

Contrast visual acuity in patients with retinitis pigmentosa assessed by a contrast sensitivity tester

Maho Oishi, Hajime Nakamura, Masanori Hangai, Akio Oishi, Atsushi Otani, Nagahisa Yoshimura

Purpose: To assess contrast visual acuity (CVA) in patients with retinitis pigmentosa (RP) and compare the result with standard visual acuity (VA), retinal thickness, status of inner segment/outer segment junction, and central visual field. **Materials and Methods:** Thirty-nine eyes of 39 patients with RP and 39 eyes of 39 healthy individuals were studied. To see the difference in CVA between RP patients and normal controls, only subjects with standard VA of 1.0 (20/20) or better were included. This was a cross-sectional study. CVA in various light conditions was measured with CAT-2000 and was compared between patients and controls. CVA of patients was further analyzed for association with other parameters including foveal retinal thickness, outer nuclear layer thickness, the status of inner segment/outer segment junction measured with optical coherence tomography (OCT), and visual field mean deviation (MD) measured with Humphrey field analyzer 10-2 program. **Results:** CVA impairment was evident in RP patients compared to controls ($P < 0.01$, in all measurement conditions). Multivariate analysis showed association of logarithm of the minimum angle of resolution (logMAR) with CVAs in several conditions. None of the OCT measurements was associated with CVA. When patients were divided into three groups based on MD, the most advanced group (MD worse than or equal to -20 dB) showed impairment of mesopic CVA ($P < 0.05$, under mesopic condition of 100% without glare, with glare, and 25% without glare). **Conclusion:** CVA impairment was confirmed in RP patients, especially in advanced cases. CVA measured with CAT-2000 may be a useful tool for assessing foveal function in RP patients.

Key words: Contrast sensitivity, contrast visual acuity, retinitis pigmentosa

Retinitis pigmentosa (RP) is a hereditary disease that manifests with night blindness and visual field defects in the midperipheral area. Although the disease primarily affects rod photoreceptors, foveal cone photoreceptors also gradually degenerate over time. Since the disease causes peripheral visual field restriction, the remaining function of the central macula is critical for the quality of the patients' daily life.^[1]

Central visual function in RP patients can be assessed in several ways, including best-corrected visual acuity (BCVA), central visual field, focal macular electroretinogram (fmERG), and contrast visual acuity (CVA). While standard VA measurements assess central vision by evaluating the maximum VA in ideal conditions, the CVA may be able to evaluate more minute decreases in central visual function prior to visual acuity (VA) loss.^[2] In fact, previous studies have reported that CVA or contrast sensitivity (CS) measurements in RP patients are reduced even when their VA losses are mild.^[3-8]

Recently, a commercially available device for CVA measurement, Contrast Sensitivity Accurate Tester (CAT-2000, Neitz, Tokyo, Japan), has been developed. This instrument is highly practical for clinical use because the examination

method is a simple extension of the standard VA test, which is familiar to patients. The device retains the conventional test's advantage of an immediate check on the patient's accuracy.

In the present study, we measured CVA in patients with RP to assess whether CVA measurement can detect abnormalities of central vision in eyes with normal BCVA. In addition, as CVA is considered to reflect macular function,^[9] we analyzed the correlations between CVA and other clinical parameters to clarify the clinical significance of the CVA test in the management of patients with RP.

Materials and Methods

The study adhered to the tenets of the Declaration of Helsinki. This study was approved by the Institutional Review Board and Ethics Committee of our institution. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. Informed consent was obtained from each subject after explanation of the study protocol.

