Predicting retinal sensitivity using optical coherence tomography parameters in central serous chorioretinopathy

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Abstract

Purpose To predict changes in retinal sensitivity using optical coherence tomography (OCT) in eyes with central serous chorioretinopathy (CSC).

Methods Twenty-three eyes in 23 patients with CSC were enrolled. Retinal sensitivity was measured twice using microp-erimetry in all the examined eyes. Spectral domain OCT measurements were simultaneously conducted. The relationship between retinal sensitivity and the thicknesses of (i) the retinal nerve fiber layer plus the ganglion cell layer (RNFL + GCL), (ii) the inner nuclear layer (INL), (iii) the outer nuclear layer (ONL), and (iv) the serous retinal detachment height (SRDH) were investigated in a point-wise manner. The associations between the change in retinal sensitivity and the OCT parameters at baseline were also investigated.

Results The mean age of the participants was 49.8 ± 10.7 years. The mean SRDH was significantly lower (p < 0.001), and the mean retinal sensitivity (p < 0.001) was significantly higher at the second examination, compared with the first; however, the logMAR visual acuity (VA) did not differ significantly between the two examinations (p = 0.063). The logMAR VA was associated with retinal sensitivity at both the first and second examinations (p < 0.001). The retinal sensitivity at the second examination was significantly correlated with the retinal sensitivity, RNFL + GCL, INL, ONL, and SRDH at the first examination and with the improvement in SRDH.

Conclusions Retinal sensitivity was associated with the retinal structure in eyes with CSC; these parameters could be useful for predicting the change in visual function prior to treatment.

Keywords Chronic central serous chorioretinopathy · Optical coherence tomography · Retinal sensitivity
Introduction

Central serous chorioretinopathy (CSC) is characterized by serous retinal detachment (SRD) in the macula accompanied by dysfunction of the retinal pigment epithelium (RPE) [1–3]. Although CSC generally resolves spontaneously, some patients complain of metamorphopsia and central scotoma even after the resolution of SRD; thus, evaluating not only visual acuity, but also retinal sensitivity and the visual field (VF) is important [4–6]. In particular, microperimetry (also known as fundus-related perimetry) is a useful tool for assessing central retinal sensitivity, as it can measure retinal sensitivity at an exact location through fundus image tracking [7–16]. Indeed, we previously reported that SRD height (SRDH) was closely correlated with the mean retinal sensitivity measured using MP-3 microperimetry (NIDEK, Co., Ltd., Japan) in CSC eyes with SRD [12]. However, this previous study had a cross-sectional design, and RS was analyzed as the mean of the whole field, rather than in a point-wise manner. Therefore, the present study enrolled CSC patients who exhibited an improvement in SRD during a follow-up period; we measured retinal sensitivity in eyes with CSC at two time points and investigated whether visual acuity and the mean retinal sensitivity were associated with the OCT parameters at each examination. Furthermore, we analyzed whether the final visual function could be predicted using the baseline OCT parameters.

Methods

This study was a retrospective observational case series and was approved by the Research Ethics Committee of the Graduate School of Medicine and Faculty of Medicine at The University of Tokyo. Written informed consent was given by all the participants. The study was conducted in accordance with the tenets of the Declaration of Helsinki.

Key messages

- Evaluating not only visual acuity, but also retinal sensitivity and the visual field is important because some patients with central serous chorioretinopathy complain of metamorphopsia and central scotoma even after the resolution of serous retinal detachment.
- The mean serous retinal detachment height was significantly associated with retinal sensitivity, but not with visual acuity.
- Retinal sensitivity is preferable to visual acuity for evaluating the disease activity of central serous chorioretinopathy.
- Retinal structure (for example, the retinal nerve fiber layer plus the ganglion cell layer, the inner nuclear layer, the outer nuclear layer, and the serous retinal detachment height) is related to visual function in patients with central serous chorioretinopathy and may predict patient outcome.

Subject

Twenty-three eyes in 23 patients (18 males, 5 females) with chronic CSC were enrolled in the current study. The mean age of the participants was 49.8 ± 10.7 years (mean ± standard deviation [SD]). All the patients underwent comprehensive ophthalmic examinations including refractive error, best-corrected visual acuity (BCVA), intraocular pressure, anterior segment examination, and fundus biomicroscopy with pupil dilation. Patients were diagnosed based on the results of OCT, fluorescein angiography (FA), and indocyanine green angiography (ICGA). Chronic CSC was defined as CSC lasting for more than 3 months. At the first examination, all the enrolled eyes exhibited subretinal fluid within the central 12 degrees; this fluid had decreased by the second examination. The exclusion criteria were as follows: (1) a history of other retinal disorders; (2) a history of laser photocoagulation or photodynamic therapy; and (3) the presence of high myopia (−6.0 diopters or greater).

