Vision-related quality of life and subscale items following intravitreal ranibizumab injections for central retinal vein occlusion

Fumiki Okamoto¹² · Tomoya Murakami¹ · Yoshimi Sugiura¹ · Shohei Morikawa¹ · Takahiro Hiraoka¹ · Tetsuro Oshika¹

Received: 9 March 2022 / Accepted: 25 August 2022 / Published online: 27 October 2022
© Japanese Ophthalmological Society 2022

Abstract

Purpose To evaluate the vision-related quality of life (VR-QOL) before and after intravitreal ranibizumab injections (IVR) for central retinal vein occlusion (CRVO) and to investigate subscale items of VR-QOL in detail.

Study design A multicenter, open-label, prospective and comparative study.

Methods Twenty-three patients with treatment naïve CRVO and 22 age-matched normal controls were included. VR-QOL was assessed by 25-Item Visual Function Questionnaire (VFQ-25) before and up to 12 months post-treatment. The VFQ-25 composite score and 12 subscales were compared between CRVO patients and normal controls.

Results The VFQ-25 composite scores of CRVO patients showed significant improvement throughout the treatment period compared with baseline. The VFQ-25 composite scores both before and after treatment for CRVO were significantly lower than in normal controls. The subscale items, including general health, general vision, near activities, social functioning, mental health, role difficulties, dependency, and peripheral vision in CRVO, were significantly lower than in the normal controls even after treatment.

Conclusion Vision-related QOL was low in patients with CRVO before treatment and improved with IVR. In spite of the improvements, several subscale items remained lower than in normal controls following treatment. Attention should be paid to the patients with CRVO and their decreased visual, social and psychological QOL.

Keywords Central retinal vein occlusion · Subscale · VFQ-25 composite scores · Vision-related quality of life

Introduction

Central retinal vein occlusion (CRVO) causes a significant loss of vision in the elderly [1], yet only limited treatments are available [2]. Since the introduction of anti-vascular endothelial growth factor (VEGF) therapy [3, 4], the visual prognosis of CRVO patients has improved, yet many patients still complain of visual impairment after anti-VEGF treatment. Poor baseline visual acuity, poor visual acuity after the initial injection, coexistence of internal carotid artery disease, and diabetic retinopathy are the factors that exacerbate visual outcomes in patients with CRVO who have undergone anti-VEGF treatment [5, 6]. Following investigations of retinal microstructure by optical coherence tomography (OCT), central retinal thickness and ellipsoid zone status at baseline [7–9], disorganization of inner retinal layers [9] and inner retinal layer reflectivity [10] are reported to be factors related to the visual prognosis of CRVO. Although the goal of the treatment of CRVO is to improve the quality of vision, including visual acuity, the ultimate aim is to improve the quality of life (QOL) of patients with CRVO.

Traditional measures of clinical outcomes, such as visual acuity, are increasingly being complemented by assessments of visual function of patients and perceived QOL. The National Eye Institute’s 25-Item Visual Function Questionnaire (VFQ-25) is a vision-related quality of life (VR-QOL) instrument designed to assess patients’ perception of their visual function and QOL [11]. VFQ-25 has been used to track outcomes of several retinal diseases, such as epiretinal
membrane (ERM) [12, 13], macular hole (MH) [14], retinal detachment (RD) [15–17], proliferative diabetic retinopathy (PDR) [18, 19], diabetic macular edema (DME) [19], and branch retinal vein occlusion (BRVO) [20, 21].

Deramo et al. assessed the VR-QOL of CRVO patients using the VFQ-25 and found that their VR-QOL was lower than normal controls and was associated with visual acuity in the better-seeing eye and the number of systemic medical conditions [22]. The CRUISE study [3] and the GALILEO/ COPERNICUS study [4, 23] used the VFQ-25 to assess VR-QOL of CRVO patients and observed improvement in VR-QOL after treatment. However, there are no reports on the relationship between VR-QOL and visual function in CRVO patients, or a detailed evaluation of changes in subscale after treatment. The purpose of the present study was to evaluate VR-QOL before and after treatment for CRVO in comparison with that of normal controls and investigate the subscale of VR-QOL in detail.

