INDIVIDUALIZED, SPECTRAL DOMAIN-OPTICAL COHERENCE TOMOGRAPHY–GUIDED FACEDOWN POSTURING AFTER MACULAR HOLE SURGERY

Minimizing Treatment Burden and Maximizing Outcome

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Purpose: To evaluate the individualized, optical coherence tomography-guided facedown posturing after macular hole (MH) surgery in minimizing the burden and maximizing outcome.

Methods: A retrospective comparative study. One hundred and seven consecutive eyes with an MH (<500 μm) received vitrectomy and gas tamponade. After surgery, optical coherence tomography examination was performed from 6 hours to postoperative Day 2. In Group A, with a pro re nata posturing protocol, the duration of facedown posturing was determined from the optical coherence tomography findings. Group A was subdivided as follows: Group A1, facedown posturing required postoperatively and Group A2, no posturing required. When MH closure was confirmed, facedown posturing (if any) was discontinued. If the MH did not close, additional posturing was advised. Group B was the control group, consisted of 42 consecutive eyes with traditional 7 days of posturing.

Results: After a single surgery, Group A had the MH closure rate of 96.2%, 95.8% in Group A1 and 97.1% in Group A2, whereas Group B had the MH closure rate of 95.2%. The average posturing period was 42 hours for Group A, 57 hours for Group A1 and 10 hours for Group A2 ($P < 0.001$). The MH size was correlated significantly with the closure time (R = 0.47, $P = 0.005$, Spearman correlation coefficient).

Conclusion: A pro re nata posturing protocol achieves a high MH closure rate with a significant reduction of posturing time especially for pseudophakic eyes.

RETINA 34:1367–1375, 2014

In the original report of Kelly and Wendel,[1] the anatomical closure rate of macular hole (MH) after vitrectomy with 1 week of maintaining a posturing was 58%. Current MH surgery usually consists of pars plana vitrectomy with the removal of all traction around the MH, gas tamponade, and posturing. This has increased the closure rate to ~90%.[2,3] Tornambe et al first addressed the lack of need for a facedown posturing, and other studies suggested a shortening of the posturing period.[4–11] A recent, multicenter randomized controlled study showed that the MH closure rate without facedown posturing was ~90% for small idiopathic MHs.[12] Despite these improvements, there are still concerns that a shorter duration of posturing might lead to failure in some eyes.[7,13] To maximize the success rate of MH closure, while minimizing the inconvenience on patients, an individualized program would be preferable to a uniform protocol, that is, a pro re nata (PRN) approach.

The key to developing an individualized posturing regimen is an early evaluation of the status of MH during the gas-filled period after the surgery. Previously, we showed that spectral domain optical coherence tomography (SD-OCT) was a reliable method in determining whether MH was closed in gas-filled eyes.[14] Since then, there have been several confirmatory reports.[15–20]

The purpose of this study was to compare the MH closure rates and duration of facedown posturing after vitrectomy with PRN posturing to that with conventional 7 days prone positioning. We studied 107 eyes and shall show that PRN posturing achieves a high MH closure rate with a significant reduction of posturing duration especially for pseudophakic eyes.

Subjects and Methods

The procedures used were approved by the Institutional Review Board of Kagoshima University Hospital (Kagoshima, Japan), Kyushu Medical Center (Fukuoka, Japan), and Beppu Medical Center (Oita, Japan), and the procedures conformed to the tenets of the 1989 Declaration of Helsinki. After a detailed explanation of the surgical procedures, a written informed consent was obtained from all subjects to perform these surgical procedures. The patients also agreed to allow us to use the data for any future analyses. This was a retrospective consecutive case series and included 107 consecutive eyes of 104 patients treated for MHs at Kagoshima University Hospital, Kyushu Medical Center, and Beppu Medical Center between July 2008 and December 2012. The primary inclusion criterion was patients with Stage 2, 3, or 4 small-to-medium–sized idiopathic MHs, that is, <500 μm. The exclusion criteria included secondary MHs, previously operated retinal disorders, myopia >6 diopters, other interfering ocular pathology, and inability to maintain a posturing.

