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Can Perifoveal Pseudocyst Area be a Prognostic Factor in Macular Hole Surgery?

A Prospective Study With Quantitative Data

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Abstract: To evaluate the effect of perifoveal pseudocysts on the anatomical outcomes of the idiopathic macular hole surgery as a prognostic factor.

Twenty-one eyes of 20 consecutive patients with a Gass stage 3 or 4 idiopathic macular hole were enrolled in this prospective study between March 2012 and May 2013. Demographic data, medical history, and ocular examinations were recorded preoperatively and on postoperative day 1, week 1, and month 1, 3, and 6. Five spectral domain optical coherence tomography (SD-OCT) parameters were analyzed: macular hole (MH) basal diameter, MH minimum diameter, MH height, macular hole index, and a new parameter, the area of macular pseudocysts via the software of SD-OCT device at the widest cross section of the MH formation.

The mean preoperative best-corrected visual acuity was 0.86 ± 0.29 logarithm of the minimum angle of resolution (LogMAR) (between 0.4 and 1.3) and improved to 0.64 ± 0.28 LogMAR (between 0.22 and 1.23) postoperatively ($P = 0.004$). There was a statistical significant difference between both MH basal diameter and MH pseudocyst area with anatomical success, respectively ($P = 0.016$ for MH basal diameter, $P = 0.004$ for MH pseudocyst area). The anatomical closure was correlated with MH basal diameter and MH pseudocyst area ($P = 0.01$ and $P = 0.001$, respectively). Spearman correlation rank coefficient between with MH basal diameter and MH pseudocyst area was $r = 0.493$ and statistically significant ($P = 0.02$).

Perifoveal pseudocysts seem to be associated with anatomic failure and may be used as a prognostic factor in MH surgery.

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Abbreviations: BCVA = best-corrected visual acuity, ILM = internal limiting membrane, ILMP = internal limiting membrane peeling, IMH = idiopathic macular hole, LogMAR = logarithm of the minimum angle of resolution, MH = macular hole, MHI = macular hole index, OCT = optical coherence tomography, RPE = retina pigment epithelium, SD-OCT = spectral domain optical coherence tomography.

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INTRODUCTION

Idiopathic macular hole (IMH) is a full-thickness defect of the neuroretina that involves the fovea, and was firstly described by Knapp[1] in 1869 with an ocular blunt trauma patient. The condition is frequently used for IMHs. Also, it may occur as a result of axial elongation in myopic eyes.[2] We used to think that this situation was untreatable before Kelly and Wendel[3], who first introduced vitreous surgery for macular holes (MH) in 1991. After that, surgery method was improved by several surgeons with some modifications.[4–6] Internal limiting membrane peeling (ILMP) played a crucial role in these modifications and was believed that there is a tangential traction in etiology of MH formation.[7] Internal limiting membrane (ILM) plays an important role in the etiology and the enlargement of the IMH.[8] As a result of this traction, while posterior hyaloid is detaching perifoveal pseudocysts may occur. ILMP relieves this traction and provides better anatomical and functional results.[9–12]

Younger age, smaller basal diameter of MH, smaller macular hole index (MHI), earlier stage, shorter duration, and better preoperative visual acuity are good prognostic criteria for anatomical closure.[13,14] In clinical practice, Gass classification is used internationally for staging the IMHs and used as a predictive factor for the anatomical and functional success.[15] However, this classification needs some modifications, because it does not include the detailed changes like accumulation of intraretinal fluid, tractional foveal cystoid space, or perifoveal pseudocysts, which may be detected via spectral domain optical coherence tomography (SD-OCT, Heidelberg Engineering, Heidelberg, Germany). On the contrary, The International Vitreomacular Traction Study Group introduced an optical coherence tomography (OCT) based anatomic classification system for diseases of the vitreomacular interface.[16] In this classification, the authors categorized the vitreomacular interface diseases as vitreomacular adhesion, vitreomacular traction and full-thickness MH. In this OCT-based anatomic classification system, staging is also based on aperture size and does not include morphological changes of MH formation. The aim of this prospective study is how these pseudocysts affect the anatomical closure success of the IMH surgeries as a prognostic factor.