Methods

Study design

This was a multicenter, open-label, prospective study conducted in accordance with the Declaration of Helsinki and with the approval of the Institutional Review Board of the University of Tsukuba Hospital and Mito Kyodo General Hospital. Before inclusion, all patients were informed of the nature of the study, and their informed consent was obtained. Treatment naïve CRVO patients referred to the Tsukuba University Hospital or Mito Kyodo General Hospital were enrolled in this study. Patient inclusion criteria were: center-involving macular edema secondary to CRVO, central foveal thickness (CFT) > 250 μm, age over 18 years and under 85 years, and patients with paper-based informed consent. The exclusion criteria were: previous history of vitreoretinal surgery, previous history of ophthalmic disorders except mild refractive errors and mild cataracts, within 90 days of macular edema treatment involving sub-Tenon triamcinolone acetonide, intravitreal bevacizumab, intravitreal aflibercept, topical steroid, carbonic anhydrase inhibitors, within 90 days of vitreoretinal surgery, previous history of ophthalmic disorder, age over 85 years, and patients with paper-based informed consent.

VR-QOL was calculated using the VFQ-25. The VFQ-25 is a validated self-reported questionnaire that assesses disease-specific quality of life. It consists of 25 questions that enable patients to assess visual symptoms and difficulties in daily activities. The answers to each of the 25 questions are scored, with 100 indicating the highest possible function or the least subjective impairment. We calculated the VFQ-25 composite score as the mean of the scores for the 11 subscales and excluded the general health subscale. The VFQ-25 composite score was used as the primary endpoint. This sample provided 80% power to detect a difference between groups (Paired t-test, two-sided α level of 5%).

Study visits and assessments

Best-corrected visual acuity (BCVA) and retinal microstructure were assessed monthly starting at pre-treatment up to 12 months post-treatment. VR-QOL was examined pre-treatment and at 3, 6, and 12 months post-treatment. BCVA measured on the Landolt chart was converted to the logarithm of the minimum angle of resolution (logMAR) and used for subsequent analysis. The retinal microstructure was assessed using spectral-domain OCT (Cirrus high-definition OCT; Carl Zeiss). Five-line Raster Cross scans were performed using the Cirrus analysis software version 3.0., and scans with signal strength of more than 6/10 were considered appropriate. The CFT was evaluated based on the OCT images.

The VFQ-25 was used to assess VR-QOL in CRVO patients; it consists of 25 items that enable patients to assess visual symptoms and difficulties in daily activities. The answers to each of the 25 questions were sorted into 12 subscales, including general health, general vision, ocular pain, near activities, distance activities, social functioning, mental health, role difficulties, dependency, driving, color vision, and peripheral vision. The subscales were scored on a scale of 0–100 points, with 100 indicating the highest possible function or the least subjective impairment. We calculated the VFQ-25 composite score as the mean of the scores for the 11 subscales and excluded the general health subscale. The VFQ-25 used in this study was the Japanese version, modified to fit Japanese culture and lifestyle. The modified NEI VFQ-25 questionnaire has been assessed for reliability and validity and is proven to accurately measure VR-QOL in a Japanese population [24].

Intraocular injections

We treated the patients using three consecutive monthly intravitreal ranibizumab injections (IVR) (0.5 mg. Lucentis; Genetech), followed by pro re nata (3 + PRN). After three injections, the subjects were evaluated monthly and treated with intravitreal injections on PRN basis according to the protocol retreatment criteria. Re-administration criteria for PRN were as follows: CFT as assessed by OCT of ≥ 300 μm in the study eye, new cystoid retinal changes,
retinal bleeding or subretinal fluid on OCT, logMAR visual acuity decrease of $>0.1$ compared with values measured on the last visit.