VF measurement

VF measurements were performed using MP-3 microperimetry. The MP-3 microperimeter test is based on the 4–2 full threshold strategy using the Goldmann III stimulus size, as previously described [13, 17]. The 25 measurement points were located within 12 degrees of the macular area, as shown in Fig. 1. All the patients underwent VF measurements during both the first and second examinations.

OCT measurement

Spectral domain (SD) OCT images were obtained using the Spectralis OCT (Heidelberg Engineering, Germany). All OCT images consisted of line scans (horizontal and vertical B-scans), raster scans, and topographic mapping. The
raster scan was performed using 25 B-scans (768 A-scans per B-scan) in a 30×20-degree area. OCT measurements were performed for each eye at both the first and second examinations. Using the OCT images, we measured the total retinal thickness (RT), the retinal nerve fiber layer plus ganglion cell layer (RNFL + GCL), the inner nuclear layer (INL), the outer nuclear layer (ONL), and the SRDH at the 25 locations corresponding to the 25 MP-3 measurement points. RT was defined as the distance between the internal limiting membrane and the RPE. SRDH was defined as the distance between the ellipsoid zone (EZ) and the RPE. The data were collected independently by two examiners (SK and YA). If the measurements made by the two examiners differed by >5 µm, a panel discussion (SK, YA, and TI) was held to reach a consensus.

**Statistical analyses**

The logMAR VA and the mean retinal sensitivity were compared between the first and second examinations (VA1 and VA2, mRS1 and mRS2). The retinal sensitivities, thicknesses (RT, RNFL + GCL, INL, and ONL), and the SRDH were also

**Fig. 1** Representative eye with chronic CSC. Retinal sensitivity was measured at the first and second examinations (after the SRD had spontaneously resolved). A OCT parameters were measured at each examination. The yellow arrows indicate the retinal structures at each measurement point. B Retinal sensitivity was measured using MP-3 microperimetry. Retinal sensitivity was measured within 12° in the CSC. The yellow circle shows the central 12° at the macula. The 4 measurement points in the upper and lower images correspond with each other. RT: retinal thickness, RNFL + GCL: retinal nerve fiber layer + ganglion cell layer, INL: inner nuclear layer, ONL: outer nuclear layer, SRDH: serous retinal detachment height, OCT: optical coherence tomography, CSC: central serous chorioretinopathy

**Table 1** Subject demographics

| Variables                        | Mean ± SD [range] | First examination | Second examination | p value |
|----------------------------------|-------------------|-------------------|--------------------|---------|
| Age (years)                      | 49.8 ± 10.5 [26 to 78] |                   |                    |         |
| Sex, male/female                 | 18:5              |                   |                    |         |
| Eye, right/left                  | 10:13             |                   |                    |         |
| LogMAR VA                        |                   | 0.038 ± 0.17 [-0.18 to 0.52] | 0.012 ± 0.17 [-0.18 to 0.52] | 0.063   |
| mRS (dB)                         | 23.7 ± 3.7 [14.2 to 28.2] | 26.2 ± 2.2 [22.4 to 29.6] | <0.001             |
| mSRDH (µm)                       | 31.0 ± 30.7       | 6.6 ± 14.1        | <0.001             |
| Point-wise analysis              |                   |                   |                    |         |
| RS (dB)                          | 23.7 ± 5.7 [0 to 34] | 26.2 ± 3.8 [0 to 32] | <0.001             |
| RT (µm)                          | 343.1 ± 61.2 [151 to 531] | 309.1 ± 46.4 [32 to 445] | <0.001             |
| RNFL + GCL (µm)                  | 67.2 ± 22.2 [0 to 132] | 66.3 ± 22.6 [0 to 120] | 0.20               |
| INL (µm)                         | 39.0 ± 11.6 [0 to 78] | 37.6 ± 11.5 [0 to 68] | <0.001             |
| ONL (µm)                         | 44.6 ± 20.5 [3 to 125] | 49.7 ± 21.1 [4 to 120] | <0.001             |
| SRDH (µm)                        | 31.0 ± 52.1 [0 to 230] | 6.6 ± 21.4 [0 to 144] | <0.001             |

