—Review—

Changes in Metamorphopsia in Patients Undergoing Treatment for Vitreoretinal Disorders

Fumiki Okamoto

Department of Ophthalmology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan

Purpose: To quantify and compare the severity of metamorphopsia in patients undergoing vitrectomy for vitreoretinal disorders.

Methods: Data were collected evaluated from 319 patients with vitreoretinal disorders, including epiretinal membrane (ERM), macular hole (MH), cystoid macular edema with branch retinal vein occlusion (BRVO-CME), CME with central retinal vein occlusion (CRVO), diabetic macular edema (DME), macula-off rhegmatogenous retinal detachment (M-off RD), and macula-on RD (M-on RD). Metamorphopsia was recorded with the M-CHARTS preoperatively and at 3 and 6 months postoperatively.

Results: Preoperative and 6-month postoperative metamorphopsia scores were 0.69 ± 0.50 and 0.50 ± 0.52, respectively. Before surgery, 94% of patients presented with metamorphopsia (score ≥0.2). Preoperative metamorphopsia scores were significantly correlated with postoperative metamorphopsia scores ($r = 0.378$, $p < 0.0001$). Preoperative metamorphopsia score was significantly higher for ERM (0.89) than for DME (0.51). Vitrectomy significantly improved metamorphopsia in ERM and MH but not in the other disorders. In contrast, treatment improved visual acuity for all disorders except CRVO-CME and M-on RD.

Conclusion: This quantitative study indicated that metamorphopsia is present in most patients undergoing surgery for vitreoretinal diseases and is most severe in ERM. In these patients, vitrectomy improved visual acuity but not metamorphopsia. (J Nippon Med Sch 2024; 91: 28–36)

Key words: metamorphopsia, vitrectomy, retinal disorders

Introduction

In ophthalmology, visual acuity has been considered central among the traditional clinical outcome measures for vitreoretinal disorders, because patients tended to have poor visual function outcomes. However, recent advances in surgical techniques for vitreoretinal disorders have improved visual acuity. Nevertheless, even after successful surgery and improvement of visual acuity, postoperative quality of vision may be unsatisfactory in some cases.

Metamorphopsia is one of the most common symptoms in macular disorders. Prior studies investigated metamorphopsia in patients with epiretinal membrane (ERM)[1–11], macular hole (MH)[10–18], cystoid macular edema (CME)[19,20], chronic central serous chorioretinopathy[21], and rhegmatogenous retinal detachment (RD)[22–24]. In addition, metamorphopsia was significantly associated with vision-related quality of life as evaluated with the 25-item National Eye Institute Visual Function Questionnaire after surgery for ERM and MH[10–12]. Therefore, assessing not only visual acuity but also metamorphopsia is of clinical importance.

Although the Amsler grid[25] has been widely used to detect and evaluate metamorphopsia in patients with macular diseases, it is difficult to use it to quantify metamorphopsia severity. In contrast, M-CHARTS is an instrument that straightforwardly quantitatively evaluates the degree of metamorphopsia associated with macular diseases; patients only need to confirm whether a line is distorted or not[8,9]. M-CHARTS has been used to track outcomes of many macular diseases[3–13,16,19,22–24]. Prior stud-

Correspondence to Fumiki Okamoto, MD, Department of Ophthalmology, Graduate School of Medicine, Nippon Medical School, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: f-okamoto@nms.ac.jp
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ies reported the effects of vitrectomy on metamorphopsia in patients with ERM[4,5,7,10,11], MH[12,13,15–18], diabetic macular edema (DME)[19], and RD[22–24]. However, no study has compared metamorphopsia and its postoperative changes in patients with vitreoretinal disorders. The purpose of this study was to compare metamorphopsia in vitreoretinal disorders and evaluate the relationship between metamorphopsia and visual function for each disorder.

