inner tear appears as a gap (Fig. 1B) on OCT images with horizontal and vertical lines passing through the center of the MH (Fig 1A). To simplify the analysis in this study, the number of foveal inner gaps (from 0−4) in the 4 directions from the center of the hole was determined for each eye. Macular hole stage 2 showing a gap in exactly 1 of the 4 directions was defined as "initial MH stage 2," which is particularly important when considering stage progression.

The direction of the foveal inner gap was evaluated by 2 retina specialists (H.S. and A.S.), and if the 2 evaluations differed, a third retina specialist (K.N.) made the final decision.

Outcome Measures

The relationship between the direction of the gap in eyes with initial MH stage 2 and PVSH was statistically investigated. Furthermore, the likelihood of an initial MH stage 2 gap based on its direction was also statistically evaluated.

Data Collection and Analysis

For each patient, data regarding age, sex, the eye with the MH (left or right), and equivalent spherical values, as well as the data collected using OCT, were analyzed. A multivariable logistic regression model was used to assess the relationships of the foveal gap with PVSH, as well as its direction among patients with initial MH stage 2. The presence or absence of the foveal gap was the dependent variable, whereas the PVSH and the direction among initial MH stage 2 patients were the independent variables. The models were adjusted for the patients' age, sex, and the variable indicating the side of the eye (right or left). Furthermore, the nonlinear association of PVSH with a restricted cubic spline with knot 3 was also assessed. The correlation between repeated measurements of single patients was addressed using Huber−White robust covariance matrix estimates. All statistical inferences were two-tailed, with a 5% significance level, and were performed using R software (https://cran.r-project.org/).

Results

Patient Characteristics

After applying the inclusion and exclusion criteria, data from 271 eyes with MH (261 patients) were included. Among patients with VMA in the contralateral eye, the length of the vitreous adhesion was ≤ 1500 μm in 40 eyes (40 patients). Therefore, data from 311 eyes (261 patients) were included in the statistical analysis (Table 1).

PVSH in the VMA and MH Groups

In the VMA and MH groups, PVSHs at a distance of 1 mm in the inferior, nasal, superior, and temporal directions from the center of the fovea or the center of the MH were calculated and presented as medians and interquartile ranges (Table 2, Fig 2). The PVSH values showed the following trend: VMA group < MH stage 1 group = MH stage 2 group < MH stage 3 group in each of the 4 directions.

