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Retinal damage extends beyond the border of the detached retina in fovea-on retinal detachment

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Abstract

Purpose: The aim of this study was to investigate the preoperative and post-operative change in retinal sensitivity in relation to the distance to the retinal detachment (RD) in patients with fovea-on RD.

Methods: We prospectively evaluated 13 patients with fovea-on RD and a healthy control eye. Preoperatively, OCT scans of the RD border and the macula were obtained. The RD border was highlighted on the SLO image. Microperimetry was used to assess the retinal sensitivity at the macula, the RD border and the retina around the RD border. At 6 weeks, 3 and 6 months postoperatively, follow-up examinations of OCT and microperimetry were performed in the study eye. Microperimetry was performed once in control eyes. Microperimetry data were overlaid on the SLO image. The shortest distance to the RD border was calculated for each sensitivity measurement. The change in retinal sensitivity was calculated as *control-study*. The relation between the change in retinal sensitivity and the distance to the RD border was assessed using a locally weighted scatterplot smoothing curve.

Results: Preoperatively, the greatest loss in retinal sensitivity was 21 dB at 3° inside the RD which decreased linearly, through the RD border, and reached a plateau of 2 dB at 4°. For 6 weeks and 3 months postoperatively, the greatest retinal sensitivity loss remained at 3° inside the RD but was 4 dB and sensitivity loss decreased linearly to a plateau of 0 dB at 5° outside the RD. At 6 months postoperatively, the greatest sensitivity loss was 2 dB at 3° inside the RD, and decreased linearly to a plateau of 0 dB at 2° outside the RD.

Conclusions: Retinal damage extends beyond the detached retina. Retinal sensitivity loss of the attached retina decreased drastically as the distance to the RD increased. Postoperative recovery occurred for both attached and detached retina.

KEYWORDS
fovea, microperimetry, OCT, retina

1 | INTRODUCTION

Vitreoretinal surgery for retinal detachment (RD) has a high reattachment rate (Williamson et al., 2014).

It is generally assumed that foveal damage is limited when the fovea is not involved, and that patients will retain their preoperative visual status after anatomical reattachment. However, vision loss in patients after successful reattachment surgery for fovea-on RD has been observed (Di Lauro et al., 2015). Moreover, vision loss may not be limited to visual acuity, but can also include other functions such as contrast acuity and metamorphopsia,

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even after excluding factors which can compromise such functions (e.g. cataract, epiretinal membrane and cystoid macular oedema) (Di Lauro et al., 2015; Okamoto et al., 2013; Zhou et al., 2017). This suggests that there are other causes besides foveal detachment for visual function loss after fovea-on RD surgery.

Animal studies reported that within 12h of RD, photoreceptor degeneration occurs in the detached retina and peaks at 2 days after RD (Arroyo et al., 2005; Wickham et al., 2018). Furthermore, animal models have also shown that photoreceptor damage is not restricted to the detached retina, but is also present at the border of the RD and in a lesser extent in the attached retina (Francke et al., 2005; Halász et al., 2021; Lee et al., 2021). These results suggest that retinal damage induced by the RD extends beyond the detached retina and can proceed towards the fovea. This may explain why patients with fovea-on RD can experience postoperative visual function loss despite no foveal involvement.

Thus, we hypothesize that distance between RD and umbo (RD-umbo distance) is associated with the preoperative severity and postoperative recovery of foveal damage and, consequently, that a greater RD-umbo distance results in less postoperative visual function loss. Therefore, the aim of this study is to investigate the preoperative and postoperative change in retinal sensitivity in relation to the distance to the RD in patients with fovea-on rhegmatogenous RD. Additionally, we investigated the relation between RD-umbo distance and the postoperative change in visual function.

2 | MATERIALS AND METHODS

2.1 | Study design

This prospective observational study was conducted in the Rotterdam Eye Hospital (Rotterdam, the Netherlands) between February 2020 and March 2021, and was approved by the Medical Ethical Committee of the Erasmus Medical Centre (Rotterdam, the Netherlands). The research followed the tenets of the Declaration of Helsinki. All included patients gave written consent prior to participation.

2.2 | Study population

Patients diagnosed with primary rhegmatogenous fovea-on RD and a healthy fellow eye were eligible to participate. All eligible patients were approached by one investigator (HN).

Exclusion criteria before surgery were the following: younger than 18 years, distance between umbo and the RD border less than 1250 μm (safety border) (Jong et al., 2017), RD border beyond the central 30° of the retina (outside the projection field of microperimetry), unclear media which prevented retinal visualization, giant tear, pre-existing maculopathy in either study or fellow eye which could compromise vision (e.g. macular hole, epiretinal membrane stage 2 or more (Govetto et al., 2019)).

Exclusion criteria after surgery were the following: recurrent RD, persistent cystoid macular oedema, persistent subfoveal fluid and epiretinal membrane (Govetto et al., 2019).

2.3 | Preoperative assessments

Best-corrected visual acuity (BCVA) measurement and fundus examination were performed in a routine outpatient setting. BCVA was measured using Snellen projector optotypes and expressed in decimal units. Fundus examination was performed after pupil dilatation with 0.5% tropicamide. Patients diagnosed with fovea-on RD were prescribed bed rest and posturing at the ward while waiting for urgent surgery (de Jong et al., 2017).