**Statistical analysis**

The mean values and standard deviations were calculated. The Shapiro-Wilk test was used to test whether the data are normally distributed. A Mann-Whitney U test was performed to compare age, BCVA, and VR-QOL scores of CRVO patients and normal controls. The chi-square test was used to check for sex-difference between CRVO patients and normal controls. A Wilcoxon signed-rank test was used to compare baseline and each time point values for BCVA, CFT, and VFQ-25 composite score. Associations between VFQ-25 composite scores and 12 subscales and BCV A at baseline and 12 months post-treatment, the number of IVR injections and age were examined by the Spearman rank correlation test. All analyses were conducted using SPSS (version 27, IBC Corp). A P-value $<0.05$ was considered statistically significant.

**Results**

We included 23 patients with CRVO and 22 normal controls. Clinical characteristics of patients with CRVO and normal controls are mentioned in Table 1. All parameters were normally distributed except for the duration of disease and the number of IVR injections. There was no difference between the two groups in terms of age or gender. The VFQ-25 composite score of CRVO patients was significantly worse than that of normal controls. No patient with CRVO discontinued treatment during the study period. The mean number of injections during the treatment period was $5.6 \pm 2.0$ (range 3–8 injections). None of the patients had ocular treatment-emergent serious adverse events such as retinal detachment, endophthalmitis, vitreous hemorrhage, iris neovascularization, and glaucoma. None of the patients underwent cataract surgery or panretinal laser photocoagulation in the affected eye or in the other eye during the follow-up period.

**Functional and anatomic outcomes**

Figure 1 shows changes from baseline BCVA and CFT. There was a significant improvement in BCVA and CFT after 1 month of treatment.

**Changes in VR-QOL in patients with CRVO**

The VFQ-25 composite score improved significantly at all observation periods compared with the baseline score ($p<0.005$ in all) (Fig. 2). The VFQ-25 composite score in patients with CRVO at baseline was $62.6 \pm 16.9$, at 3 months it was $70.6 \pm 15.6$, at 6 months it was $72.2 \pm 15.8$, and at 12 months after treatment it was $74.3 \pm 14.6$; the mean increase from baseline VFQ-25 composite score was 8.0 points at 3 months, 9.6 points at 6 months, and 11.7 points at 12 months (Fig. 2).

**VFQ-25 composite score and subscales in patients with CRVO and controls**

Table 2 shows the VFQ-25 composite scores and 12 subscales in normal controls and CRVO patients before and after treatment. The average VFQ-25 composite score in normal controls was $89.4 \pm 7.4$, and VFQ-25 composite scores in CRVO patients before and after treatment were worse than those of normal controls ($p<0.001$ in both cases). The IVR treatment for 12 months significantly improved the subscale of general vision, ocular pain, near activities, distance activities, mental health, role difficulties, dependency, and composite scores. Several subscale items, including general health, general vision, near activities, social functioning, mental health, role difficulties, dependency, and peripheral vision in CRVO patients, were significantly lower than in the normal controls after treatment as well.

**Relationship between VR-QOL and visual acuity, number of IVR injections, and age in patients with CRVO**

Table 3 shows the relationship between the VFQ-25 composite scores and 12 subscales and BCVA in CRVO patients before and after treatment. At baseline, the VFQ-25 composite score and all subscales were not significantly associated with BCVA. The VFQ-25 composite score and subscale items of social functioning and dependency

---

**Table 1** Clinical characteristics of patients with central retinal vein occlusion (CRVO) and normal controls at baseline

| CRVO          | Normal controls | $p$ values |
|---------------|-----------------|-----------|
| Age (years)   | 72.2 ± 11.1     | 65.8 ± 10.4 | $p=0.07$ |
| Sex (men / women) | 13 / 10   | 10 / 12   | $p=0.66$ |
| BCVA of CRVO eye (logMAR) | 0.79 ± 0.56 | $-0.06 \pm 0.07$ | $p<0.001$ |
| BCVA of fellow eye (logMAR) | 0.01 ± 0.13 | $-0.07 \pm 0.06$ | $p<0.001$ |
| Central foveal thickness (μm) | 770 ± 319 | -   | -   |
| VFQ-25 composite score (point) | 62.6 ± 16.9 | 89.4 ± 7.4 | $p<0.001$ |
| Duration of disease (months) | 2.1 ± 2.5 | -   | -   |