Materials and Methods

In total, 319 eyes of 319 patients (189 men and 130 women) who were diagnosed as having and treated for vitreoretinal disorders at Tsukuba University Hospital were analyzed. Their age was 60.4 ± 11.9 years (mean ± standard deviation). The patients comprised 63 patients with epiretinal membrane (ERM), 44 with macular hole (MH), 29 with cystoid macular edema with branch retinal vein occlusion (BRVO-CME), 10 with CME with central retinal vein occlusion (CRVO-CME), 17 with DME, 79 with macula-off rhegmatogenous retinal detachment (M-off RD), and 77 with macula-on RD (M-on RD), all of whom underwent pars plana vitrectomy. This research was conducted in accordance with the principles of the Declaration of Helsinki, and written informed consent was obtained from all suitable participants. This study was approved by the Institutional Review Board of the Tsukuba University Hospital (approval number: H27-70). Exclusion criteria included a previous history of vitreoretinal surgery or ocular disorders, except mild refractive errors and mild cataract. Patients with a logarithm of minimum angle of resolution best-corrected visual acuity (logMAR BCVA) of >0.7 were also excluded because the severity of metamorphopsia cannot be measured correctly in patients with a poor BCVA[8]. In patients with RD, preoperative metamorphopsia was not evaluated because of the rapid onset and severity of disturbance of visual function.

The examinations included measurements of BCVA, metamorphopsia severity, fundus examinations with indirect ophthalmoscopy, and spectral-domain optical coherence tomography (OCT) scanning (Cirrus high-definition OCT; Carl Zeiss, Dublin, CA, USA) of the retinal microstructure. All ophthalmological examinations were performed before, and at 3 and 6 months after, surgery.

Metamorphopsia severity was evaluated using M-CHARTS (Inami Co., Tokyo, Japan)[8,9]. Both the vertical and horizontal meridians were assessed, and mean values were used in the data analyses. Metamorphopsia scores were 0 in all normal eyes, and intraindividual variation of metamorphopsia scores in all ERM subjects was within 1 line (±0.1 score)[8]. Therefore, the presence of metamorphopsia was defined as a mean metamorphopsia score (metamorphopsia score) of ≥ 0.2. In addition, metamorphopsia severity was classified as mild (0.5 > metamorphopsia score ≥ 0.2), moderate (1.0 > metamorphopsia score ≥ 0.5), or severe (metamorphopsia score ≥ 1.0). The examiners administrating the M-CHARTS tests were experienced orthoptists and were masked to the fundus findings of the patients.

The indications for vitrectomy in ERM, MH, BRVO, CRVO and RD were in accordance with a previous report[11]. All surgeries were performed by 3 vitreoretinal surgeons (F.O., T.H., Y.S.) under sub-Tenon local anesthesia. In patients with ERM, the membrane was removed from the macula with intraocular forceps. After the ERM was peeled, 0.1-0.2 mL of 0.025% brilliant blue G solution was applied to the macular area. Then, the remaining internal limiting membrane was completely peeled[11].

Mean scores and standard deviations were calculated for age and visual functions in patients with vitreoretinal disorders. Associations between preoperative and postoperative parameters of visual function were examined by using Pearson's correlation coefficients. The Tukey-Kramer test was used to compare age and metamorphopsia scores among the vitreoretinal disorders. The obtained data were analyzed with repeated-measures analysis of variance (ANOVA) to assess the time course of changes in BCVA and metamorphopsia scores. If significant differences were observed, Fisher's Protected Least Significant Difference (Fisher's PLSD) test was used to find time points that significantly differed from the baseline value. A P value of <0.05 was considered to indicate statistical significance. The analyses were carried out using StatView (version 5.0, SAS Inc., Cary, NC, USA)[11].

Results

Table 1 summarizes the characteristics of patients with vitreoretinal disorders. RD patients were significantly younger than those in the other groups ($p < 0.05$).

Preoperatively, the mean metamorphopsia score for all patients was 0.69 ± 0.50, and 154 of 163 patients (94%) had metamorphopsia. The proportions of severe, moderate, mild, and no metamorphopsia were 25%, 49%, 20%, and 6%, respectively. **Figure 1** shows the preoperative distribution of metamorphopsia severity for each disorder. Over 90% of patients had metamorphopsia in the ERM, MH, and BRVO-CME groups. At 6 months postoperatively, the mean metamorphopsia score for all patients

Table 1 Characteristics of Patients with Vitreoretinal Disorders

	ERM	MH	BRVO-CME	CRVO-CME	DME	M-off RD	M-on RD
Number of eyes	63	44	29	10	17	79	77
Men/women	30/33	24/20	19/10	4/6	12/5	51/28	49/28
Age (years)	66.1 ± 9.4	65.8 ± 6.9	65.4 ± 9.6	65.6 ± 11.1	66.6 ± 7.0	56.3 ± 12.0*	52.8 ± 12.0*

ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
Values are presented as the mean ± standard deviation
* Significant difference from other groups ($p < 0.05$ Tukey-Kramer test)

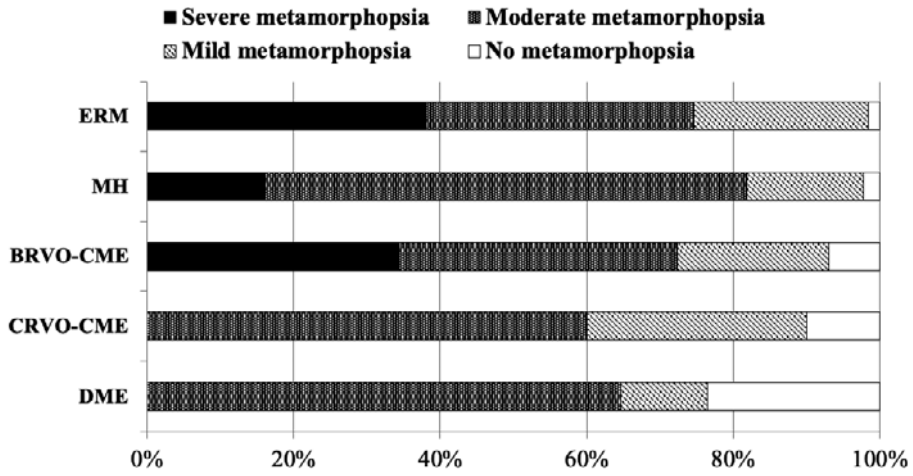

Fig. 1 Preoperative distribution of metamorphopsia severity in patients with vitreoretinal disorders.
Severe: metamorphopsia score ≥ 1.0
Moderate: 1.0 > metamorphopsia score ≥ 0.5
Mild: 0.5 > metamorphopsia score ≥ 0.2
None: 0.2 > metamorphopsia score ≥ 0
ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema.

was 0.50 ± 0.52. The proportions of severe, moderate, mild, and no metamorphopsia were 18%, 26%, 21%, and 36%, respectively. Subgroup analysis of the severity of metamorphopsia revealed that over 70% of patients had metamorphopsia for all disorders except M-on RD. Over 80% of M-on RD patients had no metamorphopsia (**Fig. 2**).

Figure 3 shows preoperative and postoperative metamorphopsia scores for each disorder. Preoperative metamorphopsia scores were significantly higher for ERM than for DME (**Fig. 3A**), and postoperative metamorphopsia scores were significantly lower for M-on RD than for the other disorders. In addition, significant differences were found between ERM and MH, MH and BRVO-CME, and BRVO-CME and M-off RD (**Fig. 3B**).

The time course of changes in metamorphopsia scores in each disorder are shown in **Figure 4**. Significant differences were observed between preoperative and 3-month postoperative values in ERM, but no significant difference existed between preoperative and 6-month values, and between 3-month and 6-month postoperative values. Preoperative values significantly differed from 3-month and 6-month postoperative values in MH, but there were no significant differences between 3-month and 6-month postoperative values.

Figure 5 shows the time course of changes in BCVA for each disorder. Preoperative values significantly differed from the 3-month and 6-month postoperative BCVA values in ERM, MH, BRVO-CME, and M-off RD, whereas no significant difference existed between 3-month and 6-month postoperative BCVA. In DME, surgery significantly improved BCVA only at 3 months postoperatively.