The subjects of the present study were patients with RP who visited our institution between March 2007 and November 2008. The patients underwent comprehensive ophthalmic examinations including BCVA, kinetic visual field test using Goldmann perimetry, funduscopy examination, and conventional electroretinogram (ERG) recorded according to the protocol recommended by the International Society for Clinical Electrophysiology of Vision (ISCEV) in 2004. RP was diagnosed by the presence of night blindness, characteristic fundus appearance, concentric, ring-shaped, or island scotoma, and non-recordable or subnormal conventional ERG. Those who had BCVA of 1.0 (20/20) or

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Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Shougoin Kawahara-cho, Sakyo-ku, Kyoto, Japan

Correspondence to: Atsushi Otani, Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Shougoin Kawahara-cho, Sakyo-ku, Kyoto, Japan. E-mail: otani@kuhp.kyoto-u.ac.jp

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better, measured with standard Landolt rings, were included in the study. Patients with myopia <-6 D, hyperopia $>+3$ D, cataract Emery grade 3 or more, glaucoma, or other retinal diseases (e.g. cystoid macular edema, macular hole, epiretinal membrane, diabetic retinopathy) were excluded from this study. Only the eye with better BCVA in each patient was used for statistical analysis. If BCVA was the same in both eyes, one was selected randomly.

The patients further underwent static visual field test [Swedish Interactive Threshold Algorithm (SITA) standard 10-2 program] using Humphrey field analyzer (Carl Zeiss Meditec, Tokyo, Japan), and optical coherence tomographic measurements with RTVue-100 (Optovue, Fremont, CA, USA). For the statistics, BCVA was measured with Landolt C and then converted to the logarithm of the minimum angle of resolution (logMAR) equivalent.

Contrast visual acuities, with and without a glare source, were measured during the same session using the Contrast Sensitivity Accurate Tester (CAT-2000, Neitz, Tokyo, Japan). LogMAR VA was measured in three contrast visual targets (100%, 25%, and 10%) under mesopic and photopic conditions. The mesopic and photopic CVAs were measured with chart lighting of 5 cd/mm² and 100 cd/mm², respectively. A glare light source of 200 lux was located at 20° around the visual axis. Following a 10-min period of dark adaptation, subjects were tested for in the following order: evening vision without glare, evening vision with glare, day vision without glare, and day vision with glare. The measurements were performed under physiologic pupillary reactions. Age-matched normal volunteers who met the inclusion and exclusion criteria, except for the presence of RP, were recruited as controls.

All patients had undergone at least two Humphrey field analyzer 10-2 program prior to enrollment in the present study and were familiar with the testing procedure. The most recent visual field data obtained within 6 months before or after CVA test were used for analysis. When the fixation loss exceeded 20% or false-positive or false-negative error rates were over 33%, the data were excluded from the study.

Foveal retinal thickness was measured and analyzed with an "MM5" grid-scanning mode of RTVue-100. The foveal retinal thickness was defined as length between the inner border of retinal pigment epithelium and the surface of inner limiting membrane. For the current study, the thickness of the foveal sector (1-mm diameter centered on the fovea) was analyzed. Photoreceptor integrity was evaluated with outer nuclear layer (ONL) thickness and an inner segment/outer segment junction (IS/OS) status. We measured the thickness of ONL on the fovea manually. The patients were divided into three groups according to the status of IS/OS within a diameter of 2 mm from the fovea as intact, disrupted, and absent as in a previous study [Fig. 1].^[10]

To investigate if there are differences between early and advanced cases, we further classified patients with visual field mean deviation (MD): better than -10 dB as mild ($n = 24$), worse than or equal to -10 and better than -20 dB as moderate ($n = 9$), and worse than or equal to -20 dB as severe ($n = 6$), and compared CVA among the three groups.

The statistical program SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive analyses