All patients had a complete preoperative ophthalmologic examination including measurement of the preoperative best-corrected visual acuity, slit-lamp examination, fundus examination, axial length measurements, and SD-OCT. The idiopathic MHs were graded according to the Gass classification.[21] Spectral domain optical coherence tomography examination was performed using the Topcon OCT (OCT-1000 MARK II; Topcon, Tokyo, Japan) or Cirrus OCT (Cirrus HD-OCT 4000; Carl Zeiss Meditec, Dublin, CA).

The preoperative MH size was determined by measuring the narrowest midhole diameter. Care was taken for the scan to pass through the center of the MH and only the largest measurement was used with the Topcon OCT with 3-dimensional scan mode (6 $\times$ 6 mm, 512 A-scan $\times$ 128 B-scan) or Cirrus OCT with 512 $\times$ 128 macular cube mode (6 $\times$ 6 mm, 512 A-scan $\times$ 128 B-scan). Early postoperative OCT images were obtained using our previously described technique.[14,19,20] Briefly, Topcon OCT with 3D-scan mode or Cirrus HD-OCT with HD 5-line raster mode (6 mm parallel lines, 1024 A-scans/B-scans and averaged 4 B-scans/image) was used. For the Cirrus OCT, several horizontal and vertical scans with 25 μm spacing were recorded to obtain clear images and evaluate the status of the MH. The MH was taken to be closed when there was an absence of a retinal gap in any OCT image, which passed through the MH.

The surgery consisted of standard pars plana vitrectomy using a 23-gauge or 25-gauge system. The internal limiting membrane was peeled in all patients after core vitrectomy and posterior hyaloid separation. Brilliant blue G was used for the internal limiting membrane staining and peeling when necessary, but indocyanine green was not used. At the end of the surgery, the vitreous cavity was filled with nonexpansile concentration ($\sim$15%) of sulfur hexafluoride gas. Phakic eyes with cataracts and patients >50 years had cataract surgery with the implantation of an intraocular lens simultaneously because postvitrectomy cataract is to be expected in most phakic eyes, especially $>90\%$ in 3 years after the MH surgery.[22,23]

The first SD-OCT examination was done 6 hours after the surgery, and the subsequent SD-OCT examinations were performed on a case-by-case basis. For example, if the surgery finished at 2:00 PM, the first SD-OCT was taken at 8:00 PM, the next SD-OCT examination was usually done at 9:00 AM next morning. Every SD-OCT examination was made with consent from the patients. From Day 1 to Day 2 postoperation (PO), SD-OCT examinations were performed every morning and evening. In gas-filled eyes, the time of MH closure was recorded as the time when no outer retinal gap on the fovea was observed in the SD-OCT images. In most cases, a clear OCT image could not be obtained from the macular area from Day 3 to Day 5 PO because of the reflections from the waterline mark. Therefore, the MH closure was confirmed on Day 7 PO with an OCT

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Supported by a grant from the Research Committee on Chorioretinal Degeneration and Optic Atrophy, Ministry of Health, Labor, and Welfare, Tokyo, Japan, and by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture of the Japanese Government.

Paper presented in part at Vail Vitrectomy meeting at Vail, CO, March 20, 2013.

None of the authors have any financial/conflicting interests to disclose.

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examination through a liquid phase. Then, the MH closure was reconfirmed at the 3-month visit after the gas bubble had been resorbed. A MH was classified as being closed only if it was seen to be closed during the last visit at ≥3 months. If a MH was not closed or reopened during the follow-up period, it was treated at the physician's discretion. Relevant data including the duration of the posturing period were collected for each case.

The eyes were divided into Group A with PRN posturing and Group B with conventional 7 days of prone positioning. Group A was subdivided into Group A1 and Group A2. Group A1 consisted of 72 eyes of 72 patients who were instructed to assume a facedown posturing immediately after surgery. Then, SD-OCT examinations were performed as described, and the facedown posturing was discontinued as soon as the MH was confirmed to be closed in the SD-OCT images. If the MH was not closed, the patients were instructed to continue the facedown posturing until the MH was closed. Group A2 consisted of 35 eyes of 32 patients. The patients were instructed not to assume a facedown posturing immediately after surgery. If the MH was not closed on the evening of Day 2 PO, they were then instructed to assume a facedown posturing. If the MH was confirmed to be closed by SD-OCT on Day 3 or Day 4 PO, the posturing was discontinued.