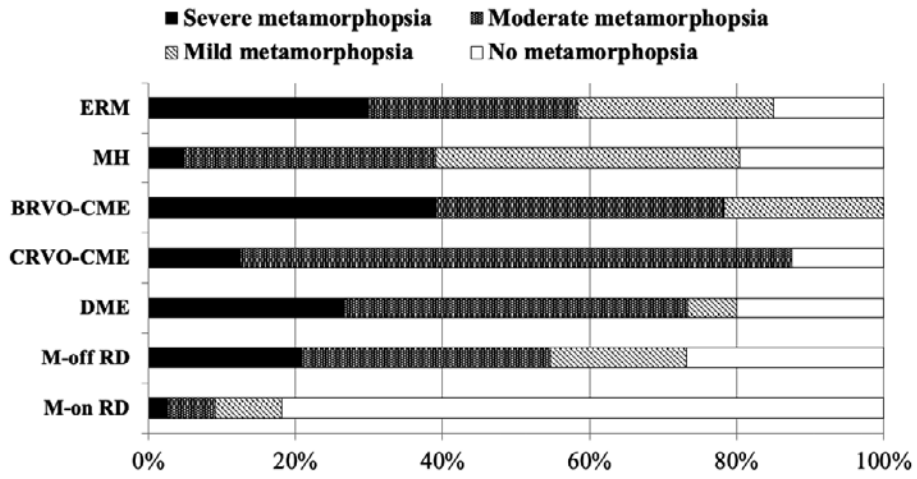

Fig. 2 Postoperative distribution of metamorphopsia severity in patients with vitreoretinal disorders.
Severe: metamorphopsia score ≥ 1.0
Moderate: 1.0 > metamorphopsia score ≥ 0.5
Mild: 0.5 > metamorphopsia score ≥ 0.2
None: 0.2 > metamorphopsia score ≥ 0
ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.

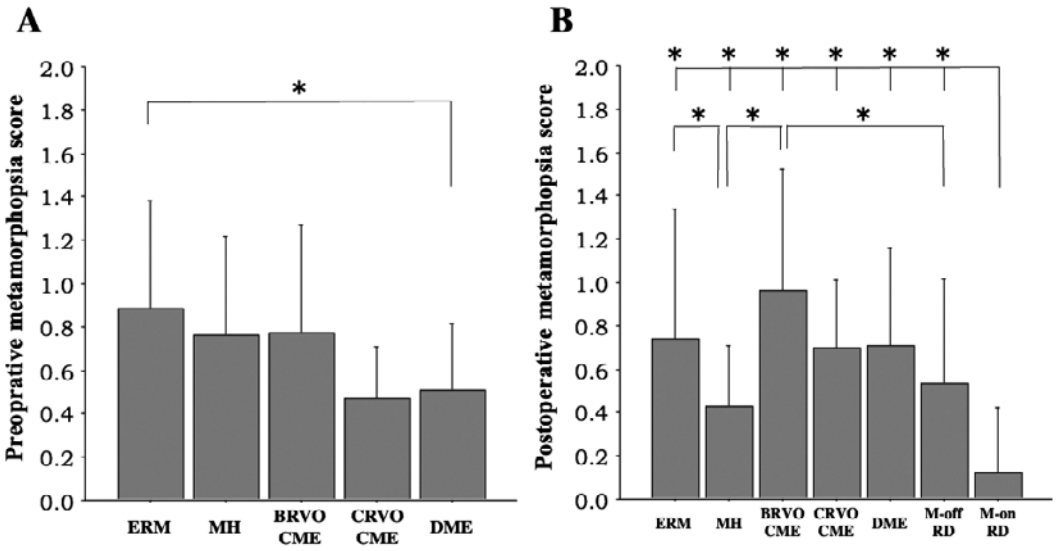

Fig. 3 Metamorphopsia scores for the vitreoretinal disorders. **A.** Preoperative metamorphopsia. **B.** Postoperative metamorphopsia.
ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
* Significant difference on Tukey-Kramer test

BCVA did not change in CRVO-CME and M-on RD.

When scores were analyzed in all patients with vitreoretinal disorders, preoperative metamorphopsia scores were significant correlated with 6-month postoperative metamorphopsia scores ($r = 0.378$, $p < 0.0001$; **Fig. 6A**). Preoperative BCVA was also significantly correlated with

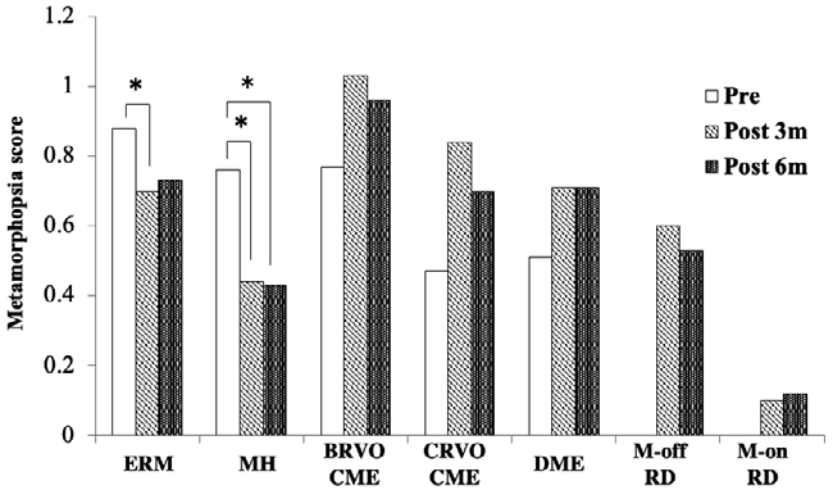

Fig. 4 Time course of metamorphopsia scores for each vitreoretinal disorder.
ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
* Significant difference on Fisher's Protected Least Significant Difference test (Fisher's PLSD)