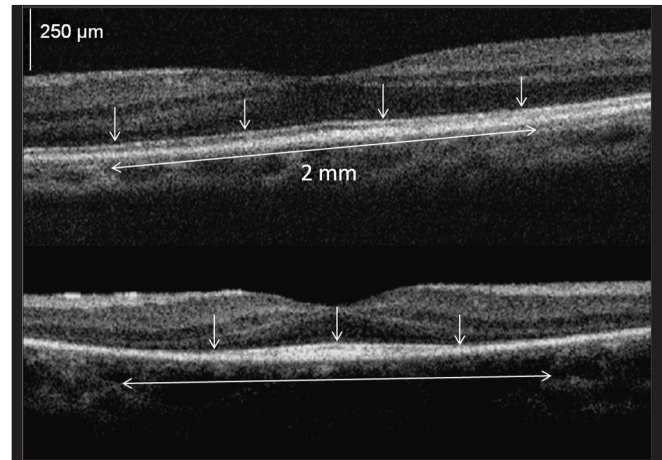


Figure 1: Optical coherence tomography images of patients with retinitis pigmentosa. We divided the subjects into three groups according to the status of inner segment (IS)/outer segment (OS) junction (arrow) within a diameter of 2 mm from the fovea as intact, disrupted, and absent. Upper: IS/OS is continuous throughout 2 mm and was classified as intact. Lower: IS/OS is not detectable at both ends in the 2 mm area and was classified as disrupted

are reported as mean \pm standard deviation unless otherwise specified. *t*-Test or Fischer's exact test was used to compare CVA between normal and RP patients as appropriate. The differences in CVAs among each MD group were tested with one-way analysis of variance (ANOVA) followed by Bonferroni test. The association between CVA and age, logMAR, visual field MD, foveal retinal thickness, ONL thickness, and the status of IS/OS was analyzed using stepwise multivariate analysis with CVA as the dependent variable. *P*-values less than 0.05 were considered statistically significant.

Results

The study sample consisted of 39 eyes of 39 patients, of whom 20 were men and 19 were women. The patients ranged in age from 15 to 65 years (38.4 ± 12.7 years). The control group consisted of 39 eyes of 9 men and 30 women. The controls ranged in age from 22 to 58 years (34.0 ± 9.80 years). There was no significant difference in age ($P = 0.133$), but the percentage of women was higher among controls ($P = 0.035$). All the participants had VA 1.0 (20/20) or better. Inheritance patterns of the RP among patients consisted of 4 autosomal dominant (10.3%), 4 autosomal recessive (10.3%), and 27 sporadic (69.2%). There was no patient with an X-linked inheritance pattern and the inheritance pattern was not identified for four patients due to the lack of detailed information collected during the interview (10.3%). Refractive error of patients and controls ranged from -5.3 to 0.5 D (-1.8 ± 2.0 D) and from -5.3 to 1.5 D (-1.9 ± 1.8 D), respectively ($P = 0.879$).

CVA in the patients and the controls

CVA of the controls and the patients was measured by 12 patterns. In general, CVA decreased as the intensity of the contrast setting decreased in both groups. CVAs of the patients were significantly worse than those of the controls in every contrast intensity in all vision modes: evening vision without and with glare, and day vision without and with glare [Fig. 2].

Next, we compared the effects of glare on the evening vision and the day vision in each group [Fig. 3]. In both groups, under evening vision, there was no difference between with and without glare in 100% contrast intensity, whereas glare caused CVA loss at the lower contrast intensities (25% and 10%) [Figs. 3a and b]. Under day vision, there was no difference in CVA between with and without glare in any contrast intensity [Figs. 3c and d]. Finally, we compared the CVA between day vision and evening vision and found significant differences in every contrast intensity in both groups [Figs. 3e and f].

CVA and other examinations

Visual field MD measured with Humphrey field analyzer ranged from -0.4 to -29.9 dB (-10.7 ± 8.4 dB). Foveal retinal thickness ranged from 213 to 327 μm (273.8 ± 27.2 μm). ONL thickness ranged from 62 to 133 μm (95.3 ± 15.9 μm). The status of IS/OS was classified as intact in 21 eyes and disrupted in 18 eyes; none of the eyes was classified as absent.