Optical coherence tomography (OCT) and microperimetry assessments were performed by one investigator within 1 h of arrival at the ward, and with the pupils still dilated for fundus examination. The interruption of posturing for both assessments was less than 30 min, and patients were transported to the devices by wheelchair.

OCT volume scans of the macula were obtained for both study and control eyes using Spectralis OCT2 (Heidelberg Engineering). The scan was acquired at a 20° × 15° fovea-centred grid with 35 μm distance between B-scans, resulting in 145 B-scans. If the scanning grid did not overlap the RD border, another OCT volume scan was acquired with a larger scanning area overlapping the RD border.

The RD border and umbo were located on the B-scans and highlighted on the scanning laser ophthalmoscopy (SLO) image using the draw tool embedded in the Heidelberg eye explorer system software (Figure 1).

The shortest distance between the umbo and RD border (RD-umbo distance) was measured on the SLO images using the measurement tool embedded in the Heidelberg eye explorer system software.

Microperimetry was performed in the study eye with the MAIA microperimetry (Centervue). The retina adjacent to the RD border was examined using a customized grid of 52 points covering the RD border and the retina on both sides (Figure 2). The foveal area was examined using the standard foveal-centred grid of 37 points in three concentric circles (2°, 6° and 10° in diameter). All examinations were performed using the 4–2 threshold strategy.

The microperimetry data of both the foveal retina and the retina adjacent to the RD border were overlaid on the SLO image with the indicated RD border (Figure 2) (Adobe Photoshop version 21.0.2). For each sensitivity measurement, the shortest distance to the RD border was calculated.

Baseline data collection included gender, age, study eye, preoperative BCVA, distance between RD and umbo, RD location and preoperative lens status, time between OCT and start of surgery and surgery technique.

2.4 | Postoperative assessments

At 6 weeks, 3 and 6 months postoperatively, patients underwent visual function assessments, OCT and microperimetry examinations.

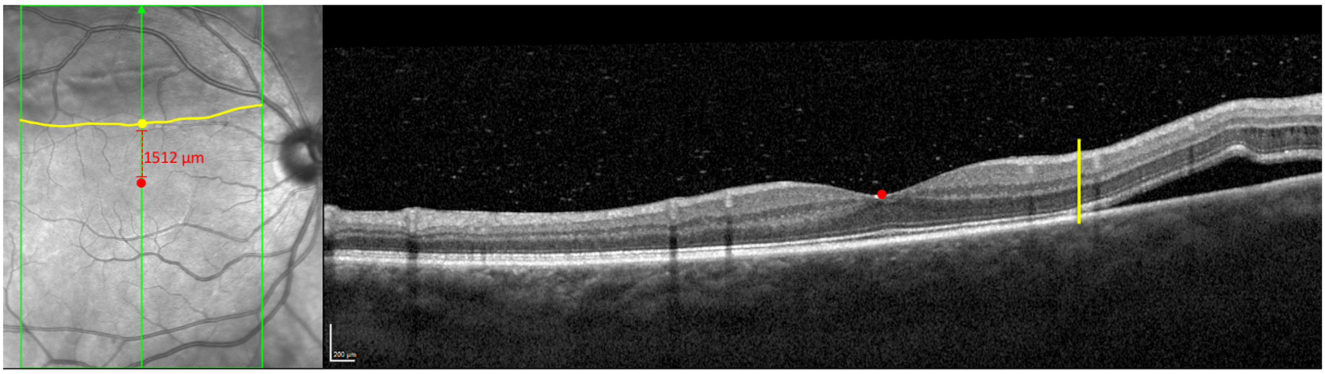

FIGURE 1 Example of a B-scan (right) with the corresponding SLO image (left) of a study eye with fovea-on RD. The yellow line in the B-scan represents the retinal detachment border, which corresponds to the yellow dot in the SLO image. The yellow line in the SLO image represents the RD border which is composed of the RD border localization of the B-scans. The red dot in the B-scan represents the umbo and corresponds to the red dot in the SLO image. The shortest distance between the umbo and RD border is 1512 μm (5.3°). RD, retinal detachment; SLO, scanning laser ophthalmoscopy.

