Significance of outer retinal undulation on preoperative optical coherence tomography in rhegmatogenous retinal detachment

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Rhegmatogenous retinal detachment (RRD) is a vision-threatening pathology. Optical coherence tomography (OCT) is useful for evaluating retinal damage and visual prognosis in patients with RRD. Outer retinal undulation (ORU) is often observed on preoperative OCT in RRD. Therefore, we evaluated the correlation between ORU seen on preoperative OCT and pre/post-operative factors in RRD. Patients with RRD (114 eyes) underwent reattachment surgery and ≥ 6 months of follow-up. According to the condition of the macula on preoperative OCT, cases were divided into macula-on RRD (65 eyes) or macula-off RRD (49 eyes). Patients were classified into acute (< 10 days), subacute (10–30 days), and chronic (> 30 days) symptom duration groups. Clinical findings, histories, and relationships with OCT findings, including ORU, were analyzed. Subacute symptom duration was significantly associated with ORU on preoperative OCT ($p = 0.001$) and had a higher prevalence of ORU (73.7%) than did acute (OR = 4.48) or chronic (OR = 7.467) durations. Ellipsoid zone (EZ) disruption was significantly associated with poorer best-corrected visual acuity (BCVA) than normal EZ integrity at 6 months postoperatively ($p = 0.012$). ORU on preoperative OCT suggests a 10–30 days morbidity duration in RRD. EZ integrity is useful for predicting postoperative BCVA in macula-off RRD.
Methods
We retrospectively reviewed the electronic medical records of 114 patients (114 eyes) who underwent surgical treatment for RRD and had a follow-up period of at least 6 months at the Keimyung University Dongsan Medical Center between January 2017 and December 2018. This study was performed in accordance with the Declaration of Helsinki and all research was performed in accordance with relevant guidelines/regulations. This study was approved by the Keimyung University Hospital Institutional Review Board (IRB no. 2020-03-037). Informed consent was obtained from all individual patients included in this study. Patients were excluded if they had an uninterpretable OCT, a history of vitrectomy or buckling surgery, or ocular diseases affecting visual acuity and visual field. With swept source OCT (Topcon DRI OCT Triton, SS-OCT, Tokyo, Japan), central macular thickness (CMT), the height of subretinal fluid (SRF), presence or absence of undulation, and ellipsoid zone (EZ) integrity were measured in the preoperative state. CMT was defined as the distance between the umbo and the outer border of the retinal pigment epithelium (RPE). The peak height of SRF was measured between the inner border of the RPE and the highest outer border of the photoreceptor outer segment. These distances were measured perpendicular to the RPE by a ruler in the IMAGEnet 6 (version 1.25; Topcon, Tokyo, Japan) software. Central retinal thickness (CRT) was calculated by subtracting the SRF height from CMT. Disruption of the EZ integrity was judged based on the discontinuity of the EZ in OCT. ORU was defined as a change in the outer retinal gradient (negative to positive) of ≥ 3 within a diameter of 6 mm (Fig. 1). Symptom duration was defined as the time between the onset of subjective visual field loss and time of retinal detachment detection on examination. The patients were classified into acute (< 10 days), subacute (10–30 days) and chronic (> 30 days) groups, according to symptom duration.

BCVA was measured preoperatively and 1, 3, and 6 months postoperatively by the Snellen chart. BCVA was then converted to the logarithm of the minimum angle of resolution (logMAR).

For subgroup analysis in the macula-off RRD group, preoperative OCT findings and postoperative clinical data for 30 eyes that had pars plana vitrectomy were included. Eyes with intravitreal silicone oil tamponade during surgery, and with postoperative complications such as proliferative vitreoretinopathy (≥ grade C), re-detachment of the retina, or endophthalmitis, were excluded.

All statistical analyses were performed with the SPSS software (version 25; IBM Corp., Armonk, NY). The correlation of undulation and retinal detachment duration was determined with the Chi-square test and Fisher’s exact test. The relationship between preoperative OCT findings and postoperative BCVA was determined with Pearson’s product moment correlation coefficient, Student’s t-test and the Kruskal–Wallis test.

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Results
One hundred and fourteen patients were enrolled. Sixty-two patients were male (54.4%) and 52 were female (45.6%). The mean (± standard deviation (SD)) age was 53.79 ± 13.48 years. The mean (± SD) symptom duration was 12.09 ± 14.25 days. According to symptom duration, groups were classified as acute (n = 65, 57.0%), subacute (n = 38, 33.3%), and chronic (n = 11, 9.7%). There were 49 patients with macula-off RRD (43.0%) and 65 patients with macula-on RRD patients (57%). On preoperative OCT, ORU was detected in 56 eyes (49.1%) (Table 1).