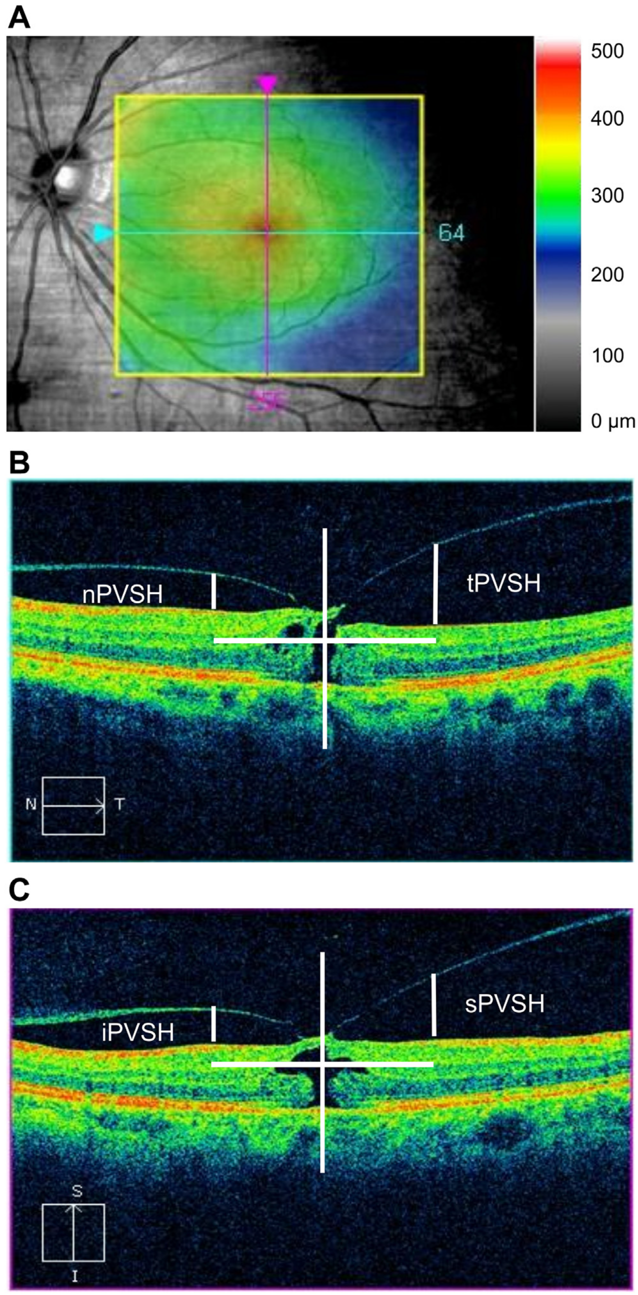

Figure 1. OCT-based measurements of the posterior vitreous separation height (PVSH), which is defined as the height of the posterior vitreous separation from the retinal surface to the posterior vitreous membrane. An example of a full-thickness macular hole is shown. **A,** The fundus image shows horizontal (blue) and vertical (red) OCT lines. **B,** PVSH values from the surface of the retina to the posterior vitreous membrane at a distance of 1 mm toward the nasal and temporal sides from the center of the macular hole were measured and recorded as nasal PVSH (nPVSH) and temporal PVSH (tPVSH) using the built-in software. **C,** PVSH values of the inferior and superior sides at 1 mm from the center of the MH were measured and recorded as inferior PVSH (iPVSH) and superior PVSH (sPVSH).

Posterior vitreous separation height tended to be smaller in the nasal direction than in the other 3 directions in all groups except for the VMA group. Regarding the MH stage 1 and MH stage 2 groups, the PVSH trends in the 4 directions were very similar (nasal < inferior = superior < temporal).

Foveal Inner Tear in MH Stage 2

A foveal inner tear in MH stage 2 appears as a gap in the horizontal and vertical lines of OCT images. The number of gaps can range from 0 to 4. Among the 118 eyes in the MH stage 2 group, 0 gaps were observed in 5 eyes (4.2%), 1 gap in 47 eyes (39.8%), 2 gaps in 38 eyes (32.2%), 3 gaps in 23 eyes (19.5%), and 4 gaps in 5 eyes (4.2%).

An initial MH stage 2 with exactly 1 gap in any of the 4 directions was observed in 47 eyes, and the direction in which the gap was identified was temporal in 27 eyes (57.4%), superior in 9 eyes (19.1%), inferior in 8 eyes (17.0%), and nasal in 3 eyes (6.4%).

Among the eyes with initial MH stage 2, the direction with the highest PVSH was temporal (23 eyes, 48.9%), followed by superior (15 eyes, 31.9%), inferior (5 eyes, 10.6%), and nasal (4 eyes, 8.5%). The direction showing the highest PVSH was consistent with the gap direction in 30 of the 47 eyes (63.8%). In 41 of the 47 eyes (87.2%), a gap was observed in the same direction in which the highest or second-highest PVSH values were observed.

Relationship Between the Presence of a Foveal Gap in the Initial MH Stage 2 and PVSH Values

The PVSH value and the presence of a foveal gap were significantly related in the initial MH stage 2 ($P = 0.002$; Fig 3A). Furthermore, the larger the PVSH, the higher the rate of recognition of the gap in that direction in the initial MH stage 2. The general likelihood of the presence of a foveal gap showed no sex difference; however, for PVSH exceeding 300 μm, the odds of a foveal gap tended to be higher in females than in males (Fig 3B). At a PVSH of 500 μm, the odds of the presence of a foveal gap were about 2.7 times higher in females than in males (calculated from logOdds = 1).