Forty-two consecutive eyes of 41 patients who had undergone MH surgery from January 2004 to June 2007 were used as control subjects. The basic procedures were almost the same except that some patients received 20-gauge pars plana vitrectomy. However, the prone positioning was begun immediately after the surgery and was maintained for 7 days. Optical coherence tomography examination was performed after Day 7 PO to confirm the MH closure.

Macular Hole Size and Closure Time

To determine the best time to begin facedown posturing to obtain the highest MH closure rate, we evaluated the relationship between the MH size and the first closure time. This analysis was performed on Group A2, the only group where no postoperative posturing was required unless the MH was found to be open by OCT.

Statistical Analyses

All statistical analyses were performed with SPSS 21 for Windows (SPSS Inc, IBM, Somers, NY). Experimental data are expressed as mean ± standard deviation. The mean and percentages were used for the description of quantitative data. The best-corrected visual acuity was measured with a Landolt C chart and then converted to logarithm of the minimal angle of resolution units. Student's *t*-tests, Mann–Whitney *U* tests, chi-square tests, or Fisher's exact tests were used to evaluate the significance of the demographic and clinical differences between groups. The relationship between the MH size and closure time was analyzed using Spearman rank correlation test. A $P < 0.05$ was considered to be statistically significant.

Results

The demographic and baseline characteristics of the groups are summarized in Table 1. Group A consisted of

Table 1. Demographic and Baseline Characteristics

	Group A (PRN Group)	Group B (Traditional Group)	*P*	Subgroup of Group A		*P*
				Group A1	Group A2	
No. eyes	107	42		72	35	
Mean age, years (SD)	67.0 (7.4)	64.4 (8.0)	0.06	67.3 (7.6)	66.4 (7.0)	0.55
Gender, male/female	48/59	14/28	0.20	30/42	18/17	0.34
Stage of MH, n (%)			0.55			0.23
2	32 (29.9)	9 (21.4)		20 (27.8)	12 (34.3)	
3	43 (40.2)	20 (47.6)		27 (37.5)	16 (45.7)	
4	32 (29.9)	13 (40.0)		25 (34.7)	7 (20.0)	
Mean MH diameter, μm (SD)	327 (111)	332 (127)	0.75	334 (109)	315 (114)	0.36
Lens status, phakia/IOL	97/10	39/3	1.0	63/9	34/1	0.27
Mean preoperative refraction, diopters (SD)	−0.18 (1.8)	−0.13 (2.2)	0.93	−0.17 (1.9)	−0.19 (1.5)	0.52
Mean axial length, mm (SD)	23.5 (1.1)	23.3 (1.2)	0.30	23.4 (1.1)	23.6 (0.9)	0.55
Mean preoperative BCVA, logMAR (SD)	0.73 (0.28)	0.82 (0.28)	0.12	0.75 (0.28)	0.69 (0.28)	0.29

BCVA, best-corrected visual acuity; IOL, intraocular lens; SD, standard deviation.

107 eyes, 72 eyes in Group A1 and 35 eyes in Group A2. Group B consisted of 42 eyes. There were no significant differences in the baseline characteristics between the groups. Preoperatively, there were 63 phakic and 9 pseudophakic eyes in Group A1, 34 phakic and 1 pseudophakic eyes in Group A2, and 39 phakic and 3 pseudophakic eyes in Group B. Concurrent cataract surgery was performed in 62 eyes in Group A1, 34 eyes in Group A2, and 39 eyes in Group B (Tables 1 and 2).

Posturing in Each Group

An algorithm of the study and flowchart of the position assumed by the patient are shown in Figure 1. The average ± standard deviation duration of posturing for all eyes was 42 ± 50 hours, with 57 ± 51 hours for Group A1 and 10 ± 30 hours for Group A2. All of Group B did a uniform posturing of 144 hours (7 days). Group A2 had a significantly shorter posturing duration than either Group A1 or Group B (Table 2; $P < 0.001$).

Macular Hole Closure Rate and Visual Acuity

After a single surgery, the closure rate was 95.8% (69 of 72 eyes) in Group A1, 97.1% (34 of 35 eyes) in Group A2, and 95.2% (40 of 42 eyes) in Group B (Figure 1). All of the unclosed MHs were closed after a second surgery. The eyes in which the MH was closed on Day 7 PO maintained the closure until the last visit with no reopening. There was no significant difference in the closure rate and the best-corrected visual acuity between the 3 groups (Table 2).