PATIENTS AND METHODS

Twenty-one eyes of 20 consecutive patients with a Gass stage 3 or 4 IMH were included in this prospective study. One patient had IMH on both eyes. All MHs had been treated with standard 3 port 23 gauge vitrectomy between March 2012 and May 2013. All patients underwent complete ophthalmic examination including measurement of best-corrected visual acuity (BCVA) via early treatment diabetic retinopathy study chart, biomicroscopy of anterior segment, dilated fundus examination, and spectral domain optical coherence tomography (SD-OCT) preoperatively and postoperative 1 day, 1 week, 1, 3, and 6 month. Postoperative SD-OCT assessments were made firstly in 1, 3, and 6 month, respectively. All patients had been operated by the same surgeon (ATY) in Beyoglu Eye Research and Training Hospital. Inclusion criteria was stage 3 and 4 IMH according to the Gass classification. Exclusion criteria were higher than −6.00 D a refractive error, traumatic MH, macular retina pigment epithelium (RPE) atrophy, history of past ocular surgery except phacoemulsification, and other systemic and ocular diseases. All patients had given written informed consent before surgery, all the procedures were approved by the institutional ethics committee, and the study adhered to the tenets of the Declaration of Helsinki.

Surgery

All patients underwent standard 3 port 23 gauge pars plana vitrectomy with triamcinolone acetonide-assisted posterior vitreous detachment, if it was not already present. ILM removal were performed using 0.2 mL of dye brilliant blue G (Brilliant-Peel; Geuder, Heidelberg). The area of removal of the ILM was intended to be 2 to 3 disc diameters surrounding the MH. Fluid-air exchange through an extrusion cannula was performed to flatten the hole. The procedure was completed by an intraocular tamponade with 15% perfluoropropane (C_3F_8) or 20% sulfur hexafluoride (SF_6). Patients were asked to maintain a prone position for 5 days postoperatively. Anatomic success was defined as the complete closure of the MH and absence of subretinal fluid on SD-OCT.

OCT Measurements

Based on previous studies, 4 OCT parameters were analyzed: MH basal diameter, MH minimum diameter, MH height, MHI, and a new parameter: the area of macular pseudocysts.[17–22] Basal hole diameter was defined as the hole diameter at the level of the RPE (Figure 1). Minimum hole diameter was determined between the nearest walls of hole. MH height was measured from the RPE to the top of the MH. The MHI (hole height/basal hole diameter) was calculated according to a previously described method.[17] The area of pseudocysts were calculated by a software option of SD-OCT at the widest cross-section of the MH formation (Figure 2). The borders of the pseudocysts were marked by the observer and the software programme gives the areas of the pseudocysts. The calculations were made by a single observer (YSG) for each patient.

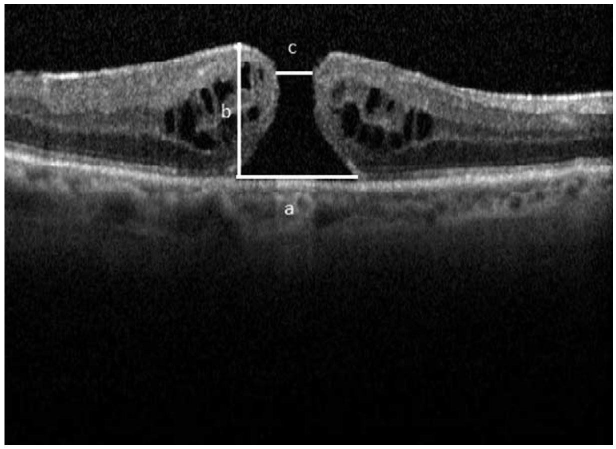

FIGURE 1. Measurements of parameters on OCT. Basal hole diameter (A) was defined as the hole diameter at the level of the retinal pigment epithelium. Minimum hole diameter (C) was calculated between the nearest walls of hole. Hole height (B) was the highest measurement from the RPE to vitreoretinal interface. OCT = optical coherence tomography, RPE = retina pigment epithelium.

Statistical Analysis

The patients were evaluated for the anatomical outcome with 1 surgical procedure. The anatomical success was defined as the complete closure of the MH and absence of subretinal fluid on SD-OCT. The cases were analyzed with Mann–Whitney test in terms of 5 SD-OCT parameters: MH base diameter, MH minimum diameter, MH height, MHI, and MH pseudocyst area. Symptom duration as weeks, age, preoperative BCVA were also analyzed. The BCVA values were converted to logarithm of the minimum angle of resolution (LogMAR) values for statistical analyses. The patients with preoperative and postoperative BCVA were assessed with Wilcoxon signed-rank test. Spearman rank coefficient was calculated to assess correlation between anatomical closure and preoperative