Likelihood of a Foveal Gap in the Initial MH Stage 2 According to the Direction

In the initial MH stage 2 group, a foveal gap was observed in only 1 direction from the fovea on the OCT image. This gap was more likely to be present on the temporal side than on the nasal side ($P = 0.002$; Fig 4). Thus, when an FTMH initially develops, the likelihood of a gap on the temporal side is high.

Discussion

The results of this study revealed interesting and important findings regarding the relationship between perifoveal posterior vitreous detachment and the onset of FTMH. In this study, it was newly found that the greater the PVSH, the higher the likelihood of a foveal inner tear occurring in eyes with initial MH stage 2. Additionally, it was newly found that a tear was more likely to be observed on the temporal side with the fovea as the center. Since PVSH on the

Table 1. Characteristics of the Patients with VMA and MH Stages 1−3

	Level	VMA	MH1	MH2	MH3	Overall	Missing (%)
n		40	36	118	117	311	
Age (years, median [IQR])		68.26 [64.01, 72.11]	67.34 [64.25, 72.19]	65.73 [63.11, 72.64]	66.57 [63.55, 69.91]	66.25 [63.42, 71.24]	0.0
Sex % (freq)	Female	65.0 (26)	77.8 (28)	63.6 (75)	54.7 (64)	62.1 (193)	0.0
	Male	35.0 (14)	22.2 (8)	36.4 (43)	45.3 (53)	37.9 (118)	
Eye % (freq)	Left	72.5 (29)	58.3 (21)	48.3 (57)	53.8 (63)	54.7 (170)	0.0
	Right	27.5 (11)	41.7 (15)	51.7 (61)	46.2 (54)	45.3 (141)	
Spherical equivalent value (diopter, median [IQR])		0.80 [−0.06, 1.63]	0.00 [−1.18, 0.75]	0.00 [−1.00, 1.10]	0.00 [−1.45, 1.00]	0.00 [−1.05, 1.05]	0.0

freq = frequency; IQR, interquartile range; MH1 = macular hole stage 1; MH2 = macular hole stage 2; MH3 = macular hole stage 3; n = number; VMA = vitreomacular adhesion.

temporal side is larger than that on other sides, a foveal inner tear is more likely to occur on the temporal side. Unexpectedly, progression from MH stage 1 to stage 2 was observed in the absence of significant changes in PVSH.

Posterior vitreous detachment first occurs in the paramacular area. In the paramacular area, a space is created between the inner surface of the retina and the posterior vitreous cortex. In the context of MH formation, the expansion of the vitreous detachment to the perifovea and the adhesion of the vitreous cortex to the fovea in the macula is quite important. If the adhesion in the fovea is dislodged, then vitreous detachment leads to the adhesion of the optic disc and vitreous membrane. Complete posterior vitreous detachment is achieved when adhesion to the optic nerve head is dislodged.[15] We hypothesized that MH formation may occur as a byproduct of these physiological posterior vitreous detachment processes; this hypothesis is in agreement with the findings of other studies.[15,16]

Among the posterior vitreous detachment processes mentioned, expansion of perifoveal posterior vitreous detachment and continuation of the attachment of the posterior vitreous membrane and fovea may be involved in the occurrence of FTMH. During this process, the optic disc and vitreous membrane continue to adhere. According to the results of our present study, PVSH was larger on the temporal side in MH stages 1 and 2, and a foveal inner tear was likely to occur on the temporal side in the initial MH stage 2. The increase in PVSH on the temporal side is considered to be related to the shape of the perifoveal posterior vitreous detachment during the process of posterior vitreous detachment. In MH stage 1, the posterior vitreous membrane is attached to the optic disc and fovea, resulting in perifoveal posterior vitreous detachment. In the horizontal OCT section, the posterior vitreous was attached to the optic disc toward the nasal side from the fovea; however, no attachment was noted on the temporal side because of the physical possibility that the posterior vitreous membrane forms an arc with a large radius in the horizontal section on the temporal side and the high likelihood of an increase in PVSH at a distance of 1 mm from the fovea on the temporal side. Furthermore, we hypothesized that the movement of the vitreous gel is involved in the formation of FTMH. There is room for the PVSH to increase on the temporal side. Moreover, the movement of the vitreous gel is considered to be involved in defining the actual PVSH value. The vitreous gel moves with the movement of the eye, and the posterior vitreous membrane has an inward moving force. When the gel is attached to the optic disc and fovea, the movement of the vitreous gel is higher in a direction away from the fovea, especially on the temporal side, and the PVSH tends to be large on the temporal side, where there is no attachment.

