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 postoperatively at 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 $0.86 \pm 0.29$ logarithm of the minimum angle of resolution (LogMAR) (between 0.4 and 1.3) and improved to $0.64 \pm 0.28$ LogMAR (between 0.22 and 1.23) postoperatively ($P = 0.004$). There was a statistically 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 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.

INTRODUCTION

Idiopathic macular hole (IMH) is a full-thickness defect of the neuroretina that involves the fovea, and was firstly described by Knapp 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.

We used to think that this situation was untreatable before Kelly and Wendel, who first introduced vitreous surgery for macular holes (MH) in 1991. After that, surgery method was improved by several surgeons with some modifications. 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. Internal limiting membrane (ILM) plays an important role in the etiology and the enlargement of the IMH. 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.

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. In clinical practice, Gass classification is used internationally for staging the IMHs and used as a predictive factor for the anatomical and functional success.

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).

The International Vitreomacular Traction Study Group introduced an optical coherence tomography (OCT) based anatomic classification system for diseases of the vitreomacular interface.

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 −6.00D 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 (C₃F₈) or 20% sulfur hexafluoride (SF₆). 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. 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. 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.

**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
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 6 cases were stage 4 according to the Gass classification. 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 postsurgically, 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. 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, μm² | 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.
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 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 μm and MH pseudocyst area was 0.5075 μm². However, the MH basal diameter and MH pseudocyst area was 958 μm and 0.1824 μm² 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, 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

![FIGURE 3. Case 21; MH pseudocyst area was 0.73 μm² 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 μm² 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.](image)

**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, μm² | 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 pseudocyst areas, 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\(^{23}\) 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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