Values are presented as the mean ± standard deviation

BCVA: best-corrected visual acuity, logMAR: logarithm of the minimum angle of resolution, VFQ-25: the 25-Item National Eye Institute Visual Function Questionnaire

* Significantly different from the normal controls (Mann-Whitney U test)
The VFQ-25 composite score improved from 62.6 points before treatment to 74.3 points 12 months after treatment in this study. In a study by Deramo et al. the VFQ-25 composite score in CRVO at baseline was 66.9 points [22], and in the COPERNICUS study it was 77.4 points [23]; the scores showed a significant correlation with BCVA 12 months after treatment. In addition, the VFQ-25 composite scores were not significantly associated with the number of IVR injections ($r = 0.025$, $p = 0.920$) and age ($r = 0.333$, $p = 0.177$).

**Discussion**

The VFQ-25 composite score improved from 62.6 points before treatment to 74.3 points 12 months after treatment in this study. In a study by Deramo et al. the VFQ-25 composite score in CRVO at baseline was 66.9 points [22], and in the COPERNICUS study it was 77.4 points [23]; the scores showed a significant correlation with BCVA 12 months after treatment. In addition, the VFQ-25 composite scores were not significantly associated with the number of IVR injections ($r = 0.025$, $p = 0.920$) and age ($r = 0.333$, $p = 0.177$).
Table 2  The National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25) composite score and 12 subscales of normal controls and patients with CRVO before and after intravitreal ranibizumab treatment

| VFQ-25 Questionnaire scale | Normal controls Baseline | Patients with CRVO Post-treatment | p-value compared with normal controls | p-value compared with baseline value | p-value compared with normal controls |
|---------------------------|--------------------------|-----------------------------------|--------------------------------------|-------------------------------------|--------------------------------------|
| General health            | 64.8 (16.7)              | 43.2 (11.4)                      | <0.001*                              | 0.206                               | 0.027*                               |
| General vision            | 78.2 (10.5)              | 46.4 (17.9)                      | <0.001*                              | 0.013†                              | <0.001*                               |
| Ocular pain               | 86.9 (13.1)              | 72.2 (22.8)                      | 0.029*                               | 0.008†                              | 1.000                                |
| Near activities           | 85.6 (12.4)              | 47.6 (26.4)                      | <0.001*                              | 0.033†                              | <0.001*                               |
| Distance activities       | 86.0 (13.0)              | 63.5 (21.5)                      | <0.001*                              | 0.036†                              | 0.062                                |
| Social functioning        | 94.0 (8.9)               | 72.6 (17.1)                      | <0.001*                              | 0.133                               | 0.002*                               |
| Mental health             | 95.5 (7.3)               | 52.8 (21.8)                      | <0.001*                              | 0.004†                              | <0.001*                               |
| Role difficulties         | 91.5 (10.5)              | 62.5 (22.8)                      | <0.001*                              | 0.004†                              | 0.048*                                |
| Dependency                | 98.5 (4.2)               | 68.6 (20.2)                      | <0.001*                              | 82.4 (16.9)                         | 0.004†                                |
| Driving                   | 85.6 (12.3)              | 61.5 (27.2)                      | 0.013*                               | 73.1 (25.8)                         | 0.057                                |
| Color vision              | 94.3 (10.7)              | 83.8 (14.7)                      | 0.013*                               | 85.9 (12.8)                         | 0.414                                |
| Peripheral vision         | 87.5 (18.5)              | 65.2 (20.5)                      | <0.001*                              | 69.4 (20.2)                         | 0.257                                |
| Composite score           | 89.4 (7.4)               | 62.6 (16.9)                      | <0.001*                              | 73.9 (14.7)                         | 0.002†                                |