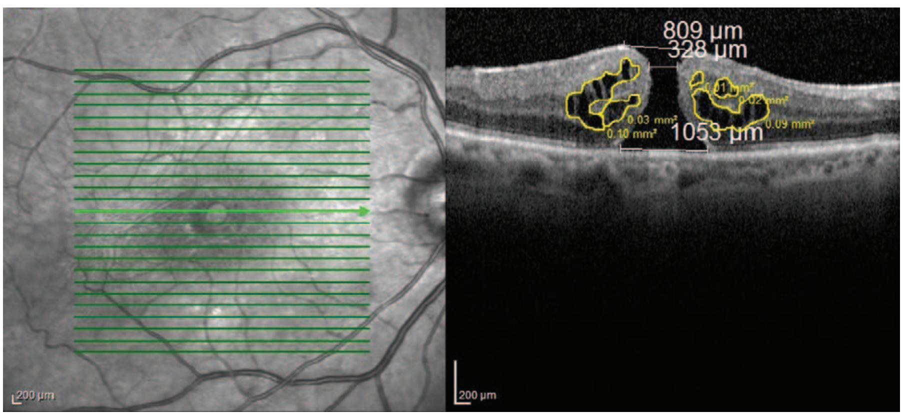

FIGURE 2. The area of pseudocysts is calculated as in micrometer square at the widest cross section of the macular hole formation.

variables such as MH base diameter, MH minimum diameter, MH height, MHI, MH pseudocyst area, preoperative BCVA, and age. A P value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics and OCT parameters of study participants were presented in Table 1. Between study participants, 6 (30.0%) were male and 14 (70.0%) were female. Five cases were stage 3 and 16 cases were stage 4 according to the Gass classification.[15] Additionally, 3 of 5 stage 3 cases have vitreomacular traction. Mean age is 67.7 ± 7.3 years ranging from 57 to 85. Sixteen eyes were phakic and 5 eyes were pseudophakic. Three patients developed significant cataract during follow-up and underwent phacoemulsification with an intraocular lens implantation. Comparing the lens status between study groups, no significant impact on the anatomical outcome was found ($P = 0.182$, Wilcoxon–Mann–Whitney test). Phacoemulsification with an intraocular lens implantation was combined with MH surgery in 2 cases. Thereby no significant influence of a combined surgery on the anatomical outcome was found ($P = 0.253$, Wilcoxon–Mann–Whitney test). Perfluoropropane (C_3F_8) was used in 16 patients and sulfur hexafluoride (SF_6) was used in 5 patients as a tamponade. There was not a significant difference between the eyes in which C_3F_8 or SF_6 were used as a tamponade regarding the anatomical outcome ($P = 0.897$, Wilcoxon–Mann–Whitney test).

The mean preoperative BCVA was 0.86 ± 0.29 LogMAR and improved to 0.64 ± 0.28 LogMAR postoperatively ($P = 0.004$). In 14 out of 21 eyes (66%), BCVA was improved by at least 1 early treatment diabetic retinopathy study line after surgery. In 6 eyes, BCVA remained unchanged, and in 1 eye, BCVA worsened. Among the group of eyes who had unchanged BCVA, 2 had open MH. One of them had undergone to second surgery and 1 of them had refused second surgery. The patient who experienced a decrease in her visual acuity had an open MH and had refused the second surgery. Primary and final anatomical success rate was 81% (17/21) and 90.5% (19/21), respectively. Overall, 4 patients remained open MHs after first surgery and were suggested a second surgery (Figure 3). Two of them could not maintain prone position for 5 days postoperatively, and did not accept second surgery.

MH basal diameter and MH pseudocyst area showed statistical significance between anatomical success and failure ($P = 0.016$ and $P = 0.004$, respectively). Other variables such as MH minimum diameter, MH height, MHI, age, stage, and preoperative BCVA and symptom duration showed no statistical significance (Table 2). The anatomical closure is correlated with MH basal diameter and MH pseudocyst area ($P = 0.01$, $r = -0.541$, and $P = 0.001$, $r = -0.652$, respectively). Also, there is a positive correlation between MH basal diameter and MH pseudocyst area ($P = 0.02$, $r = 0.493$).

Postoperative BCVA is correlated with MH basal diameter and MHI ($P = 0.02$, $r = -0.488$ $P = 0.02$, $r = 0.485$, respectively), but not with MH pseudocyst area ($P = 0.61$). Also, Spearman correlation rank coefficient between postoperative BCVA and preoperative BCVA is 0.421, but it is not statistically significant ($P = 0.05$).