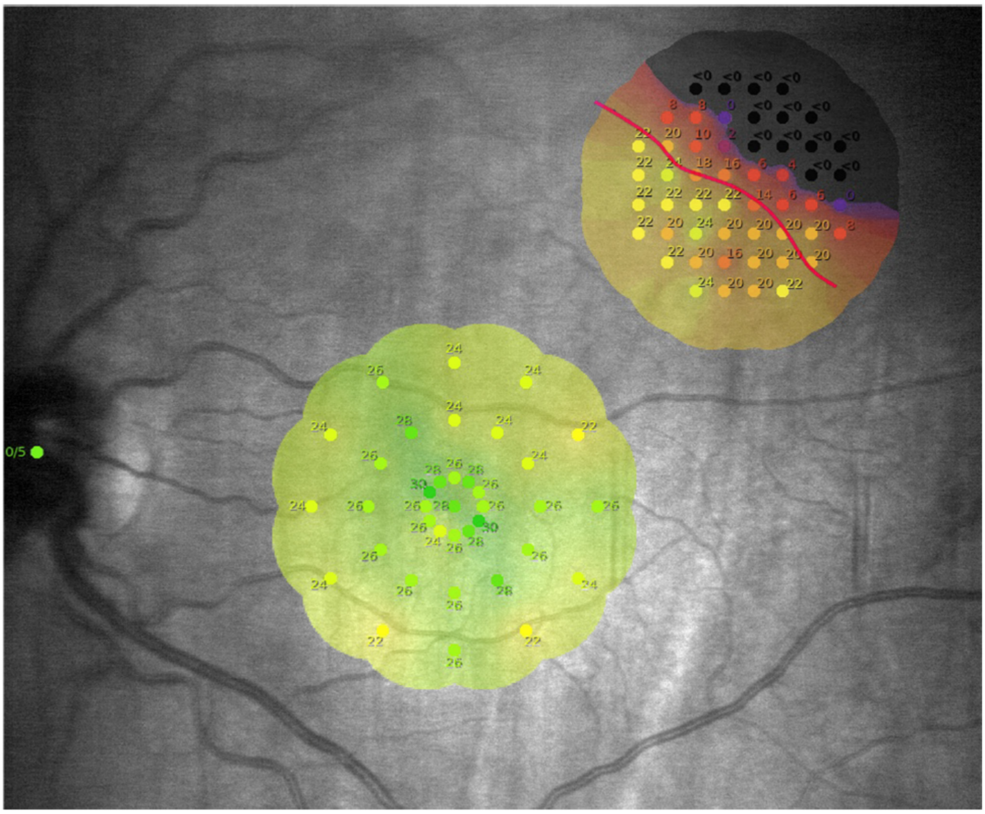

FIGURE 2 Example of microperimetry data overlaid on the SLO image with the RD border (red line). RD, retinal detachment; SLO, scanning laser ophthalmoscopy.

The following visual function assessments were performed for both study and control eyes without pupil dilatation: BCVA and low-contrast BCVA were measured using conventional and 10% ETDRS charts and expressed as the logarithm of minimal angle of resolution (logMAR). Metamorphopsia was assessed by the M-CHARTS (Inami Co.) in horizontal and vertical direction. Aniseikonia was assessed by the New Aniseikonia Test in horizontal and vertical direction. Macropsia was defined as aniseikonia of at least +2% and micropsia was defined as aniseikonia of −2% or worse (Ichikawa et al., 2018). For colour vision assessment, we used the Hardy Rand Rittler test (fourth edition, Richmond Products). The test score was equal to the number of correctly identified figures (Ng et al., 2020; Zhao et al., 2015). Stereopsis was examined using Titmus Fly Test. Absence of gross stereopsis was regarded as 6000 seconds of arc for statistical analysis (Han et al., 2016). The assessments for metamorphopsia, aniseikonia, colour vision and stereopsis were all performed at 30 cm with refraction corrected for this distance.

Microperimetry was performed after pupil dilatation with 0.5% tropicamide. For the study eye, follow-up examinations were performed for both preoperative examinations. For the fellow eye, two microperimetry examinations were performed covering the same areas as the study eye. The fellow eye was examined during one postoperative visit, as the repeatability of sensitivity measurements in healthy eyes is high (Barboni et al., 2018).

OCT examination was performed with the pupils still dilated for microperimetry. For both study and control eyes, macular volume scans were obtained to detect macular abnormalities using the same method as described preoperatively.

2.5 | Surgical procedures

Each surgery, pars plana vitrectomy or scleral buckling, was carried out by one of five experienced vitreoretinal surgeons.

Standard 23-gauge vitrectomy was carried out with vitreous traction release around breaks, subretinal fluid drainage and endolaser photocoagulation. In phakic study eyes, phacoemulsification was conducted according to the surgeon's preference.

Scleral buckling included drainage and indentation by a local radial or circular explant (with or without encircling band) and injection of a 25% sulphur hexafluoride gas to prevent hypotony and to tamponade retinal tears. Either preoperative cryocoagulation or postoperative laser was performed.

Gas tamponade was either sulphur hexafluoride or octafluoropropane, and patients were instructed to posture 6 h a day for 1 week, in a manner to reduce the risk of macular folds.

2.6 | Statistical analysis

Categorial variables were presented as frequencies and percentages. Continuous variables were expressed as mean ± SD in case of normal distribution, or as median (IQR) otherwise. Significant differences between study and control eyes were determined with the paired Student's *t*-test in case of normal distribution, the Wilcoxon signed-rank test for non-normal distribution and the McNemar test in case of categorial variables.

In order to calculate the change in retinal sensitivity and visual function in study eyes due to fovea-on RD, we would need the values of these parameters before the RD occurs. As these values were not available, the values of the healthy fellow eyes were used as a proxy.

For retinal sensitivity, the proxy for the sensitivity measurements in the study eye was obtained from the corresponding locations in the control eye. Sensitivity values below 0 dB were considered as 0 dB for statistical analysis. The change in retinal sensitivity was calculated as the difference between control and study eye (*control – study*). The relation between the change in retinal sensitivity and the distance to the RD border was assessed using a locally weighted scatterplot smoothing (LOWESS) curve.

The change in BCVA, low-contrast BCVA, colour vision and metamorphopsia was also calculated as the difference between control and study eye (*control – study*).

For aniseikonia and stereopsis, there were no control values as those were binocular assessments. The relation between RD-umbo distance and the change in visual function was evaluated by bivariate analysis using Spearman's rank correlation coefficient.

Preoperative visual acuity values were transformed from decimal to logMAR equivalents, and RD-umbo distance measurements were converted from micrometre to degree (Kolb et al., 1995).