Mean (standard deviation)

* Significantly different from the normal controls (Mann-Whitney U test)
† Significantly different from the postoperative values (Wilcoxon signed-ranks test)

Table 3  The relationship between the National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25) composite score and 12 subscales of normal controls and patients with CRVO before and after intravitreal ranibizumab treatment

| VFQ-25 Questionnaire scale | VFQ-25 vs. BCVA at baseline | VFQ-25 vs. BCVA at 12-month | BCVA at 12-month post-treatment |
|---------------------------|----------------------------|----------------------------|---------------------------------|
|                           | r                          | p                          | r                              | p                              |
| General health            | 0.243                      | 0.276                      | 0.013                          | 0.603                          |
| General vision            | 0.018                      | 0.938                      | 0.025                          | 0.089                          |
| Ocular pain               | -0.102                     | 0.652                      | 0.050                          | 0.850                          |
| Near activities           | -0.140                     | 0.545                      | 0.340                          | 0.182                          |
| Distance activities       | -0.230                     | 0.317                      | 0.409                          | 0.103                          |
| Social functioning        | -0.026                     | 0.912                      | 0.577                          | 0.015*                         |
| Mental health             | 0.036                      | 0.873                      | 0.424                          | 0.090                          |
| Role difficulties         | -0.207                     | 0.356                      | 0.453                          | 0.068                          |
| Dependency                | -0.389                     | 0.073                      | 0.543                          | 0.024*                         |
| Driving                   | -0.061                     | 0.829                      | 0.440                          | 0.176                          |
| Color vision              | -0.427                     | 0.060                      | 0.389                          | 0.152                          |
| Peripheral vision         | -0.363                     | 0.115                      | 0.330                          | 0.196                          |
| Composite score           | -0.184                     | 0.412                      | -0.554                         | 0.021*                         |

BCVA: best-corrected visual acuity

* Significantly correlation between two parameters (Spearman rank correlation test)

observed in our study were lower than those of the COPERNICUS study.

In this study the mean increase from baseline VFQ-25 composite score was 9.5 points after 6 months, and 11.7 points after 12 months of treatment. In the GALILEO study the mean increase from the baseline VFQ-25 composite score after 6 months of treatment was 7.1, points [4], in the COPERNICUS it was 7.2 points [23], and in the CRUISE study it was 7.1 points [3, and after 12 months these scores were 7.8, 7.5, and 7.1 points respectively. In our study, the mean number of injections for 12 months was 5.6, lower than 9.8 in the CRUISE study [3], and 11.8 in the GALILEO study [4]. Despite these results, there was a greater improvement in the VFQ-25 composite score in the present study than in other studies, suggesting that 3 + PRN is acceptable as a standard treatment for CRVO in terms of QOL.

The VR-QOL has been investigated in patients with various retinal diseases, including ERM [12, 13], MH [14], RD [15–17], PDR [18, 19], DME [19], and BRVO [20, 21]. The mean increase from baseline VFQ-25 composite score were 11.7 points in ERM [13], 6.9 points in MH [14], 10.8 points in PDR [19], 6.0 points in DME [19], and 9.0–9.4 points in BRVO [21, 25]. Despite differences in the observation periods and inclusion criteria, the improvement in the VFQ-25 composite score of patients with CRVO was nearly similar to that of patients with other retinal diseases after treatment, suggesting that anti-VEGF treatment in patients with CRVO has clinical significance.