In the univariate analysis, age, sex, macula status, retinal break size, preoperative BCVA, and postoperative BCVA were not significantly different with respect to on the presence or absence of ORU. ORU was however significantly associated with symptom duration (P = 0.001). The subacute group had a higher incidence of ORU (73.7%) than the acute (P = 0.001, OR = 4.48) and chronic (P = 0.01, OR = 7.467) groups. There was no significant
difference between the acute and chronic groups in the incidence of ORU (Fig. 2) (Table 1). In the multivariate analysis, additionally, the absence of ORU was significantly associated with older age and better preoperative BCVA (Table 2). Age, sex, and retinal hole size were not significantly different with respect to symptom duration. The longer the symptom duration, the higher the preoperative BCVA and the higher the macula-off rate (Table 3).

Table 1. Patient characteristics and comparison of the presence or absence of outer retinal undulation with all RRD. ¹Student’s t-test. ²Chi-square test. ³Fisher’s exact test. RRD rhegmatogenous retinal detachment, OD oculus dexter, OS oculus sinister, BCVA best-corrected visual acuity, PPV pars plana vitrectomy.

| Baseline data                          | Outer retinal undulation | P-value |
|---------------------------------------|--------------------------|---------|
|                                       | Absence (n = 58)         | Presence (n = 56) |
| Age, mean ± SD, years                 | 56.10 ± 12.82            | 51.39 ± 13.83 | 0.062¹ |
| Sex, eyes, n (%)                      | Male                     | 29 (46.8)   | 33 (53.2)   | 0.354² |
|                                       | Female                    | 29 (55.8)   | 23 (44.2)   |         |
| Eyes, eyes, n (%)                     | OD                       | 26 (53.1)   | 23 (46.9)   | 0.709² |
|                                       | OS                       | 32 (49.2)   | 33 (50.8)   |         |
| Symptom duration, ± SD, days          | 11.59 ± 15.52            | 12.61 ± 12.92 | 0.704¹ |
| Symptom duration, eyes, n (%)         | Acute (< 10 days)        | 40 (61.5)   | 25 (38.5)   |         |
|                                       | Subacute (10–30 days)    | 10 (26.3)   | 28 (73.7)   | 0.001² |
|                                       | Chronic (> 30 days)      | 8 (72.7)    | 3 (27.3)    |         |
| Macula-off, eyes, n (%)               | On                       | 37 (56.9)   | 28 (43.1)   | 0.185² |
|                                       | Off                      | 21 (42.9)   | 28 (53.1)   |         |
| Retinal hole size, ± SD, disc diameter| 1.35 ± 1.39              | 1.28 ± 1.21 | 0.779⁴ |
| Pre-op BCVA (LogMAR) ± SD             | 0.75 ± 0.77              | 1.08 ± 1.12 | 0.070⁴ |
| Post-op 6 months BCVA (LogMAR) ± SD   | 0.24 ± 0.25              | 0.25 ± 0.21 | 0.750⁴ |
| Surgical procedure, eyes, n (%)       | PPV                      | 30 (43.5)   | 39 (56.5)   | 0.118³ |
|                                       | Buckling                 | 26 (61.9)   | 16 (38.1)   |         |
|                                       | PPV + buckling           | 2 (66.7)    | 1 (33.3)    |         |

Figure 2. Presence of outer retinal undulation (ORU) in each group on preoperative optical coherence tomography. ¹Chi-square test; ³Fisher’s exact test.
In the subgroup analysis of macula-off RRD with pars plana vitrectomy (n = 30), the mean ± SD age was 57.80 ± 9.94 years and the mean ± SD symptom duration was 12.77 ± 12.41 days. On preoperative OCT, ORU was detected in 20 of these eyes (66.7%). Twelve patients (40.0%) from this subgroup had disruption of the EZ integrity, and 18 patients (60.0%) had normal EZ integrity. The mean ± SD CRT was 0.26 ± 0.15 mm, and the mean ± SD baseline SRF height was 1.35 ± 0.91 mm (Table 4).

Only EZ integrity was significantly associated with postoperative BCV A (P = 0.014). Symptom duration, extent of detachment, ORU, CRT, and SRF had no significant correlation with postoperative BCV A (Table 4).

In previous studies, many preoperative factors have been reported to be significantly correlated with visual outcome for patients with RRD. These factors include patient age, preoperative visual acuity, duration of macular detachment, extent of retinal detachment, height of macular detachment, location and size of the retinal break, and proliferative vitreoretinopathy. After the advent of OCT, the integrity of the photoreceptor outer segment layer, external limiting membrane integrity, and height of retinal detachment at the central fovea were reported to be correlated with postoperative BCV A. In our study, EZ integrity was significantly associated with postoperative BCV A in patients with macula-off RRD with pars plana vitrectomy (P = 0.014).