Diagnosable OCT images in gas-filled eyes were obtained from 93 of 107 eyes (86.9%) in Group A, Group A1 was 80.6% and Group A2 was 100%. The causes of the poor quality of OCT image of 14 eyes were: a gas cataract in 1 eye, hyphema in 1 eye, and corneal edema or Descemet membrane folds in 11 eyes. In these 93 eyes, the MH was closed by Day 2 PO in 80 of 93 eyes (86.0%); 51 of 58 eyes (87.9%) in Group A1 and 29 of 35 eyes (82.9%) in Group A2 (Table 2). All of the patients with a closed MH were informed that maintaining a facedown posturing was not necessary thereafter.

In Group A, 13 of 93 eyes had an opened MH on the evening of Day 2 PO; 7 patients in Group A1 were instructed to continue with the facedown posturing and 6 patients in Group A2 were instructed to begin the facedown posturing. Among these 13 eyes, 11 eyes were found to have a closed MH on Day 7 PO (Table 3).

Macular hole closure was confirmed in 60% of the cases on the morning of Day 1 PO, and the closure rate increased slowly over time (Figure 2). However, there was no apparent difference between those with immediate posturing (Group A1) and posturing only if needed (Group A2).

In 16 eyes whose OCT images were clear enough to follow the course of MH closure, the subretinal fluid cuff disappeared first and retinal cystic change gradually became more obscure and disappeared. Soon thereafter, the MH decreased in size and closed (Figures 3 and 4).

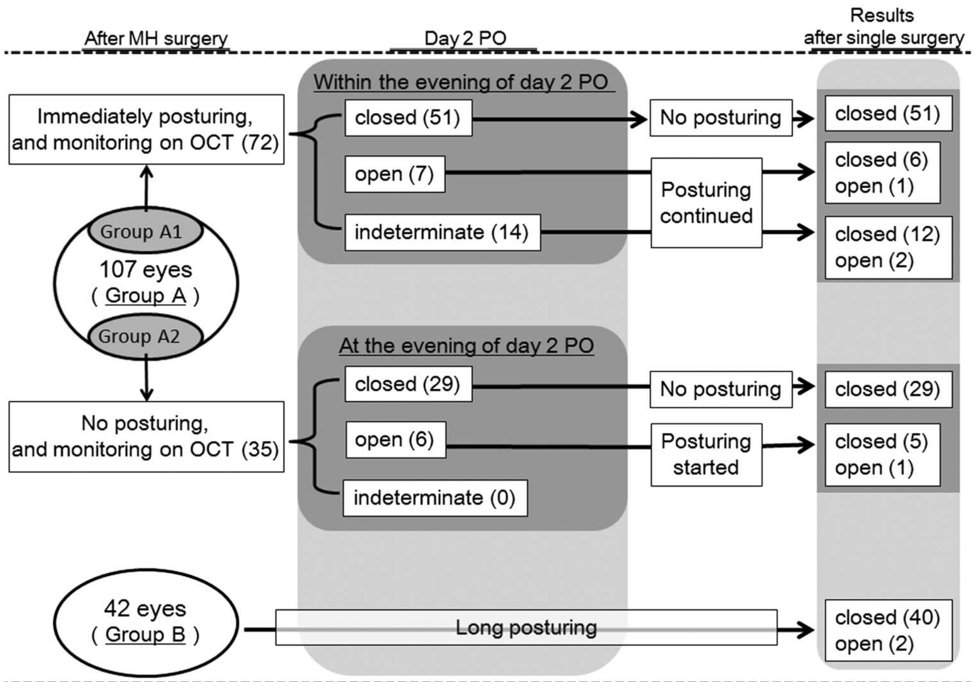

Fig. 1. Algorithm and flowchart of posturing regimen.