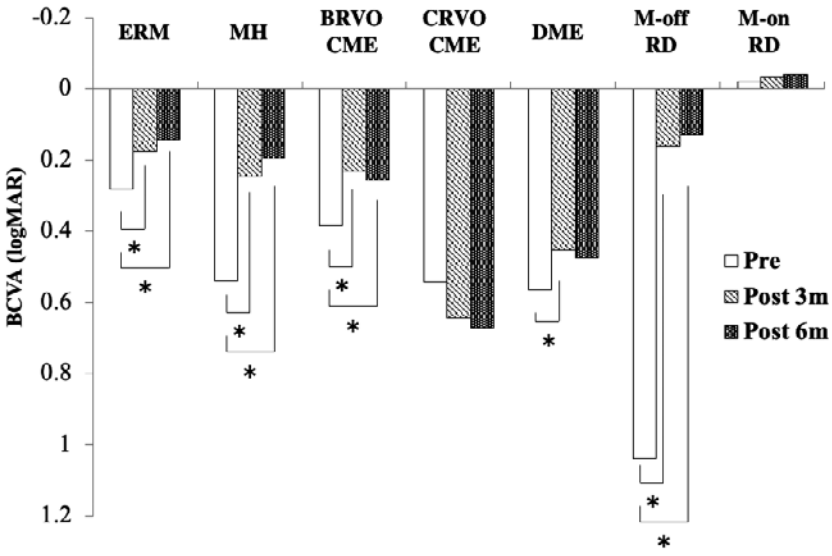

Fig. 5 Time course of visual acuity scores for each vitreoretinal disorder.
BCVA = best-corrected visual acuity, ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
* Significant difference on Fisher's Protected Least Significant Difference (Fisher's PLSD).

6-month postoperative BCVA ($r = 0.353$, $p < 0.0001$; **Fig. 6B**). Subgroup analysis showed a significant correlation of preoperative with 6-month postoperative metamorphopsia scores in BRVO-CME. Preoperative BCVA was significantly correlated with postoperative BCVA in all disorders except MH (**Table 2**). Metamorphopsia scores were significantly associated with BCVA both preoperatively and postoperatively overall. Postoperative meta-