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### Discussion

In previous studies, many preoperative factors have been reported to be significantly correlated with visual outcome for patients with RRD. These factors include patient age, preoperative visual acuity, duration of macular detachment, extent of retinal detachment, height of macular detachment, location and size of the retinal break, and proliferative vitreoretinopathy. After the advent of OCT, the integrity of the photoreceptor outer segment layer, external limiting membrane integrity, and height of retinal detachment at the central fovea were reported to be correlated with postoperative BCV A. In our study, EZ integrity was significantly associated with postoperative BCV A in patients with macula-off RRD with pars plana vitrectomy (P = 0.014).

ORU is another OCT finding in patients with RRD. Cho et al. found that the presence of ORU on preoperative OCT is predictive of poorer visual acuity both preoperatively and one month postoperatively. However, Kang et al., Hagimura et al., and Karacorlu et al. could not find a correlation between the presence of ORU on preoperative OCT and postoperative visual outcome. A study of experimental RRD in the owl monkey, the authors reported that edema could cause posterior protrusion and a wavy, shagreen-like appearance. ORU is presumed to come from the disparity of the amount of edema between the inner and outer retina in RRD. The disparity of edema is probably because retinal damage is more severe in the outer retina than the inner retina due to the mechanical牵涉.
to the physiologic dependency of the outer retina on the RPE and choroid; SRF is adjacent to the outer retina, and tangential expansion of the inner retina is possibly limited by the internal limiting membrane. Many studies have reported that poorer visual outcomes are associated with a longer duration of preoperative retinal detachment. Hassan et al. did not find an effect on postoperative visual acuity in the first 10 days of detachment, but did find a decrease in visual outcome 10 days after symptoms were reported. Enders P et al. reported poorer visual acuity after symptoms which lasted more than 30 days compared to a shorter symptom duration. Other studies have defined days 5 or 10 after the onset of symptoms as important thresholds for adverse visual outcomes. The current study found that the subacute group (10–30 days) had a higher incidence of ORU than did the other groups. Based on our results, ORU can be used to determine retinal detachment duration in patients with unknown duration of symptoms.

In the current study, ORU did not have a significant influence on visual outcome in patients with macula-off RRD. As mentioned above, in previous studies, there has been controversy about the relationship between ORU and visual outcome. This may be due to the different compositions of the enrolled patients in each study. For example, if many acute cases are included, ORU could be a prognostic indicator of bad vision. However, if many chronic cases are included, ORU could be a good prognostic factor for vision, or may have no significance if the distribution of case duration is even. In their study, Cho et al. included only acute and subacute cases (average of 11 days, range 1–30 days) and found that the presence of ORU on preoperative OCT was predictive of poorer visual acuity. However, Kang et al. (average 12.2, range 0–60 days) and Hagimura et al. (average 16 days, range 2–60 days) did not find a correlation between ORU and postoperative visual outcome. In their study, Kara-corlu M et al. primarily included only acute cases (average 6 days, range 3–13 days) and did not find a correlation between the presence of ORU and postoperative BCVA.

In the multivariate analysis, the presence of ORU was significantly associated with younger age and better preoperative BCVA. Due to the more rapid progression to atrophy in older patients, the group with ORU is thought to be younger and have better BCVA. The number of patients in the chronic group was relatively small; the absence of ORU had a better preoperative BCVA associated with the acute group (Table 2).

Table 4. Characteristics of patients with macula-off RRD with PPV and preoperative factors influencing BCVA 6 months postoperatively. RRD rhegmatogenous retinal detachment, PPV pars plana vitrectomy, OD right eye, OS left eye, BCVA best-corrected visual acuity, SRF subretinal fluid, EZ ellipsoid zone, ILM inner limiting membrane. 1 Pearson’s product moment correlation coefficient. 2 Student’s t-test. 3 Kruskal-Wallis test. 4 Paired sample t-test.
In conclusion, the presence of ORU on preoperative OCT may be associated with the duration of retinal detachment. Integrity of the EZ is useful to predict postoperative BCVA in macula-off RRD, and preoperative OCT images are a useful tool for the assessment of the duration and prognosis of RRD.

Data availability
The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Author contributions
Y.D.Y. conceived and designed the study. Y.C.K. initiated and supervised the project. Both authors wrote, reviewed and approved the manuscript, and equally contributed as first authors.

Competing interests
The authors declare no competing interests.

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