Table 2. Results After Macular Hole Surgery

	Group A (PRN Group)	Group B (Traditional Group)	*P*	(Subgroup of Group A) Group A1	Group A2	*P*
Closure rate of MH after the single surgery, n/n (%)	103/107 (96.2)	40/42 (95.2)	0.67	69/72 (95.8)	34/35 (97.1)	1.0
Lens status, phakia/IOL	1/106	0/42	1.0	1/71	0/35	1.0
Diagnosable gas-OCT images, n/n (%)	93/107 (86.9)	—	—	58/72 (80.6)	35/35 (100)	0.004
MH closure within the evening of day 2 PO, n/n (%)	80/93 (86.0)	—	—	51/58 (87.9)	29/35 (82.9)	0.55
Mean duration of posturing, hours (SD)	42 (50)	144 (–)	<0.001	57 (51)	10 (30)	<0.001
Mean postoperative BCVA, logMAR (SD)	0.20 (0.22)	0.27 (0.23)	0.19	0.20 (0.23)	0.19 (0.21)	0.58
Improvement of ≥0.2 logMAR in VA, n/n (%)	97/107 (90.7)	38/42 (90.4)	1.0	67/72 (93.0)	30/35 (85.7)	0.29
Mean follow-up period, months (range)	7.2 (3–39)	5.7 (3–40)	0.53	8.1 (3–39)	5.4 (3–12)	0.61

BCVA, best-corrected visual acuity; gas-OCT, SD-OCT on gas-filled eye; IOL, intraocular lens; SD, standard deviation; VA, visual acuity.

Macular Hole Size and Closure Time

In Group A2, the MH size was significantly and positively correlated with the time of closure (R = 0.47, P = 0.005, Spearman correlation coefficient; Figure 5). Fourteen of the eyes in Group A1 with an MH <250 μm were closed on the evening of Day 1 PO. The mean closure time in these 14 eyes was 18.6 hours. The mean closure time in 17 eyes with a smaller MH (≤300 μm) was 19.8 hours and that for 17 eyes with a medium MH (300–500 μm) was 45.4 hours ($P < 0.01$; Figure 5).

Unclosed Macular Hole and Complications

In Group A, there were 3 eyes in Group A1 and 1 eye in Group A2 whose MH had not closed at 1 week PO. In Group B, there were 2 eyes whose MH had not closed at 1 week PO. They were all closed with an additional surgery.

Retinal breaks occurred in 6 eyes in Group A (5.6%) and 3 eyes in Group B (7.1%), which were all repaired with laser treatment intraoperatively. A retinal detachment developed in 2 eyes in Group A (1.8%) and 1 eye in Group B (2.3%), which were repaired with a second vitrectomy. There was no endophthalmitis, corneal opacity, or uncontrollable intraocular pressure rise. There was no imbalance of systemic adverse events among the groups.

Discussion

These results suggest that individualized facedown posturing by the SD-OCT images can significantly

Table 3. Characteristics of 13 Eyes Observed the Residual MH on the Evening of Day 2 PO

Patient (Group-Case)	Stage	MH Size, μm	MH Status Another Day (Day 3 PO)	MH Status 1 week PO	Duration of posturing, hours
A1-3	4	382	Indeterminate	Closed	168
A1-8	2	376	Indeterminate	Closed	115
A1-16	3	359	Indeterminate	Closed	129
A1-22	2	423	Indeterminate	Closed	116
A1-43	3	415	Open	Open	152
A1-45	3	455	Indeterminate	Closed	144
A1-46	3	407	Open	Closed	144
A2-1	2	384	Open	Closed	73
A2-5	3	353	Open	Open	144
A2-9	2	367	Close	Closed	43
A2-11	3	354	Open	Closed	93
A2-21	3	422	Close	Closed	57
A2-22	3	409	Close	Closed	60
Mean (SD)	—	393 (32)	—	—	111 (43)

SD, standard deviation.

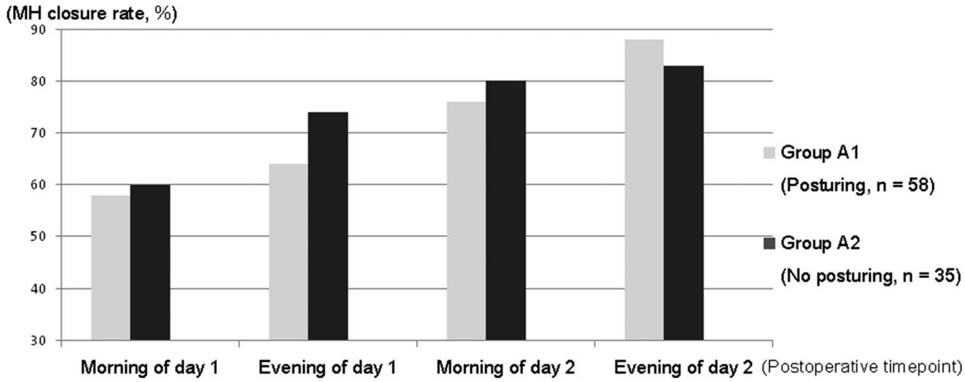

Fig. 2. Macular hole closure rate determined by SD-OCT from Day 1 to Day 2 PO. Macular hole closure was confirmed in ∼60% on the morning of Day 1 PO, and the closure rate increased gradually over time. There is no apparent difference between those with immediate posturing (Group A1) and posturing only if needed (Group A2).