The IVR treatment for CRVO improved BCVA and CFT immediately after treatment and was maintained throughout the following 12 months. In the present study, the improvement in BCVA at 12 months was 0.2 logMAR (10 letters). In the CRUISE study BCVA at 12 months after anti-VEGF treatment was 13.9 and in the GALILEO study [4], it was 16.9 letters from baseline. The reason for less improvement in BCVA in our study compared to that in other studies may be the inclusion criteria. As mentioned earlier, CRVO patients
in the CRUISE and GALILEO studies had a BCVA of 20/40 to 20/320 [3, 4], whereas, in the present study, the range of BCVA of the patients at baseline was 20/20 to 20/2000. When CRVO patients were divided into the good VA group (baseline BCVA < 1 logMAR, 12 cases) and the poor VA group (baseline BCVA ≥ 1 logMAR, 11 cases), the improvement in BCVA at 12 months in the good VA group was 0.89 logMAR (18 letters) and in the poor VA group was 0.37 logMAR (8 letters). There was a significant difference between the two groups (p < 0.0001, unpaired t-test). The improvement in BCVA was lower than in the abovementioned studies because our study included patients with extremely poor vision and patients with good vision.

We observed that the baseline VFQ-25 composite score was not associated with BCVA. Consistently, Deramo VA et al. also report that the VR-QOL of pre-treatment CRVO patients was not associated with visual acuity [22]. Visual acuity and VR-QOL are related in common eye diseases [26]; however, the relationship between VR-QOL and visual functions except for visual acuity has been indicated in many retinal diseases. The VR-QOL in ERM [13, 19] and MH [14] was associated with metamorphopsia and not visual acuity. In PDR [18, 19], DME [19], after RD [15], and vitreous floaters [27], contrast sensitivity affected the VR-QOL. Moreover, stereopsis was associated with VR-QOL after RD surgery [17]. Visual dysfunctions such as metamorphopsia [28] and aniseikonia [29] are reported in CRVO patients; hence, visual function factors other than visual acuity may be involved in the deterioration of VR-QOL. On the other hand, the post-treatment VFQ-25 composite score showed a significant correlation with post-treatment BCVA. This discrepancy cannot be explained. No significant correlation was found between the post-treatment BCVA and age (r = 0.312, p = 0.223), duration of disease (r = 0.283, p = 0.272), the number of IVR injections (r = 0.343, p = 0.178).

In the present study, IVR treatment for CRVO patients significantly improved subscale items of general vision, ocular pain, near activities, distance activities, mental health, role difficulties, and dependency. At baseline, all subscale items were lower in patients with CRVO than in normal controls. Even after treatment, subscale items, including general health, general vision, near activities, social functioning, mental health, role difficulties, dependency, and peripheral vision in CRVO, were significantly lower than those in the normal controls. In addition, the VFQ-25 composite score and subscale items social functioning, and dependency after treatment showed a significant correlation with BCVA. Most subscale items in pre-treatment in patients with CRVO were lower than in normal controls, consistent with previous reports [22]. Although anti-VEGF treatment for CRVO improved many subscale items, those related to the quality of vision (general vision, near activities, and peripheral vision) and psychosocial functioning (social functioning, mental health, role difficulties, and dependency) were more impaired than those in normal controls even after treatment. Attention should be paid to the patients with CRVO and their decreased visual, social and psychological QOL.

The limitations of this study were a small sample size, short follow-up duration and the lack of classification of patients into ischaemic or non-ischaemic CRVO. We evaluated the patients for 12 months after treatment. In the COPERNICUS study, BCVA in CRVO patients treated with intravitreal aflibercept injection at 24 months was 3.2 letters less than that at 12 months [30]. Since CRVO is a retinal disease with a poor prognosis, it is important to monitor visual functions and QOL in the long term. In our study, we could not classify CRVO into ischemic or non-ischemic types because we did not perform fluorescein angiography or OCT-angiography. Changes in VR-QOL following treatment are believed to differ between ischemic and non-ischemic CRVO. In addition, CRVO patients are relatively more likely to have diabetes, hypertension, and stroke. Although this study excludes patients with severe diabetes, hypertension and stroke, it includes patients with mild diabetes and hypertension. It is difficult to accurately investigate QOL based on CRVO alone, because patients with mild DM or HT may have poorer QOL than healthy subjects even if they do not have CRVO. Future studies with larger sample size, longer follow-up duration and classification of CRVO will further improve our understanding of VR-QOL in patients with CRVO.