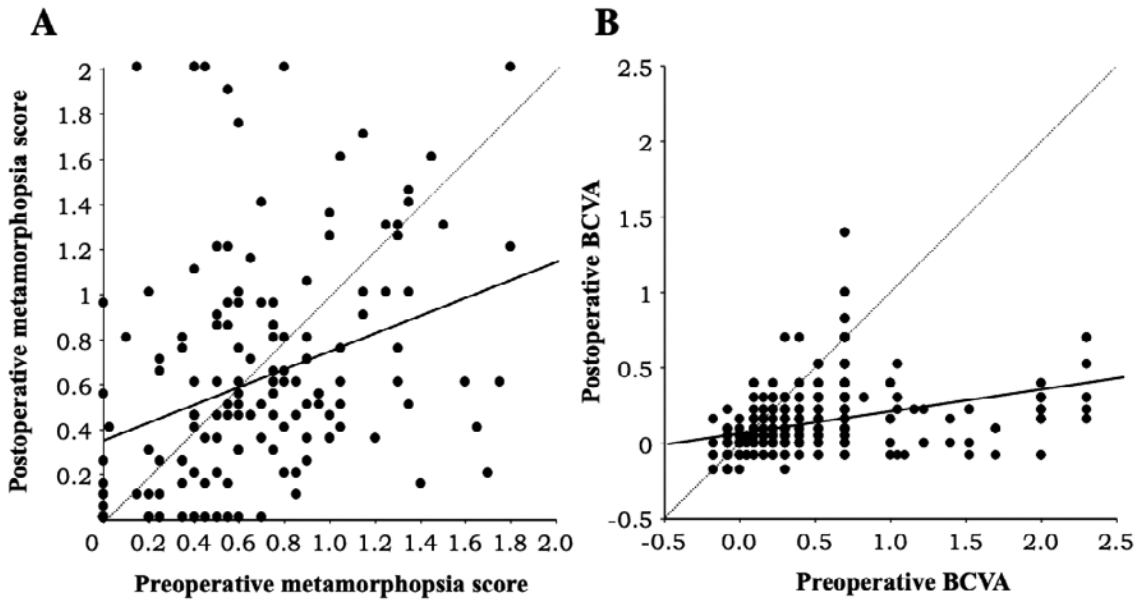

Fig. 6 **A.** Preoperative metamorphopsia scores versus postoperative metamorphopsia scores in all patients. **B.** Preoperative best-corrected visual acuity (BCVA) versus postoperative BCVA in all patients.

Table 2 Subgroup Analysis: Associations between Preoperative and 6-month Postoperative Visual Function

	Preoperative and postoperative metamorphopsia score		Preoperative and postoperative BCVA	
	r	p value	r	p value
ERM	0.199	0.128	0.346	< 0.01*
MH	0.188	0.242	0.304	0.053
BRVO-CME	0.473	< 0.05*	0.707	< 0.0001*
CRVO-CME	0.661	0.075	0.752	< 0.05*
DME	0.419	0.122	0.556	< 0.05*
M-off RD	-	-	0.381	< 0.001*
M-on RD	-	-	0.239	< 0.05*

BCVA = best-corrected visual acuity, ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
* Significant difference in Pearson's correlation coefficient

Table 3 Associations of Metamorphopsia Scores with BCVA

	Preoperative metamorphopsia score and preoperative BCVA		Postoperative metamorphopsia score and postoperative BCVA (6-month)	
	r	p value	r	p value
All cases	0.209	< 0.005*	0.335	< 0.0001*
ERM	–0.003	0.981	0.014	0.918
MH	0.194	0.234	0.417	< 0.01*
BRVO-CME	0.179	0.356	–0.116	0.602
CRVO-CME	–0.247	0.505	0.427	0.308
DME	0.114	0.667	0.206	0.470
M-off RD	-	-	0.343	< 0.005*
M-on RD	-	-	0.074	0.522

BCVA = best-corrected visual acuity, ERM = epiretinal membrane, MH = macular hole, BRVO-CME = cystoid macular edema with branch retinal vein occlusion, CRVO-CME = cystoid macular edema with central retinal vein occlusion, DME = diabetic macular edema, M-off RD = macula-off rhegmatogenous retinal detachment, M-on RD = macula-on rhegmatogenous retinal detachment.
* Significant difference in Pearson's correlation coefficient

morphopsia scores were significantly correlated with postoperative BCVA in MH and M-off RD (**Table 3**).

Discussion

The present study used M-CHARTS to assess preoperative and postoperative metamorphopsia in patients with retinal disorders, and the values were compared. Almost all patients (94%) had metamorphopsia preoperatively, and approximately 25% had severe metamorphopsia (metamorphopsia score ≥1.0). In ERM and BRVO, severe metamorphopsia was obvious, whereas most patients with MH, BRVO-CME, and VRVO-CME had moderate metamorphopsia.

The overall proportion of metamorphopsia decreased

to 64% after surgery. In ERM, MH, BRVO-CME, and DME, however, more than 80% of patients had metamorphopsia. In addition, over 70% of patients with DME and M-off RD had metamorphopsia postoperatively. The proportion of patients with severe metamorphopsia decreased after surgery in ERM and MH but increased in BRVO-CME, CRVO-CME, and DME. Metamorphopsia was more prevalent in disorders that accompanied macular impairment, and metamorphopsia severity varied widely by disease.

In a comparison among disorders, preoperative metamorphopsia score was significantly higher for ERM (0.89) than for DME. In previous studies, the preoperative metamorphopsia score for ERM was reported to be 0.32-1.00[3–11], which was consistent with the present results. In addition, 80% to 85% of ERM patients reported moderate to severe distortion[26,27]. Previous findings and the high proportion of patients with severe metamorphopsia suggest that ERM is characterized by the presence of metamorphopsia. The preoperative metamorphopsia scores for MH and DME were 0.76 and 0.51, respectively, and these values are consistent with prior findings for MH (0.45-0.92)[12,13,16] and DME (0.64)[19].