decrease the duration of facedown posturing without compromising the results. The eyes in the PRN Group A2 required a shorter facedown posturing duration than that in the other groups. The overall success rate of MH closure with PRN posturing was comparable with that of the traditional 7 days of prone positioning. This suggests that immediate posturing after surgery is not required, and posturing may be imposed when needed as determined by the SD-OCT images.

Several recent studies have modulated the facedown posturing durations after MH surgery based upon OCT images of gas-filled eyes.[14,16,17,20] To the best of our knowledge, our study contains the largest number of patients using this protocol. In addition, we were able to document the chronologic progress of MH closure under gas, and determine the relationship between the MH size and closure time using SD-OCT imaging of gas-filled eyes.

Several no posturing protocols have been attempted to minimize the postoperative inconveniences.[4,11,12,24–28] The results of recent comparative studies[12,26–28] suggested no statistically significant difference in the closure rates between no posturing or short-term posturing and standard posturing. However, there

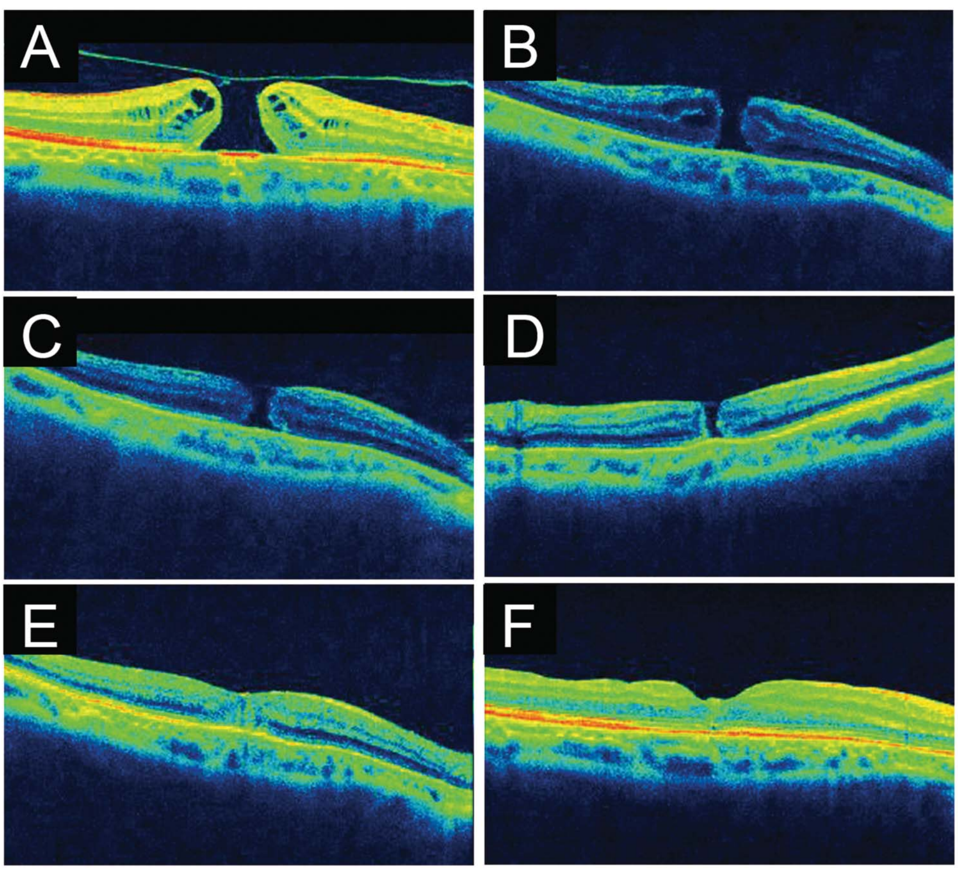

Fig. 3. Spectral domain optical coherence tomography images after MH surgery obtained from Case 17 (Group A2). **A.** A 63-year-old woman with a Stage 3 MH. Posturing was not assumed after surgery. **B.** After 6 hours, the MH was still open in the intraocular gas OCT image, but subretinal fluid cuff had resolved. The macula cysts resolved after 17 hours (**C**), the MH is smaller after 22 hours (**D**), and closed after 28 hours (**E**). **F.** After 6 months, MH remained closed.