We presumed that the reason for the increased likelihood of a foveal inner tear on the temporal side in the initial MH stage 2 is based on the same principle. The posterior vitreous membrane is attached to the optic disc and fovea. Considering the vicinity of the foveal attachment, the traction on the temporal side is greater than that on the nasal side when the gel vibrates due to eye movement. Therefore, in the initial MH stage 2, the likelihood of the occurrence of

Table 2. Posterior Vitreous Separation Height

		VMA	MH1	MH2	MH3
n		40	36	118	117
PVSH (μm) (median [IQR])	inferior	81 [20, 166]	240 [161, 332]	259 [154, 383]	415 [279, 525]
	nasal	84 [52, 167]	199 [146, 299]	230 [143, 300]	342 [232, 463]
	superior	116 [65, 167]	248 [195, 363]	279 [199, 342]	469 [329, 593]
	temporal	104 [56, 151]	298 [222, 408]	329 [198, 419]	446 [337, 564]

IQR = interquartile range; MH1 = macular hole stage 1; MH2 = macular hole stage 2; MH3 = macular hole stage 3; n = number; PVSH = posterior vitreous separation height; VMA = vitreomacular adhesion.

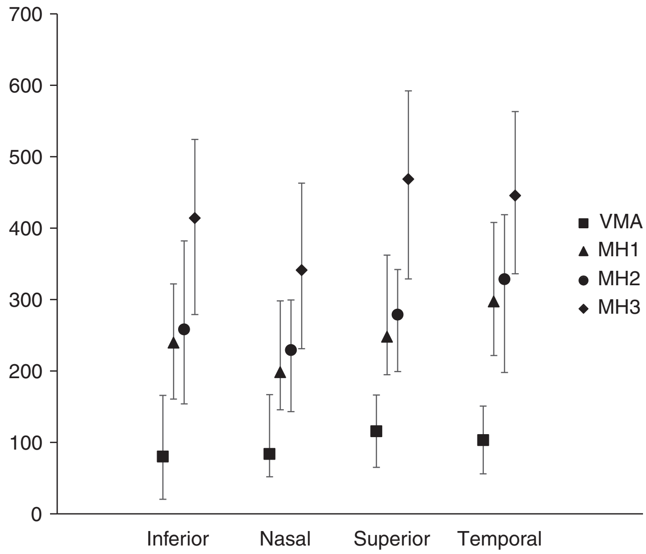

Figure 2. Comparison of the median posterior vitreous separation heights of the vitreomacular adhesion (VMA) and macular hole (MH) groups. MH1, macular hole stage 1; MH2, macular hole stage 2; MH3, macular hole stage 3. Error bars: interquartile ranges.