A *p*-value below 0.05 was considered statistically significant. We corrected for multiple testing using the Bonferroni correction to adjust the threshold for statistical significance. This applies to the comparison of postoperative visual functions between study and control eyes (four comparisons, the threshold for statistical significance was adjusted to 0.013) and the correlation between RD-umbo distance and the change in visual function parameters (24 correlations, the threshold for statistical significance was adjusted to 0.002).

Statistical analyses were performed using SPSS statistics version 24.0, except for the LOWESS curves, which were produced using R version 3.6.1.

3 | RESULTS

We approached 27 eligible patients of which 23 patients were initially included and four patients were unwilling to participate. Of the 23 initially included patients, 10 patients were excluded due to distance between umbo and the RD border was less than 1250 μm (n=2), RD border was beyond the central 30° of the retina (n=6), presence of preoperative ERM stage 1 (n=1) and presence of postoperative ERM stage 3 (n=1). This resulted in 13 patients for analysis.

3.1 | Patient characteristics

Of the 13 patients, nine were male (69%) and the mean age was 60 years (Table 1). Most patients underwent vitrectomy (85%).

Preoperative lens status was predominantly phakic (62%). One patient had phacoemulsification combined with vitrectomy, whereas two patients had phacoemulsification during follow-up, which resulted in 8 (62%%) pseudophakic and 5 (38%) phakic study eyes at 6 months postoperatively.

3.2 | Preoperative change in retinal sensitivity in relation to the distance to the RD border

The greatest difference in retinal sensitivity was 21 dB at 3° inside the RD which decreased approximately linearly, through the RD border, to 4 dB at 2° outside the RD (Figure 3). The difference further decreased outside the RD until it reached a plateau of 2 dB at 4°.

3.3 | Postoperative change in retinal sensitivity in relation to the distance to the RD border

At 6 weeks postoperatively, the shape of the LOWESS curve was more flattened compared with the preoperative

TABLE 1 Patient characteristics.

Characteristics		*p*-Value
Total patients	13	
Gender, *n* (%)		
Male	9 (69)	
Age (years), mean ± SD	60 ± 7	
Study eye, *n* (%)		
OD	7 (54)	
Preoperative BCVA (logMAR), median (IQR)		
Study eye	0.02 (0.0–0.1)	0.05
Control eye	−0.04 (0.0–0.1)	
Distance between RD and umbo (°), mean ± SD	12 ± 5	
RD location, *n* (%)		
Superior	4 (31)	
Nasal	4 (31)	
Inferior	1 (7)	
Temporal	4 (31)	
Preoperative lens status, phakic/pseudophakic, *n* (%)		
Study eye	8 (62)/5 (38)	
Control eye	10 (77)/3 (23)	0.5
Time between OCT scan and start surgery (hours), median (IQR)	20 (6–22)	
Surgery technique, *n* (%)		
Scleral buckling	2 (15)	
Vitrectomy only	10 (77)	
Vitrectomy combined with phacoemulsification	1 (8)	
Gas tamponade		
Sulphur hexafluoride	9 (69)	
Octafluoropropane	4 (31)	

Abbreviations: IQR, interquartile range; logMAR, logarithm of the minimal angle of resolution; OCT, optical coherence tomography; RD, retinal detachment; SD, standard deviation.

LOWESS curve (Figure 3). The greatest difference in retinal sensitivity remained at 3° inside the RD but decreased to 4 dB and, in a similar trend as preoperatively, the difference decreased approximately linearly to 2 dB at 2° outside the RD and the plateau of 0 dB started around 5°.

At 3 months postoperatively, the LOWESS curve was similar to the LOWESS curve at 6 weeks postoperatively.

At 6 months postoperatively, the curve was even more flattened compared with 6 weeks and 3 months postoperatively and the greatest difference in retinal sensitivity was approximately 2 dB at 3° inside the RD, and decreased linearly to a plateau of 0 dB at 2° outside the RD.

The 95% confidence interval increased starting from 18° for all three LOWESS curves.

3.4 | Visual function during 6-month follow-up

At 6 weeks postoperatively, BCVA, low-contrast BCVA and colour vision were worse in study eyes compared with control eyes (Figure 4). The values of the study eyes improved and at 6 months postoperatively, BCVA, low-contrast BCVA and colour vision of study and control eyes were not statistically significantly different (BCVA $p = 0.3$, low-contrast BCVA $p = 0.2$, colour vision $p = 0.7$) (Table 2). Stereopsis scores also improved during 6-month follow-up.

For metamorphopsia in study eyes, both scores and prevalence decreased during follow-up. Metamorphopsia was not present in control eyes during follow-up, and although metamorphopsia was present in two study eyes at 6 months postoperatively, there was no measurable evidence that there was a difference between both eyes ($p = 0.5$).

Even though median aniseikonia scores remained stable during follow-up, the prevalence of aniseikonia increased from 31% ($n = 4$) at 6 weeks postoperatively to 54% ($n = 7$) at 6 months postoperatively.

3.5 | The relation between RD-umbo distance and the change in visual function

At 6 weeks postoperatively, RD-umbo distance showed the highest correlation with horizontal metamorphopsia difference and stereopsis ($|r| = 0.7$ for both), followed by BCVA difference, low-contrast BCVA difference and vertical metamorphopsia difference ($r = 0.6$ for all three) (Table 3 and Figure 5). These correlations decreased during follow-up.