Acknowledgements This study was supported by Novartis Pharma K.K., Tokyo, Japan. No additional external funding was received for this study. The sponsor had no role in the design or conduct of this research. Previous Posting This manuscript was posted as a preprint on ResearchSquare on July 20, 2021. doi: https://doi.org/10.21203/rs.3.rs-724586/v1.

Declarations
Conflict of interest F. Okamoto, None; T. Murakami, None; Y. Sugiyura, None; S. Morikawa, None; T. Hiraoka, None; T. Oshika, None.

References
1. Klein R, Wang Q, Klein BE, Moss SE, Meuer SM. The relationship of age-related maculopathy, cataract, and glaucoma to visual acuity. Invest Ophthalmol Vis Sci. 1995;36:182–91.
2. Mohamed Q, McIntosh RL, Saw SM, Wong TY. Interventions for central retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2007;114:507–19, 524.
3. Brown DM, Campochiaro PA, Bhistikul RB, Ho AC, Gray S, Saroj N, et al. Sustained benefits from ranibizumab for macular edema following central retinal vein occlusion: twelve-month outcomes of a phase III study. Ophthalmology. 2011;118:2041–9.
4. Korobelnik JF, Holz FG, Roider J, Ogura Y, Simader C, Schmidt-Erfurth U, et al. Intravitreal aflibercept injection for macular edema resulting from central retinal vein occlusion: one-year results of the Phase 3 GALILEO study. Ophthalmology. 2014;121:202–8.

5. Nagasato D, Muraoka Y, Osaka R, Iida-Miya Y, Mitamura Y, Tabuchi H, et al. Factors associated with extremely poor visual outcomes in patients with central retinal vein occlusion. Sci Rep. 2020;10:19667.

6. Etheridge T, Blodi B, Oden N, Van Veldhuisen P, Scott IU, Ip MS, et al. Spectral domain optical coherence tomography predictors of visual acuity in the study of Comparative treatments for REtinal vein Occlusion 2 (SCORE2). Ophthalmol Retina. 2021;5:991–8.

7. Tang F, Qin X, Lu J, Song P, Li M, Ma X. Optical coherence tomography predictors of short-term visual acuity in eyes with macular edema secondary to retinal vein occlusion treated with intravitreal conbercept. Retina. 2020;40:773–85.

8. Ciulla TA, Kapik B, Grewal DS, Ip MS. Visual acuity in retinal vein occlusion, diabetic, and uveitic macular edema: central subfield thickness and ellipsoid zone analysis. Ophthalmol Retina. 2021;5:633–47.

9. Chan EW, Eldeen M, Sun V, Thomas D, Omar A, Kapusta MA, et al. Disorganization of retinal inner layers and ellipsoid zone disruption predict visual outcomes in central retinal vein occlusion. Ophthalmol Retina. 2019;3:83–92.

10. Greenlee TE, Cutler NE, Mehta N, Hom GL, Wai K, Conti FF, et al. Inner retinal layer reflectivity as predictor of retinal vein occlusion visual acuity outcomes. Ophthalmol Retina. 2020;4:3434.

11. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD. Development of the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol. 2001;119:1050–8.

12. Khanna RK, Pichard T, Pasco J, Dorvault M, Cook AR, Pisella PJ, et al. Monocular and binocular visual parameters associated to vision-related quality of life in patients with epiretinal membrane: a prospective cohort. Graefes Arch Clin Exp Ophthalmol. 2021;259:1723–30.

13. Okamoto F, Okamoto Y, Hiraoka T, Oshika T. Effect of vitrectomy for epiretinal membrane on visual function and vision-related quality of life. Am J Ophthalmol. 2009;147:869 – 74, 874.e1.

14. Fukuda S, Okamoto F, Yuasa M, Kunikata T, Okamoto Y, Hiraoka T, et al. Vision-related quality of life and visual function in patients undergoing vitrectomy, gas tamponade and cataract surgery for macular hole. Br J Ophthalmol. 2009;93:1595–9.