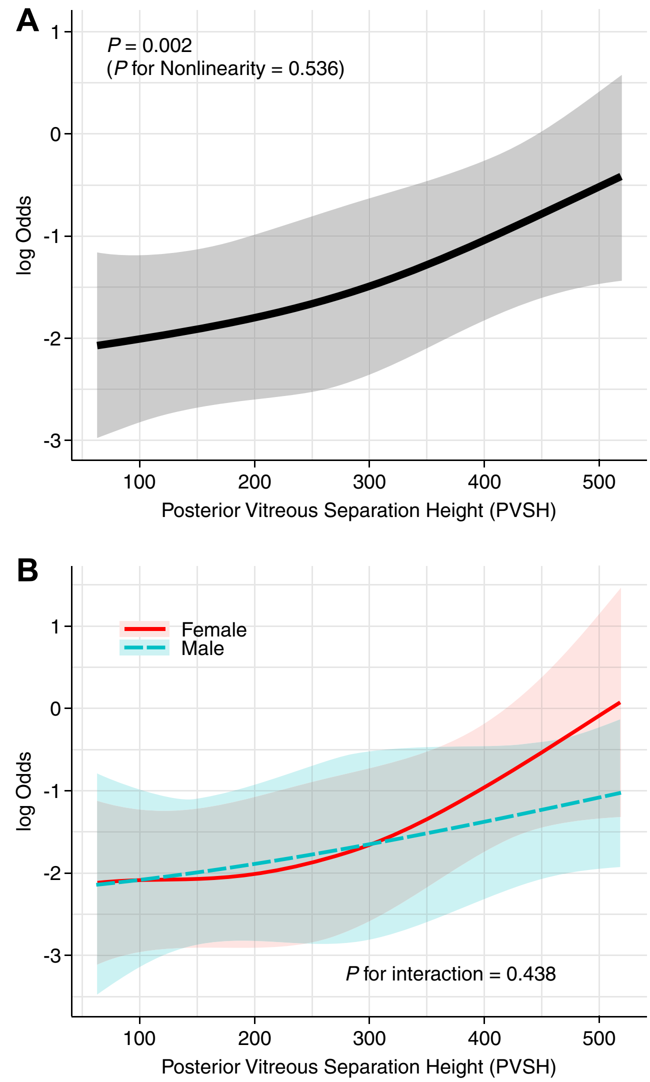

Figure 3. Relationship between the presence of a foveal gap and the magnitude of the posterior vitreous separation height (PVSH) in eyes with initial macular hole stage 2. **A,** An increase in PVSH increases the odds of a foveal gap ($P = 0.002$). The dark gray area shows the interquartile range. **B,** The general likelihood of the presence of a foveal gap shows no sex difference, but for PVSH exceeding 300 μm, the odds of a foveal gap tend to be higher in females than in males. At a PVSH of 500 μm, the odds of the presence of a foveal gap are about 2.7 times higher in females than in males (calculated from logOdds = 1).

a foveal inner tear is thought to be higher on the temporal side. The positional relationship between the optic disc and fovea, which is the site where the posterior vitreous membrane is attached, and the traction associated with the movement of the gel in the vicinity of the parafovea contribute to the shape of the perifoveal posterior vitreous detachment and to the size of the PVSH.

Based on the results of our study, we speculated about the progression from the VMA stage to MH stage 1 and stage 2. A few perifoveal posterior vitreous detachments can be observed during the VMA stage (Fig 5A). Perifoveal posterior vitreous detachment and increased space between the posterior vitreous membrane and the retinal surface layer can be detected on OCT images. Retinal detachment or cyst-like changes may occur in the foveal area (Fig 5B). This condition is called MH stage 1. When the size of the posterior vitreous membrane remains almost unchanged, a foveal inner tear, that is, FTMH, occurs in the direction in which the space between the posterior vitreous membrane and the retinal surface layer is larger (Fig 5C). As the distance between the posterior vitreous membrane and the retinal surface is larger on the temporal side, there is increased likelihood of foveal inner tears occurring on the temporal side. When the tear occurs, it expands; consequently, the vitreous attachment on the fovea is released, and the MH progresses to stage 3.

Various theories about the origin of traction have been proposed. The vitreous traction involved in MH formation was considered by Mori et al.[17] to be the dynamic traction generated by posterior cortical vitreous movements during eye rotation. The temporal side has a greater range of motion than the nasal side, to which the optic disc is attached, with more movement of the posterior vitreous cortex. Therefore, we hypothesized that traction is stronger on the temporal side, and foveal inner tears are more likely to occur.