Although the correlation between horizontal metamorphopsia and RD-umbo distance also decreased at 3 and 6 months postoperatively, the correlation was the highest among the visual function parameters at both time points.

None of the correlations analysis remained statistically significant after correction for multiple testing.

4 | DISCUSSION

This prospective study showed that the retinal damage induced by a RD is not restricted to the detached retina, but extends beyond the border to the attached retina in patients with fovea-on retinal detachment. This supports the findings of previous animal studies by Halász, Lee and Francke who demonstrated that retinal damage is found not only in the detached retina but in lesser extent also in the attached retina (Francke et al., 2005; Halász et al., 2021; Lee et al., 2021).

The results of the current study are consistent with our hypothesis that the distance to the RD is associated with the severity of retinal damage: We have shown that retinal sensitivity loss of the attached retina decreased drastically as the distance to the RD increased and reached a plateau starting at four degrees away from the RD. Postoperative recovery of retinal sensitivity occurred for both attached and detached retina, but was slightly better for the attached retina which was at least two degrees away from the RD border. Translated to clinical practice, it means that the risk of foveal damage increases remarkably if the RD is <4° (1152 μm) away from the umbo, thus if the RD has extended to more than the half of the parafovea (Kolb et al., 1995). In

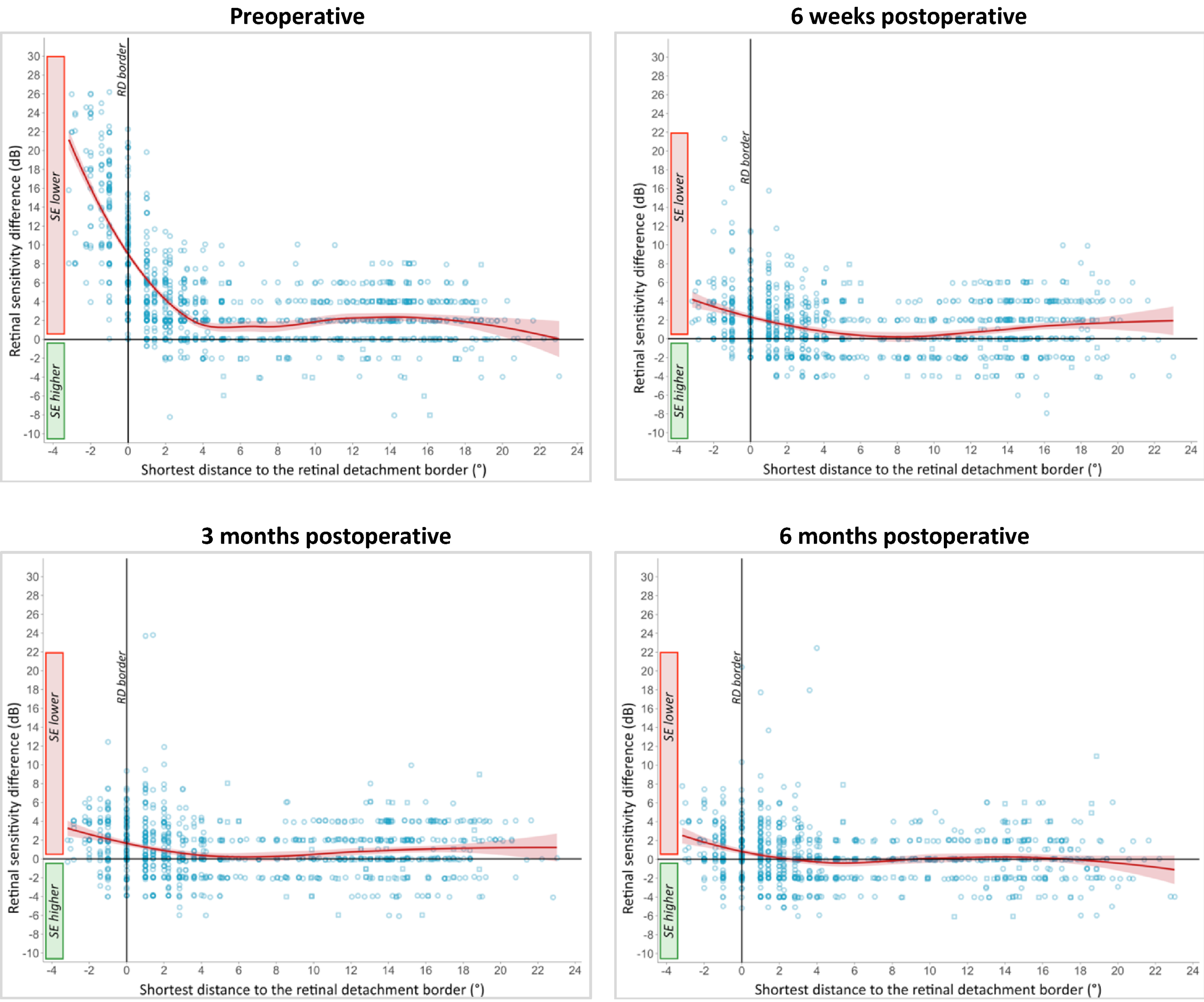

FIGURE 3 Retinal sensitivity difference in relation to the distance to the retinal detachment border in patients with fovea-on retinal detachment (*n* = 13). The red line is the locally weighted scatterplot smoothing curve. The light red area around the curve represents the 95% confidence interval. RD, retinal detachment; SE, study eye.

other words, foveal damage can already occur without foveal detachment. Fortunately, it seems that the retinal damage can recover postoperatively and the recovery is better if the retina was not detached preoperatively. However, the improvement of retinal sensitivity values can also be caused by the removal of media opacification due to vitrectomy or learning effects (Díaz-Barreda et al., 2021). The presence of gas tamponade or gas cataract can also negatively influence the retinal sensitivity measurement.