DISCUSSION

There is a tangential traction in the etiology of MH formation, induced by vitreous shrinkage as observed by Gaudric et al.[7] As a result of this traction, while posterior hyaloid is detaching, perifoveal pseudocysts may occur in the inner

TABLE 1. Demographic Characteristics, Ophthalmic Characteristics, and OCT Parameters

Case Number	Age, Years	Sex	Gass Stage	Symptom Duration, Weeks	Preoperative BSCVA, LogMAR	Basal Diameter, μm	Minimum Diameter, μm	Hole Height, μm	MHI	Perifoveal Pseudocyst Area, μm^2	Anatomic Success With First Surgery
1	63	F	3	28	0.4	853	344	497	0.58	0.13	Yes
2	75	M	4	40	1	1161	251	416	0.36	0.31	No
3	65	F	3	40	0.8	400	222	408	1.02	0.1	Yes
4	64	F	4	18	0.8	962	341	416	0.43	0.11	Yes
5	85	F	4	4	0.7	917	520	351	0.38	0.14	Yes
6	69	F	4	36	1	1235	632	411	0.33	0.15	Yes
7	69	F	4	28	0.7	2203	647	670	0.30	0.59	No
8	70	F	4	20	0.52	897	398	428	0.48	0.19	Yes
9	58	F	3	4	1	751	229	410	0.55	0.16	Yes
10	62	F	3	64	1.7	932	292	405	0.43	0.18	Yes
11	57	F	4	40	1	1181	682	443	0.38	0.34	Yes
12	72	F	4	24	0.7	745	236	477	0.64	0.31	Yes
13	59	F	4	40	0.8	1188	418	504	0.42	0.40	No
14	73	F	4	8	1.3	1260	210	507	0.40	0.13	Yes
15	63	F	4	16	0.7	1480	671	500	0.34	0.20	Yes
16	63	M	3	22	0.7	764	284	508	0.66	0.24	Yes
17	64	F	4	22	0.7	1019	491	453	0.44	0.19	Yes
18	71	M	4	14	0.7	1053	328	809	0.77	0.25	Yes
19	65	M	4	18	0.7	967	356	447	0.46	0.25	Yes
20	75	M	4	17	1.0	884	417	346	0.39	0.03	Yes
21	81	M	4	10	1.3	2627	747	1313	0.50	0.73	No

F = female, M = male, MHI = macular hole index, OCT = optical coherence tomography.

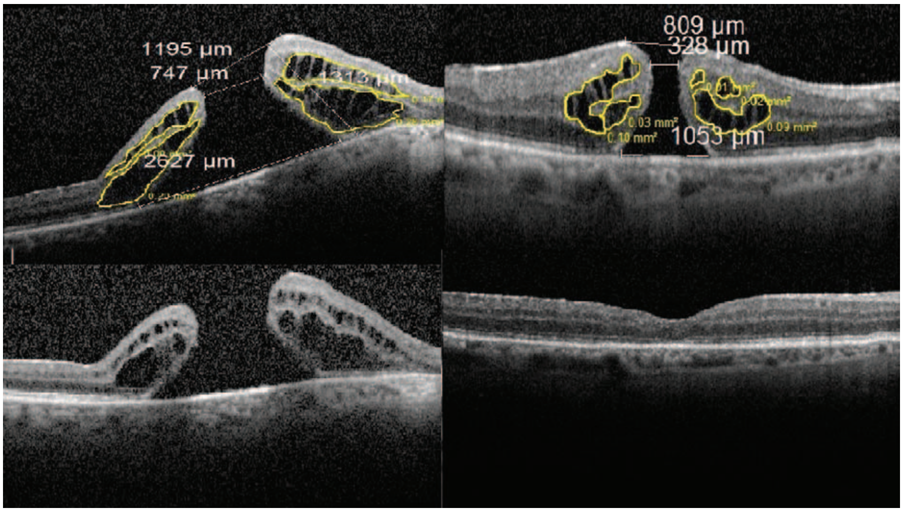

FIGURE 3. Case 21; MH pseudocyst area was 0.73 μm^2 and MH basal diameter was 2627 µ (top left) and postoperative 7. Month SD-OCT with anatomical failure (bottom left). Case 18; MH pseudocyst area was 0.25 μm^2 and MH basal diameter was 1053 µ (top right) and postoperative 4. Month SD-OCT with anatomical success (bottom right). MH = macular hole, SD-OCT = spectral domain optical coherence tomography.

nuclear layer. The objective of this prospective study was to evaluate the effect of these pseudocysts on the anatomical outcome, therefore, we measured the area of the pseudocyst via the software of Spectralis OCT, (Heidelberg Engineering, Heidelberg, Germany). To our knowledge, this is the first study to assess the pseudocyst areas quantitatively and the anatomical outcome (from a *PubMed* and *Medline* search in December 2013).