Hikichi et al.[10] reported that spontaneous healing within 1 year was observed in 48% of patients and that progression to FTMH occurred in 23% of patients with MH stage 1. The study by de Bustros et al.[8] reported a 40% progress to FTMH in eyes with MH stage 1 within 2 years. Kim et al.[11] reported that natural healing of MH stage 2 occurred in 16% of cases within 1 year whereas progression to stage 3 was observed in 74% of cases. In MH stages 1 and 2, the height of the posterior vitreous cortex does not change, and it seems that the same

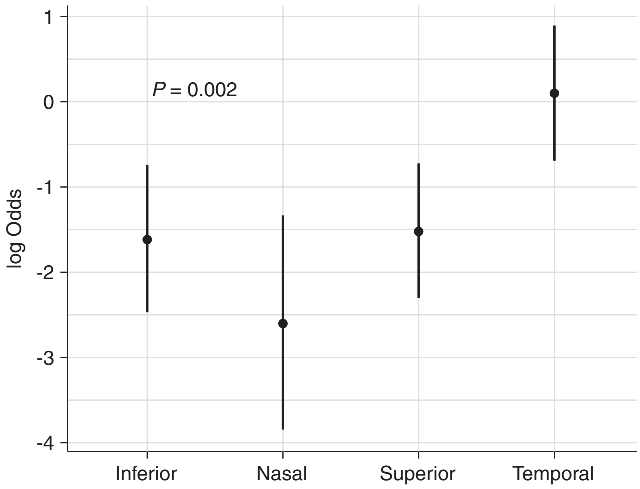

Figure 4. Likelihood of a foveal gap in the initial macular hole stage 2 based on the direction. A foveal gap is more likely to be present on the temporal side than on the nasal side ($P = 0.002$). Error bars: interquartile ranges.

continuous traction force is applied to the foveal surface. However, MH stage 1 is considered to show high stability against vitreous traction because of the absence of a retinal tear; in many cases, vitreous traction is released, progression to FTMH is prevented, and the pathological condition is naturally relieved. Conversely, in MH stage 2, a retinal tear has already occurred, and the MH expands due to the continuous traction of the posterior vitreous detachment. Transition to MH stage 3 is expected to eventually occur.

Regarding MH development, there is a debate regarding whether the fovea degenerates or foveal traction is present. Our results suggest that foveal traction occurs first and the continuous traction changes the structure of the fovea. Previous reports showed the frequent occurrence of MH in females[18–20] with thin retinas[21–23]. Our data also showed that a foveal inner tear is more likely to occur in females than in males with large PVSH. These data can be understood with this mechanism and may prove it.

The present results suggest that patients with a large PVSH are at high risk of developing MH stage 2 (an odds ratio about 2.7 times [calculated from logOdds = 1] higher than that of PVSH of 100 μm for a PVSH of 400 μm) and the odds of developing MH stage 2 tend to be higher in females than in males for PVSH exceeding 300 μm. Ophthalmologists must be aware that as PVSH increases, the odds ratio of progression to MH stage 2 increases more in female than in male patients.

Our data indicate that the average PVSH does not change substantially between MH stages 1 and 2. Thus, patients with MH stage 1 with a high PVSH should be followed up carefully for signs of progression to MH stage 2, keeping in mind that the PVSH may remain unchanged. Based on the results of this study, we suggest the following strategy for patients with MH stage 1 or VMA. The OCT findings are important. Patients with VMA are at a lower risk if the PVSH is small; however, when it increases, MH stage 1 may occur. Since the next stage, MH stage 2, requires surgery, progression to MH stage 2 is an important change, and 2 points should be considered: patients may proceed to MH stage 2 even if the PVSH does not increase and a foveal inner tear can occur in the direction of the large PVSH or on the temporal side. Macular hole stage 1 likely progresses to MH stage 2 even when the PVSH remains in the same state. Special attention should be paid to the direction with the highest PVSH as it is associated with a high probability of foveal inner tears and progression to MH stage 2. Thus, we suggest that the physical observational window should be changed to closely examine the posterior vitreous membrane for patients with MH stage 1 or VMA with a large PVSH.