It is generally assumed that a fovea-on RD will not compromise visual acuity as the fovea is not involved. However, we have found that BCVA was lower in study eyes compared with control eyes at 6 weeks and 3 months after surgery. This is consistent with the study of Di Lauro et al. (2015) who evaluated the visual acuity of patients at 3 months after macula-on RD surgery and found visual acuity loss without explanatory factors. It is possible that a follow-up of 3 months was too short, as we have shown that the BCVA in study eyes improved to values of the healthy control eyes at 6 months postoperatively. We have also found that a fovea-on RD can negatively affect low-contrast BCVA, colour vision, stereopsis, metamorphopsia and aniseikonia, which is comparable to previous studies (Lina et al., 2016, Nork et al., 1995, Okamoto et al., 2013, Okamoto et al., 2014a, Okamoto et al., 2014b). In addition, we have shown that these visual functions improve during 6 months after surgery, with low-contrast BCVA, colour vision and metamorphopsia restoring to levels of the healthy control eyes. However, although not statistically significantly different from control eyes, metamorphopsia was present in 15% of the study eyes, and aniseikonia was perceived by 54% of the patients at 6 months postoperatively. Thus, although visual function can improve during 6 months after surgery, visual function loss can be present despite fovea-on RD. Even though the exact pathophysiology of visual function loss after fovea-on RD is not clear, we believe it is important that it is acknowledged as visual function loss can negatively impact vision-related quality of life (Hanumunthadu et al., 2021; Lina et al., 2016; Ng et al., 2020; Okamoto et al., 2008).

In our study, the prevalence of metamorphopsia at 6 months postoperatively was 15% and was consistent with previous studies as they reported a prevalence of 13%–26% (Okamoto et al., 2014b; Okuda et al., 2018; Saleh et al., 2018; Zhou et al., 2017).