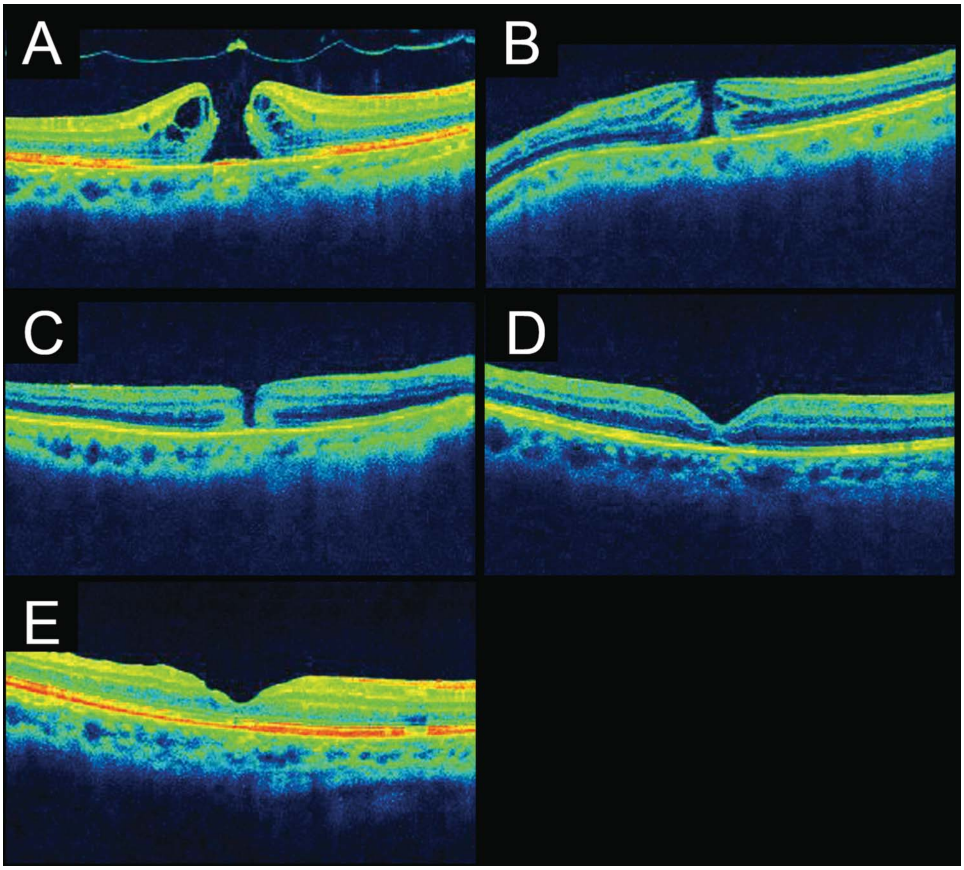

Fig. 4. Spectral domain optical coherence tomography images after MH surgery obtained from Case 11 (Group A2). **A.** A 57-year-old woman with a Stage 3 MH. Posturing was not assumed after surgery. **B.** After 15 hours, the MH was still open in the intraocular gas OCT image. On the evening of Day 2 PO (37 hours after surgery, **C**), the macula cysts resolved and the MH is smaller, however the MH is still open. She was then instructed to start the facedown posturing and continued. **D.** On Day 7 PO, the MH is closed. **E.** After 6 months, MH remained closed.

was a tendency for the closure rate to be better with standard posturing than with no or short-term posturing, for example, posturing versus no posturing was 97.4% versus 87.5% in a study by Guillaubey et al[26]; 94.1% versus 91.4% in a study by Tadayoni et al[12]; and 93.3% versus 60% in a study by Lange et al.[27] Nonetheless, these results must be questioned