This study has some limitations. First, VMA causes no abnormalities in visual function, and many patients do not visit the hospital until their visual function deteriorates to MH stages 2–4. Therefore, patients were often not followed up as they progressed from VMA to MH stage 3, and data regarding the course of progression could not be obtained. To obtain more information on this population, this study had a cross-sectional design. Second, a radial scan would have been more effective in evaluating MH and the direction of the inner tear. According to Schneider

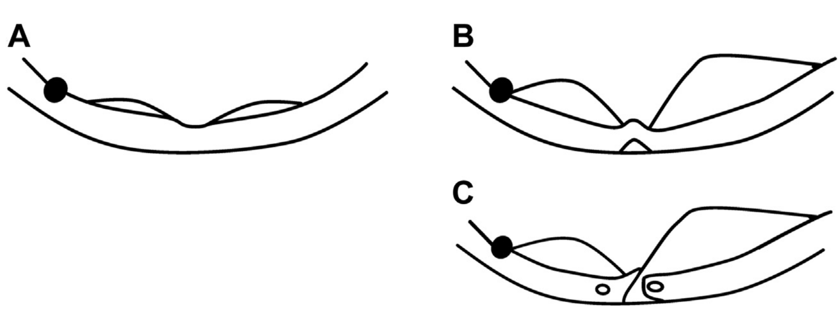

Figure 5. Relationship between the state of the posterior vitreous membrane and macular hole (MH) stage. **A,** Vitreomacular adhesion stage. There are few perifoveal posterior vitreous detachments. **B,** MH stage 1. In this stage, the height of the perifoveal posterior vitreous detachment is increased, especially on the temporal side. **C,** MH stage 2 (full-thickness macular hole). In this stage, the height of the perifoveal posterior vitreous detachment is also high, especially on the temporal side; however, this value is not significantly different from that in stage 1 (**B**). A foveal inner tear arises from the direction with a larger height of the posterior vitreous separation between the retinal surface and the posterior vitreous membrane, mostly present on the temporal side.

et al.,[24] high-density radial scanning demonstrated superior detection rates of small FTMHs compared with standard raster volume scanning. This may be attributable to the greater foveolar scan density attained with radial scan patterns. A radial scan, especially a high-density radial scan, would prevent any inner tear from being missed and allow a more detailed and accurate examination of its range, direction, and other parameters. Third, patients with secondary or traumatic MH were excluded from the study. Furthermore, patients with large adhesions of the vitreous cortex on the macular surface and those with high myopia were excluded; consequently, it is unclear how MHs develop in such patients. Macular hole progresses in some cases even if the fovea is similarly pulled by the vitreous body, whereas the pulling is relieved and the disease recovers spontaneously in other cases. In this study, we evaluated VMA and MH stage 1, which are likely to recover spontaneously, and we included cases that did not progress to MH stage 2 and spontaneously improved during follow-up.

In conclusion, when MH stage 2 (i.e., FTMH) occurs, a foveal inner tear is likely to occur from the direction where the posterior vitreous detachment is larger or from the temporal side.

Footnotes and Disclosures

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HUMAN SUBJECTS: Human subjects were included in this study. The institutional review board of Osaka University Hospital approved the study protocol. All research adhered to the tenets of the Declaration of Helsinki. Due to the retrospective nature of the study, patient consent was not obtained. No animal subjects were used in this study.

Author Contributions:

Conception and design: Sakaguchi, Sakimoto, Nishida

Data collection: Sakaguchi, Sakimoto, Shiraki, Fujimoto, Fukushima, Hara.
Analysis and interpretation: Sakaguchi, Kabata, Shintani. Obtained funding: N/A

Overall responsibility: Sakaguchi, Kabata, Sakimoto, Shiraki, Fujimoto, Fukushima, Hara, Shintani, Nishida

Abbreviations and Acronyms:
FTMH = full-thickness macular hole; **MH** = macular hole; **PVSH** = posterior vitreous separation height; **VMA** = vitreomacular adhesion; **VMT** = vitreomacular traction.

Keywords:
Full-thickness macular hole, Optical coherence tomography, Macular hole, Vitreomacular adhesion, Posterior vitreous detachment.

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