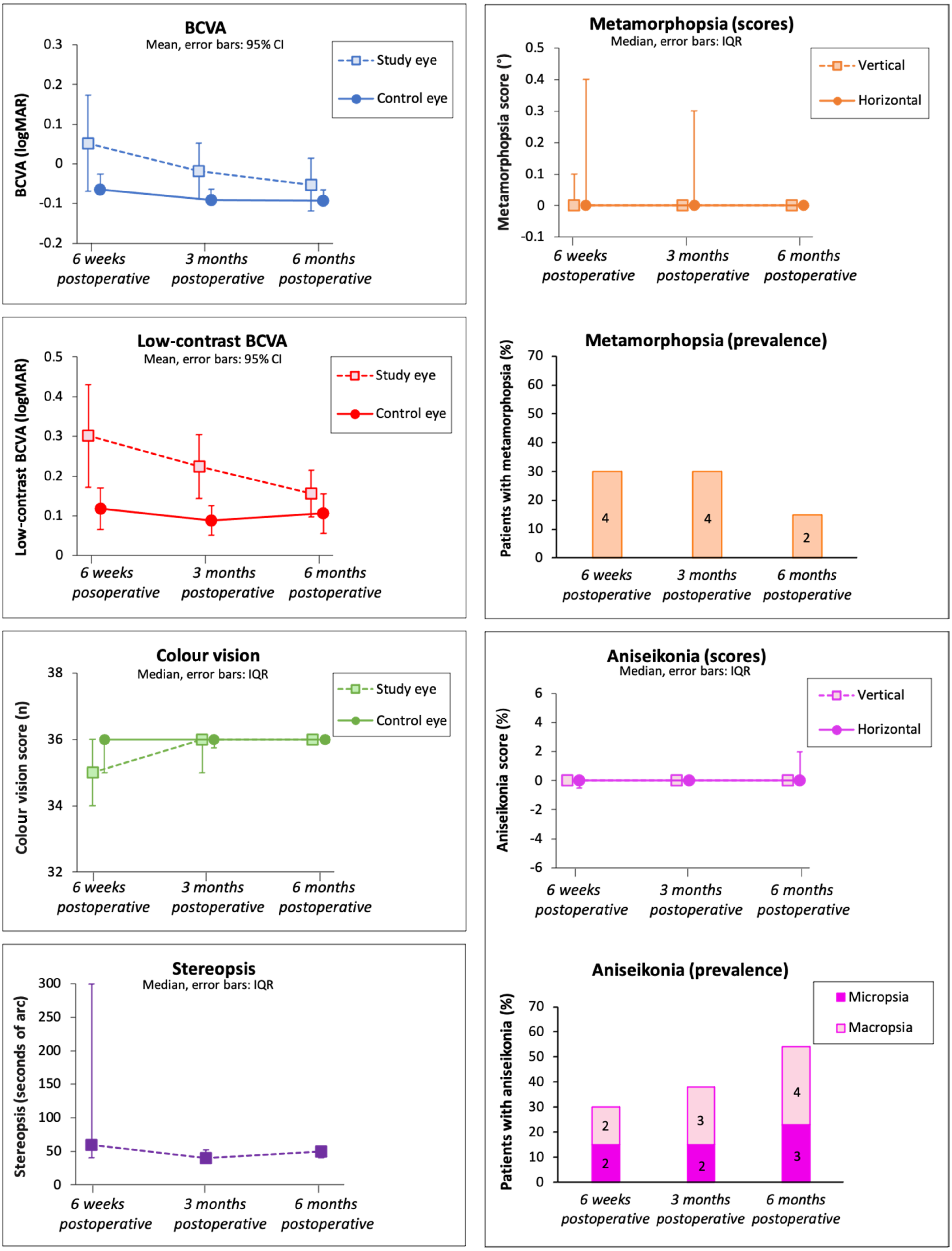

FIGURE 4 Visual function in healthy control eyes and eyes after fovea-on retinal detachment during 6-month follow-up. The numbers within the prevalence graphs represent the frequencies. BCVA, best-corrected visual acuity, CI, confidence interval; IQR, interquartile range; logMAR, logarithm of the minimal angle of resolution.

Comparable to our study, Zhou et al. and Okamoto et al. reported metamorphopsia in patients after macula-on RD surgery without abnormal foveal structures on postoperative OCT (Okamoto et al., 2014b; Zhou et al., 2017). Postoperative metamorphopsia was explained by Okamoto et al. by brief detachment of the macula

TABLE 2 Visual function 6 months postoperatively in study eye and fellow eye.

Visual function	Study eye	Control eye	*p*-Value
BCVA (logMAR), mean ± SD	−0.05 ± 0.1	−0.09 ± 0.05	0.3
Low-contrast BCVA (logMAR), mean ± SD	0.2 ± 0.03	0.1 ± 0.03	0.2
Colour vision (*n*), median (IQR)	36 (36–36)	36 (36–36)	0.7
Metamorphopsia			
Present, *n* (%)	2 (15)	0 (0)	0.5
Aniseikonia[a]			
No aniseikonia, *n* (%)	7 (54)		
Micropsia, *n* (%)	3 (23)		
Macropsia, *n* (%)	3 (23)		
Stereopsis[a] (seconds of arc), median (IQR)	50 (40–50)		

Abbreviations: A_H, aniseikonia horizontal; A_V, aniseikonia vertical; BCVA, best-corrected visual acuity; IQR, interquartile range; logMAR, logarithm of the minimal angle of resolution; M_H, metamorphopsia horizontal; M_V, metamorphopsia vertical; SD, standard deviation.

[a]Binocular test.

TABLE 3 Correlation between RD-umbo distance and the change in visual function[a]

	6 weeks Postoperative		3 months Postoperative		6 months Postoperative	
Visual function	*p*	*r*	*p*	*r*	*p*	*r*
BCVA difference	0.009	0.6	0.2	0.3	0.4	0.1
Low-contrast BCVA difference	0.02	0.6	0.2	0.3	0.2	0.3
Colour vision difference	0.2	−0.3	0.2	−0.3	0.3	0.1
Metamorphopsia vertical difference	0.02	0.6	0.2	0.3	0.4	0.08
Metamorphopsia horizontal difference	0.008	0.7	0.01	0.6	0.01	0.6
Aniseikonia vertical	0.1	−0.4	0.1	−0.3	0.5	−0.04
Aniseikonia horizontal	0.05	−0.5	0.2	−0.2	0.3	−0.2
Stereopsis	0.008	−0.7	0.06	−0.5	0.3	−0.1

Abbreviations: BCVA, best-corrected visual acuity; *p*, *p*-Value; *r* = Spearman's rank correlation coefficient.

[a]Bonferroni correction for multiple testing was applied to adjust the significant *p*-value at 0.002.

during surgery (Okamoto et al., 2014b), while Okuda et al. explained it by a possible preoperative macular detachment as these patients had a superior quadrant RD close to the fovea (Okuda et al., 2018). Indeed, progression of a RD is possible, especially for superior-located RD (de Jong et al., 2017). Hence, our patients were prescribed bed rest and posturing while waiting for urgent surgery, as these interventions have been shown to limit the progression of the RD (Jong et al., 2017). Moreover, foveal detachment in the short interval to surgery was precluded based on the progression rates of the study by De Jong et al. and the fact that we excluded patients with detachments closer than 1250 μm to the umbo (Jong et al., 2017). Hence, we hypothesize that the loss of retinal function in the attached retina is due to cellular damage mechanisms in the detached retina which spreads into the attached retina. Our hypothesis is supported by previous animal studies which have reported damage to the synapse between photoreceptor and bipolar cells in both attached and detached retina (Halász et al., 2021; Townes-Anderson et al., 2017; Wang et al., 2016). This synaptic damage is due to rods retracting their presynaptic terminals and cones losing their synaptic invaginations (Halász et al., 2020). Reattachment of the retina does not restore all the synapses so it has been proposed that the synaptic changes can be the cause of incomplete visual recovery after anatomical successful reattachment surgery. The synaptic damage, although the mechanism is not known, is linked to activation of the RhoA pathway by the RD (Wang et al., 2016). Therefore, it has been suggested that inhibition of the RhoA pathway can improve visual outcomes after reattachment surgery (Halász et al., 2020).