Because each of the factors was considered to be confounded,

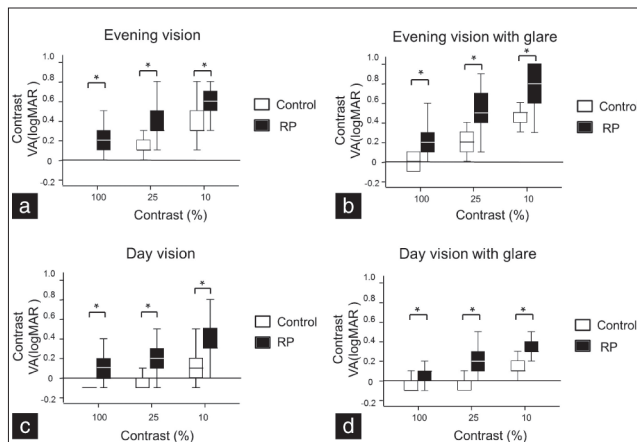


Figure 2: Comparisons of contrast VA between patients and controls: (a) evening vision (b) evening vision with glare (c) day vision (d) day vision with glare. There were statistically significant differences in all the comparisons (**P* < 0.001)

CVA values were evaluated with multivariate linear regression analysis. Among the investigated parameters, logMAR showed significant associations with CVA in several settings [Table 1]. None of the OCT measurements in this study was associated with CVA.

We further investigated the difference between early and

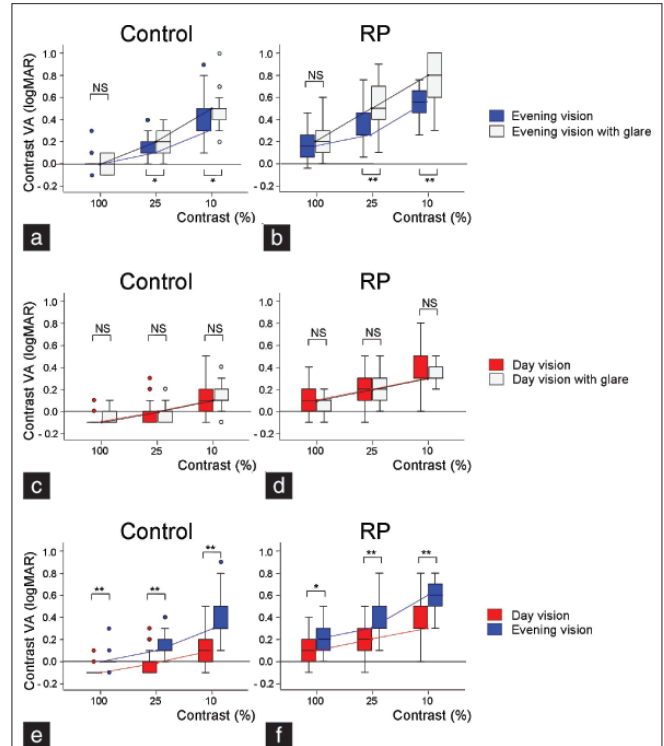


Figure 3: Comparisons between with and without glare: in controls (a, c) and in patients (b, d) Glare loading impaired the CVA in evening vision but not in day vision. Comparison between day vision and evening vision in RP patients and controls (e, f) The CVAs of the patients were significantly worse at all three contrasts (**P* < 0.01, ***P* < 0.001)

Table 1: Results of multivariate linear regression analysis

| | Adjusted R2 for the model | Contributing factors | Standardized regression coefficient | P-value |
|-------|---------------------------|----------------------|-------------------------------------|------------|
| E100 | 0.20 | logMAR, age | 0.44, 0.23 | 0.01, 0.03 |
| E25 | 0.20 | logMAR | 0.45 | 0.02 |
| E100G | 0.16 | logMAR | 0.40 | 0.03 |
| D100G | 0.13 | MD | -0.40 | 0.04 |

E: Evening, the number following the letter E indicates contrast intensity, D: Day, G: With glare, Measurement settings that did not show significant correlation were omitted

Table 2: Contrast visual acuity of three groups divided by visual field mean deviation score

| | E100 | E25 | E10 | E100G | E25G | E10G |
|--------------------------|--------------|--------------|-------------|--------------|-------------|-------------|
| Mild (<i>n</i> = 24) | 0.15 ± 0.13* | 0.34 ± 0.16 | 0.56 ± 0.17 | 0.20 ± 0.17 | 0.49 ± 0.20 | 0.80 ± 0.25 |
| Moderate (<i>n</i> = 9) | 0.12 ± 0.10* | 0.29 ± 0.15* | 0.57 ± 0.16 | 0.13 ± 0.11* | 0.46 ± 0.15 | 0.80 ± 0.15 |
| Severe (<i>n</i> = 6) | 0.30 ± 0.14 | 0.47 ± 0.19 | 0.67 ± 0.27 | 0.37 ± 0.18 | 0.57 ± 0.16 | 0.82 ± 0.16 |