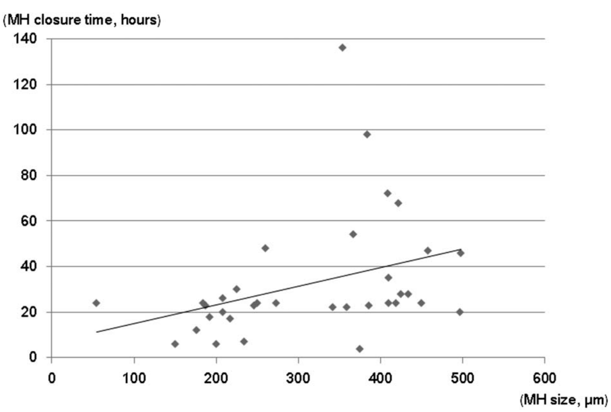

Fig. 5. Macular hole size and closure time in Group A2. The MH size is significantly and positively correlated with closure time (R = 0.47, P = 0.005, Spearman's correlation coefficient). All MHs <250 μm (14 eyes) had closed by the evening of Day 1 PO. One eye with unclosed MH was excluded from this analysis.

because ~800 cases are theoretically required to achieve a 95% confidence interval.[28] The sample size in these studies was not adequate to be conclusive. It should be noted that our results also do not provide conclusive evidence regarding the closure rate of PRN posturing protocol being the same as that of the traditional 7-day posturing.

The OCT images showed that ~60% of MHs were closed by the morning of Day 1 PO, >75% by the morning of Day 2 PO, and some 85% by the evening of Day 2 PO (Figure 2). Notably, neither the chronology nor the anatomy of MH closure differed between the 2 PRN groups. This suggests that for some MH cases, no facedown posturing is needed after surgery and that the presumed drying effect of the gas bubble is sufficient even without facedown posturing.[25,29,30]

The MH of 13 of 107 eyes (12.1%) had not closed by the evening of Day 2 PO, and facedown posturing was then imposed. As a result, 10 of 13 eyes (9.3%) had closed within 1 week after an additional facedown posturing. Therefore, it seems that a facedown posturing is necessary for ~10% eyes. This finding may explain the difference, when calculated as an aggregate, for the tendency of the closure rate to be better with traditional posturing compared with no posturing or short-term posturing in some studies, even though the differences were not statistically significant.[12,26,27]

However, a uniform prone posturing protocol would place an unnecessary inconvenience on many patients, therefore it seems reasonable to use the SD-OCT findings to individualize the postoperative posturing.[12,13,27–29] Our results also showed that a smaller MH required a shorter posturing duration after surgery, which would indicate that the traditional posturing duration may not be necessary for small MHs. This is consistent with earlier reports that no posturing or short-term posturing has the same closure rate for small MHs than traditional 7-day posturing.[12,13,26–28] To the best of our knowledge, this is the first direct confirmatory evidence supported by clear OCT images obtained from every gas-filled eye. These data further support an individualized postoperative strategy.

Examination of the correlations between the MH size and closure times (Figure 5) showed that there seems to be 2 clusters; 1 with MH size <300 μm and the other >300 μm. Every MH of the former group closed within 24 hours without facedown posturing, but some of the latter group required an additional posturing after Day 2 PO. Therefore, there might be a clinically important threshold MH size of 300 μm. This is consistent with the finding that smaller MHs close without posturing or gas tamponade just after the release of vitreomacular traction with ocriplasmin.[31]

This study has important limitations. The retrospective nature of this study may have introduced sampling bias. Although the basic surgical technique was the same, individual surgeon variables cannot be excluded. Almost all of the eyes were pseudophakic after surgery, and it is always easier to obtain a clear image of a gas-filled eye from a pseudophakic eye compared with a phakic eye.[20] Thus, this protocol is more suitable for pseudophakic eyes.

The frequent examinations after surgery is a time-consuming protocol, however, our results provide important information that could determine the future individualized protocol. Additionally, the Group B control group was not perfectly matched because these surgeries were performed at a different time. Even though the comparison was made on only a limited number of issues which were expected not to be affected by the postoperative frequent OCT examinations of study groups, this limitation should be remembered.

In conclusion, our data support using an individualized approach based on the intraocular-gas OCT findings for the postoperative management of patients with MH to maximize outcome and minimize the inconvenience for the patient.

Key words: facedown posturing, macular hole, SD-OCT, vitrectomy, intraocular gas OCT.

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