SD standard deviation. Log MAR VA logarithm of the minimal angle of resolution visual acuity, mRS mean retinal sensitivity, RT retinal thickness, RNFL retinal nerve fiber layer, GCL ganglion cell layer, INL inner nuclear layer, ONL outer nuclear layer, SRDH serous retinal detachment height
compared between the first and second examinations (RS1 and RS2, RT1 and RT2, RNFL+GCL1 and RNFL+GCL2, INL1 and INL2, ONL1 and ONL2, SRDH1 and SRDH2, respectively), at all 25 measurement points. Among 6 variables (age, RNFL + GCL1, INL1, ONL1, SRDH1, and the improvement in SRDH (dSRDH)), variables associated with retinal sensitivity at the second examination were identified using the corrected Akaike information criterion (AICc) model selection; the optimal model was selected from 2^6 patterns [18]. The AICc is a well-known statistical measure that allows optimal variables to be determined without an over-fit problem, unlike the coefficient of determination [19]. All statistical analyses were performed using the statistical programming language “R” (R version 3.1.3; The Foundation for Statistical Computing, Vienna, Austria).

### Results

The baseline patient characteristics are summarized in Table 1. The interval between the first and second examinations was 87.8 ± 85.6 days (range, 26–440 days). The mean SRDH values at the first and second examinations (mSRDH1 and mSRDH2, respectively) were 31.0 ± 30.7 μm and 6.6 ± 14.1 μm, respectively; this difference was significant (p < 0.001, Wilcoxon signed rank test). Among the 23 eyes, 13 eyes exhibited a complete resolution of SRD within the central 12° at the time of the second examination. In the remaining 10 eyes, the SRD improved but had not resolved completely at the time of the second examination. No significant difference between VA1 and VA2 was seen, although the p value approached significance (p = 0.063, Wilcoxon signed rank test). On the other hand, a significant improvement in mRS2, compared with mRS1, was observed (p < 0.001, Wilcoxon signed rank test). mRS1 was significantly correlated with VA1, and mRS2 was also associated with mSRDH2 (p = 0.043) was seen. However, mRS1 was significantly associated with mSRDH1 (p = 0.041), and mRS2 was also associated with mSRDH2 (p = 0.0069; Table 2).

In the pointwise analysis (25 × 23 measurement points), significant differences were observed between RT1 and RT2, between INL1 and INL2, between ONL1 and ONL2, and between SRDH1 and SRDH2 (p < 0.001, respectively), but not between RNFL + GCL1 and RNFL + GCL2 (p = 0.20, Wilcoxon signed rank test). Univariate analyses suggested that age, RS1, ONL1, SRDH1, and dSRDH were significantly correlated with RS2 (p = 0.031, p < 0.0001, p < 0.0001, and p = 0.00012, respectively), whereas RNFL + GCL1 and INL1 were not associated with SR2 (p = 0.31, p = 0.33, respectively, linear mixed model). However, in a multivariate analysis followed by AICc model selection, the optimal model for RS2 included age, RS1, RNFL + GCL1, INL1, ONL1, SRDH1, and dSRDH (Table 3), as follows.

\[ RS_2 = 22.9 - 0.53 \times \text{age} \quad (\text{standard error: SE}=0.026)+0.21 \times \text{RS1} \quad (SE=0.027)-0.0099 \times \text{RNFL+GCL1} \quad (SE=0.0054)+0.027 \times \text{INL1} \quad (SE=0.012)+0.021 \times \text{ONL1} \quad (SE=0.0070)-0.070 \times \text{SRDH1} \quad (SE=0.0066)-0.067 \times \text{dSRDH} \quad (SE=0.0072) \quad (\text{AICc}=2749.4).\]

### Table 2 OCT measurements at first and second examinations

| Variable | First examination | Second examination |
|----------|-------------------|--------------------|
|          | Correlation | p value | Correlation | p value |
| Age      | 0.413       | 0.050  | 0.305       | 0.157   |
| LogMAR VA |          |        |            |        |
| mRS      | -0.739     | <0.0001| -0.591     | 0.0030  |
| mSRDH    | 0.067      | 0.76  | 0.173      | 0.43    |

LogMAR VA: logarithm of the minimal angle of resolution visual acuity, mRS: mean retinal sensitivity, mSRDH: mean serous retinal detachment height.

### Table 3 AICc model selection for RS at the second examination

| Variable | Coefficient | SE | p value | Coefficient | SE |
|----------|-------------|----|---------|-------------|----|
| Age      | -0.094      | 0.041| 0.031   | -0.053      | 0.026 |
| RS1      | 0.295       | 0.026| <0.0001 | 0.21        | 0.027 |
| RNFL + GCL1 | 0.0093      | 0.0092| 0.31   | -0.0099     | 0.0064 |
| INL1     | 0.014       | 0.014| 0.33    | 0.027       | 0.012 |
| ONL1     | 0.050       | 0.0076| <0.0001| 0.021       | 0.0070 |
| SRDH1    | -0.028      | 0.0031| <0.0001| -0.070      | 0.0066 |
| dSRDH    | -0.014      | 0.0037| 0.00012| -0.067      | 0.0072 |

SE: standard error, AICc: corrected Akaike information criterion, RS: retinal sensitivity, RNFL: retinal nerve fiber layer, GCL: ganglion cell layer, INL: inner nuclear layer, ONL: outer nuclear layer, SRDH: serous retinal detachment height, dSRDH: the change of SRDH (SRDH2-SRDH1).