15. Okamoto F, Okamoto Y, Hiraoka T, Oshika T. Vision-related quality of life and visual function after retinal detachment surgery. Am J Ophthalmol. 2008;146:85–90.

16. Ng H, Vermeer KA, van Meurs JC, La Heij EC. Visual acuity inadequately reflects vision-related quality of life in patients after macula-off retinal detachment surgery. Invest Ophthalmol Vis Sci. 2020;61:34.

17. Potic J, Bergin C, Giacuzzo C, Konstantinis L, Daruich A, Wolfensberger TJ. Application of modified NEI VFQ-25 after retinal detachment to vision-related quality of life. Retina. 2021;41:653–60.

18. Okamoto F, Okamoto Y, Fukuda S, Hiraoka T, Oshika T. Vision-related quality of life and visual function following vitrectomy for proliferative diabetic retinopathy. Am J Ophthalmol. 2008;145:1031–6.

19. Okamoto F, Okamoto Y, Fukuda S, Hiraoka T, Oshika T. Vision-related quality of life and visual function after vitrectomy for various vitreoretinal disorders. Invest Ophthalmol Vis Sci. 2010;51:744–51.

20. Campochiaro PA, Heier JS, Feiner L, Gray S, Saroj N, Rundle AC, et al. Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study. Ophthalmology. 2010;117:1102-12.e1.

21. Clark WL, Boyer DS, Heier JS, Brown DM, Haller JA, Vitti R, et al. Intravitreal aflibercept for macular edema following branch retinal vein occlusion: 52-week results of the VIBRANT study. Ophthalmology. 2016;123:330–6.

22. Deramo VA, Cox TA, Syed AB, Lee PP, Fekrat S. Vision-related quality of life in people with central retinal vein occlusion using the 25-item National Eye Institute Visual Function Questionnaire. Arch Ophthalmol. 2003;121:1297–302.

23. Brown DM, Heier JS, Clark WL, Boyer DS, Vitti R, Berliner AJ, et al. Intravitreal aflibercept injection for macular edema secondary to central retinal vein occlusion: 1-year results from the phase 3 COPERNICUS study. Am J Ophthalmol. 2013;155:429 – 37.e7.

24. Suzukamo Y, Oshika T, Yuzawa M, Tokuda Y, Tomidokoro A, Oki K, et al. Psychometric properties of the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25), Japanese version. Health Qual Life Outcomes. 2005;3:65. doi:https://doi.org/10.1186/1477-7525-3-65.

25. Brown DM, Campochiaro PA, Bhisitkul RB, Ho AC, Gray S, Saroj N, et al. Sustained benefits from ranibizumab for macular edema following branch retinal vein occlusion: 12-month outcomes of a phase III study. Ophthalmol. 2011;118:1594–602.

26. Ishii K, Kabata T, Oshika T. The impact of cataract surgery on cognitive impairment and depressive mental status in elderly patients. Am J Ophthalmol. 2008;146:404–9.

27. Mamou J, Wa CA, Yee KM, Silverman RH, Ketterling JA, Sadun AA, et al. Ultrasound-based quantification of vitreous floats correlates with contrast sensitivity and quality of life. Invest Ophthalmol Vis Sci. 2015;56:1611–7.

28. Manabe K, Osaka R, Nakano Y, Takasago Y, Fujita T, Shigami C, et al. Metamorphopsia associated with central retinal vein occlusion. PLoS ONE. 2017;12:e0186737. doi:https://doi.org/10.1371/journal.pone.0186737.

29. Okamoto F, Sugura Y, Okamoto Y, Hiraoka T, Oshika T. Anisokonia in various retinal disorders. Graefes Arch Clin Exp Ophthalmol. 2017;255:1063–71.

30. Heier JS, Clark WL, Boyer DS, Brown DM, Vitti R, Berliner AJ, et al. Intravitreal aflibercept injection for macular edema due to central retinal vein occlusion: two-year results from the COPERNICUS study. Ophthalmology. 2014;121:1414-20.e1.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.