E: Evening, 100 = 100% contrast, G: With glare, mild: visual field MD >-10 dB, moderate: visual field MD ≤-10 dB, >-20 dB, severe: visual field MD ≤-20 dB, **P* < 0.05 compared to severe group. No difference was noted between mild and moderate groups

advanced cases. Severely affected eyes showed significant impairment of CVA under evening vision of 100% without glare, with glare, and 25% without glare, compared to mildly and moderately affected eyes [Table 2]. There was no significant difference in CVA between eyes with mild and those with moderate disease.

Discussion

We showed that CAT-2000 enabled the detection of CVA loss of RP patients with normal VA. CVA loss was significantly more severe than that of the normal controls in various test conditions. Our results suggested that a decline in CVA exists before clinically apparent VA impairment and the measurement of CVA is useful to detect early damage of retinal functions in RP patients.

RP patients often complain of difficulty seeing in bright light, a phenomenon known as photoaversion.^[11] Although one study with a relatively small sample did not show a significant effect of light scatter on VA and contrast sensitivity,^[11] increased glare can have a pronounced effect on visual performance when there are peripheral glare sources.^[12-14] Control of glare and determination of the proper luminance for activities of daily living, such as reading and driving, is important for the patients' care.^[15,16] In the current study, our results showed that adding glare caused a significant decrease of CVA in evening vision. On the other hand, in day vision, the effect of a glare source on CVA was minimal. To soften the glare, prescribing absorptive lenses designated for the evening condition might be beneficial for some RP patients.

In the present study, with multivariate linear regression analysis, logMAR was associated with CVA in several conditions even though the participants had VA better than 1.0 (20/20). The result confirms that normal VA does not assure totally normal visual function. Although OCT-measured foveal retinal thickness, ONL thickness, and the status of IS/OS did not show significant correlation with CVA in the present study, histologic studies have reported a reduced number of foveal cone photoreceptors in RP donor eyes, even in those eyes with relatively good VA.^[17-20] Alternatively, CVA loss may reflect the subtle changes of the fovea, e.g. reduced responsiveness of cones, reduced cone photopigment optical density,^[21] or a reduction in the spatial density of cone photoreceptors in RP patients. Further investigation in detailed and specialized analysis of recent OCT images or scanning laser ophthalmoscopy with adaptive optics technology is warranted to investigate the photoreceptor changes underlying the CVA loss.

The classification with visual field MD, which has already been shown to be useful to monitor the rate of progression in RP,^[22] showed significant differences in CVA in some conditions. The result should be reasonable; the visual ability of RP patients, even if they have good VA, may be impaired in non-ideal light conditions as their central visual field deteriorates. CVA can be a quantitative measurement of practical VA in these patients with advanced central visual field loss but with good VA.

There are several limitations to the present study. The study sample consisted of relatively small number of patients and included only those with good VA to match with normal

eyes. The inclusion criteria might cause selection bias. Some sensitive examinations such as microperimetry, multifocal ERG, and autofluorescence were not assessed in the current study. In addition, there was a wide variability in the extent of contrast sensitivity impairment among patients, despite that all of them had 1.0 (20/20) or better standard VA. It is known that the inter-subject variability of contrast sensitivity is twice as greater than standard VA even in healthy subjects, which makes the interpretation of the result difficult or less sensitive.^[4] When evaluating the results, these limitations should be kept in mind.

In conclusion, CAT-2000 may be a useful device in assessing CVA in RP patients. The CVA enables detection of foveal functional loss in RP patients that can hardly be assessed with BCVA. Measurement with CAT-2000 may be useful in monitoring the progression of RP with good standard VA.

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