The postoperative score for M-on RD was significantly lower than the scores for all other disorders. This result is reasonable because M-on RD causes no damage to the macula. However, approximately 20% of M-on RD patients had metamorphopsia, perhaps because of postoperative ERM formation, transient CME, or intraoperative macular detachment. CME is a postoperative complication responsible for secondary visual impairment, and its prevalence is 4% to 11%[28–30]. The reported incidence of ERM on OCT after repair of primary RD ranged between 9.0% and 23%[28–33]. In addition, metamorphopsia can occur postoperatively if the macula detaches even briefly during vitrectomy[33]. Physicians must be mindful of the possibility of metamorphopsia after surgery, even if a patient with RD had no macular detachment.

Vitrectomy improved visual acuity and metamorphopsia in ERM and MH in a subgroup analysis on the time course of changes in visual function. The mean metamorphopsia score of ERM patients was 0.89 preoperatively and 0.76 postoperatively, which was consistent with previous findings (0.32-1.00 preoperatively and 0.23-0.72 postoperatively)[4,5,7,10,11]. In MH, the mean metamorphopsia score was 0.76 preoperatively and 0.43 postoperatively, which are similar to values in previous studies (0.45-0.92 preoperatively and 0.20-0.42 postoperatively)[11,12,16]. Despite improvement in metamorphopsia, the score did not become 0. Even when ERM was peeled or MH was closed morphologically, and visual acuity was improved by surgery, metamorphopsia remained detectable and impaired postoperative quality of vision.

After vitrectomy, metamorphopsia was unchanged in BRVO-CME, CRVO-CME, and DME, while visual acuity improved in BRCO-CME and DME. Metamorphopsia reflects a nonuniform distribution of photoreceptors[34]. Prolonged macular traction causes irreversible photoreceptor cell loss and changes the alignment of cone cells in eyes with DME or BRVO-CME[35,36]. Therefore, persistent CME likely prevents improvement in metamorphopsia.

No significant difference was found between 3-month and 6-month postoperative metamorphopsia in M-on RD and M-off RD. Previous studies reported that visual acuity in patients with RD continued to improve even at 1 to 5 years postoperatively[37,38]. In RD patients, long-term follow-up might have showed improvement of metamorphopsia.

Overall, preoperative metamorphopsia was associated significantly with postoperative metamorphopsia. Subgroup analysis revealed that preoperative metamorphopsia was significantly correlated with postoperative metamorphopsia in BRVO-CME and tended to be correlated in other disorders. This suggests that surgical treatment should be considered as early as possible after a vitreoretinal disorder is diagnosed, so that vitrectomy can be performed to prevent further deterioration of metamorphopsia[39].

Overall, preoperative metamorphopsia was significantly associated with preoperative visual acuity, and postoperative metamorphopsia was significantly associated with postoperative visual acuity. However, subgroup analysis revealed that postoperative metamorphopsia was associated with postoperative visual acuity only in MH and M-off RD. Visual acuity and metamorphopsia were not associated in some disorders.

This study had several limitations. First, the sample size was rather small, especially the numbers of patients with BRVO, CRVO, and DME. This may have influenced the metamorphopsia results. Second, patients were evaluated up to 6 months postoperatively. Previous studies reported that visual acuity in patients with ERM and RD continued to improve at 1 to 5 years postoperatively[37,38,40]. Metamorphopsia in patients after ERM surgery also improved up to 2 years postoperatively[7]. Thus, longer studies of patients after vitrectomy might yield different results regarding metamorphopsia. Third, patient selection of BRVO-CME, CRVO-CME, and DME may have been

inadequate. In this study, vitrectomy was indicated for patients with persistent CME that did not resolve after administration of corticosteroid and/or anti-VEGF agents. Therefore, it was possible that only patients with poor visual outcomes were selected. Future studies with larger sample sizes, longer follow-up, and appropriate patient selection will improve understanding of aniseikonia in patients with vitreoretinal disorders.

In conclusion, this study compared metamorphopsia in patients with vitreoretinal disorders. Metamorphopsia was present in almost all patients and was most severe in ERM. Vitrectomy improved metamorphopsia in ERM and MH. For most vitreoretinal disorders, surgery improved visual acuity but not metamorphopsia.

Conflict of Interest: The author declares no conflict of interest.

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