LogMAR VA: logarithm of the minimal angle of resolution visual acuity, mRS: mean retinal sensitivity, mSRDH: mean serous retinal detachment height.
Discussion

In the current study, MP-3 and OCT measurements were performed in patients with chronic CSC. The results showed that the mean SRD height was significantly associated with retinal sensitivity, but not with VA. We also found that the retinal sensitivity at the second examination was significantly correlated with the retinal sensitivity and retinal structural parameters (the thicknesses of RNFL + GCL, ONL, INL, and SRDH) at the first examination, suggesting that the baseline OCT parameters could be used to predict retinal sensitivity after the resolution of SRD in eyes with CSC.

In clinical settings, VA measurements are frequently used to evaluate visual function in patients with macular diseases, including CSC. However, we recently reported the benefit of using retinal sensitivity (visual field) in CSC eyes with SRD, since retinal sensitivity, but not log-MAR VA, was significantly associated with SRDH [12]. Similarly, the present study suggested no significant relationships between VA1 and mSRDH1 or between VA2 and mSRDH2; on the other hand, significant associations were seen between mRS1 and mSRDH1 and between mRS2 and mSRDH2.

In the point-wise analysis, RNFL + GCL1, ONL1, INL1, SRDH1, and dSRDH, in addition to RS1, were significantly associated with RS2. In other words, these variables were useful for predicting retinal sensitivity after the resolution of SRD in eyes with CSC. The optimal model for RS2 suggested that a younger age, a better retinal sensitivity at baseline, a thinner RNFL + GCL thickness, a thicker INL and ONL thickness, and a lower SRDH were correlated with better retinal sensitivity at the time of the second examination. Among the OCT parameters, ONL1 and INL1 were positively correlated with RS2, which was considered reasonable. On the other hand, RNFL + GCL1 and SRDH1 were negatively associated with RS2. This result is somewhat contradicting because the univariate analysis suggested that the RNFL + GCL thickness was positively correlated with RS2 (Table 3). Considering that the coefficient value of RNFL + GCL1 was much smaller than those for ONL1 and INL1, RNFL + GCL1 might be a negligible variable for RS2.

Several studies have indicated that the integrity of the EZ was correlated with visual function in patients with macular diseases. We also reported that the residual EZ index was correlated with visual acuity and retinal sensitivity in patients with resolved CSC [20]. In the present study, EZ disruption was not considered, as it can be difficult to identify the EZ line in detached retina. Instead, we measured the ONL thickness in conjunction with RNFL + GCL, INL, and SRDH during each examination; as a result, these parameters were found to be correlated with retinal sensitivity.

The present study had some limitations. First, this study had a retrospective design, and patients who had undergone treatments such as laser photocoagulation were excluded. Investigating the accuracy of OCT measurements to predict patient outcome after treatment would be interesting. Second, in the present study, fundus autofluorescence (AF) measurements were not taken into consideration. The short-wavelength AF signal is reportedly associated with retinal sensitivity in eyes with chronic CSC [21]. We also recently reported that AF measurements, especially near-infrared AF, are superior to OCT measurements (EZ disruption) for detecting the deterioration of retinal sensitivity in eyes with chronic CSC [22]. Further study is needed to investigate whether AF measurements enable a more accurate prediction of visual function.

In conclusion, retinal sensitivity is an additional measure of visual function that might reflect microstructural changes revealed by OCT measurements better than visual acuity and should be considered when monitoring patients with CSC. Measuring retinal sensitivity at baseline could be useful for predicting visual outcome in eyes with CSC.

Author contribution SK and TI were responsible for writing the protocol and report, conducting the search, screening potentially eligible studies, extracting and analyzing data, interpreting results, updating reference lists and creating the “Summary of findings” tables. HZ, RF, AS, YA, KK, MM, RO, and RA provided feedback on the report. All the authors have read and approved the manuscript.

Data availability None.

Declarations

Ethics approval and consent to participate This study was approved by the Research Ethics Committee of the Graduate School of Medicine and Faculty of Medicine at The University of Tokyo. The committee’s reference number is 2217.

Consent for publication Done.

Competing interests The authors declare no competing interests.

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