Brockman et al[23] found that MH with the presence of perifoveal pseudocysts was associated with a 3-fold higher closure rate, but presence of perifoveal pseudocysts was assessed qualitatively. In our study, we found that MH with perifoveal pseudocysts was associated with anatomic failure ($P < 0.05$). In our study group, 4 eyes did not achieve anatomical success. In addition, the mean MH basal diameter of these cases was 1794 µ and MH pseudocyst area was 0.5075 μm^2. However, the MH basal diameter and MH pseudocyst area was 958 µ and 0.1824 μm^2 in the cases with anatomical success (Figure 3). Also, there was a correlation between MH basal diameter and MH pseudocyst area ($r = 0.493$ $P < 0.05$). In the light of these findings, while MH basal diameter was increasing, also MH pseudocyst area was increasing and MH perifoveal pseudocysts were statistically relevant with the anatomical outcome. In the study by Brockman et al[23], only the presence of perifoveal pseudocysts was qualitatively assessed, and they used both Stratus and Cirrus OCT (Carl Zeiss Meditec, Dublin, CA). In Stratus OCT, perifoveal pseudocyst may not be detected because the Stratus OCT takes 6 sections of the macula, so the perifoveal pseudocysts may not intersect at the sections that the device provides. As a result of this phenomenon, while evaluating the perifoveal pseudocysts, it may not be appropriate to use time domain OCT. In the present study, the perifoveal pseudocyst areas were calculated by the software option of the

TABLE 2. Comparison of Clinical Characteristics and OCT Parameters Between Patients With Anatomic Success and Anatomic Failure

	Anatomic Success	Anatomic Failure	*P*
Number of cases	17	4	–
Age, years	67 (57–85)	71 (59–81)	0.3
Gass stage 3 : 4	5:12	0:4	0.2
Lens status, phakic : pseudophakic	14:3	2:2	0.1
Surgery, PPV : combined PPV + phaco	16:1	3:1	0.2
Tamponade, C3F8/SF6	14/3	2/2	0.8
Preoperative BCVA, LogMAR	0.84	0.94	0.3
Symptom duration, weeks	23.2	29.5	0.3
MH basal diameter, µm	958 ± 245	1794 ± 736	**0.016**
MH minimum diameter, µm	391 ± 156	515 ± 223	0.2
MH perifoveal pseudocyst area, μm^2	0.182 ± 0.078	0.507 ± 0.188	**0.004**
MH height, µm	464 ± 101	725 ± 405	0.09
MHI	0.52 (0.33–1.22)	0.39 (0.30–0.50)	0.1

BCVA = best-corrected visual acuity, LogMAR = logarithm of the minimum angle of resolution, MH = macular hole, MHI = macular hole index, OCT = optical coherence tomography, Phaco = phacoemulsification, PPV = pars plana vitrectomy. Bold values are significant at $P < 0.05$.

Spectralis OCT. Also, the pseudocysts may be detected in three-dimensional view of the macula, but it is not possible to calculate the volume of these pseudocysts via the present software.

In addition to MH perifoveal pseudocysts area, 4 OCT parameters were analyzed: MH basal diameter, MH minimum diameter, MH height, and MHI.[17–22] MH basal diameter and MHI were only 2 OCT parameters that showed a statistically significant correlation with postoperative BCVA, whereas no significant correlation was found regarding the other 3 OCT parameters including MH perifoveal pseudocyst area. Kusuhara et al[17] reported that MHI significantly correlated with the postoperative BCVA and also they postulated that MHI represents the preoperative configuration of a MH and is a prognostic factor for visual outcome. Furthermore, similar results were reported about the correlation between MHI and postoperative BCVA by Ruiz-Moreno et al.[18]

In our study, we did not find an effect of age, symptom duration, and preoperative BCVA on the anatomical outcome. Jaycock[24] and Ullrich[14] also questioned the symptom duration, and they reported similar results with ours. We think that this variable is a subjective complaint, therefore, no statistically significant effect was found on the anatomical outcome.

Various studies have shown that ILMP during MH surgery is associated with higher anatomical outcomes.[11,12] Also ILMP had been performed in all our surgeries and our final anatomical success rate is 90.5%, which was similar with the other studies in stage 3 and 4 IMHs.[25,26]

Limitation of the present study includes the relatively small numbers of patients and MH perifoveal pseudocyst areas were calculated in two-dimensional way. Strengths of the study include the fact that these MH perifoveal pseudocysts were first assessed in a quantitative way prospectively.

In conclusion, we think that MH perifoveal pseudocysts were positively correlated with MH basal diameter and propose that it may be used as a prognostic factor for the anatomical outcome of MH surgery. We used two-dimensional measurements for the perifoveal pseudocysts, new software programmes may be enhanced for measuring the three-dimensional structure of the foveal pseudocysts with larger number of patients.

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