The prevalence of aniseikonia increased from 31% at 6 weeks postoperatively to 54% at 6 months postoperatively which is higher than the prevalence of 26% reported by Okamoto et al. (Okamoto et al., 2014a). Okamoto et al. excluded patients with more than 2.0 dioptres anisometropia which may explain why they found a lower prevalence. However, aniseikonia can be induced by anisometropia (dynamic aniseikonia), but it can also be retinally induced (static aniseikonia) (McNeill & Bobier, 2017). In our study, two patients had anisometropia of −3 dioptre (spherical equivalent of the study eye was −3 higher than the control eye). These two patients had the highest anisometropia and no micropsia was measured for these patients. Therefore, we think it is unlikely that anisometropia contributed much to aniseikonia and we chose not to exclude patient with anisometropia. For future studies, it would be of additional value to differentiate between the two types of aniseikonia.

Changes in BCVA, low-contrast BCVA, metamorphopsia and stereopsis were highly correlated with

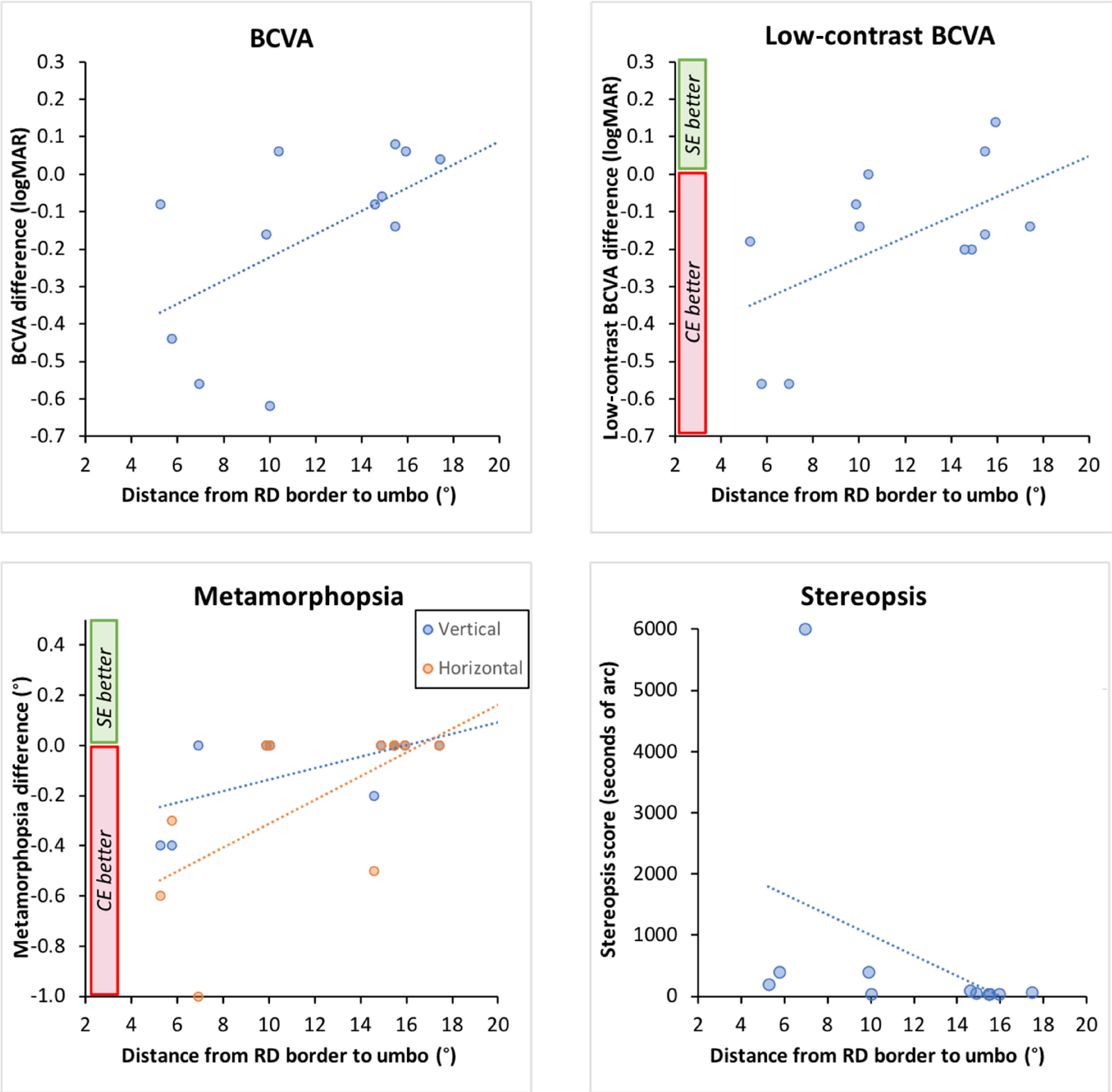

FIGURE 5 Correlation between RD-umbo distance and the change in visual function at 6 weeks postoperatively. BCVA, best-corrected visual acuity; CE, control eye; logMAR, logarithm of the minimal angle of resolution; RD, retinal detachment; SE, study eye.

RD-umbo distance at 6 weeks after surgery. Even though the correlations decreased during follow-up, the correlation between RD-umbo distance and horizontal metamorphopsia remained the highest among other visual function parameters at three and 6 months after surgery. Moreover, 15% of the patients perceived metamorphopsia at 6 months postoperatively. In clinical practice, this would mean that detachments closer to the central fovea results in more visual function loss shortly after surgery which can improve to healthy values during 6 months after surgery. However, metamorphopsia can still be perceived at 6 months after surgery, in which a RD closer to the fovea is associated with more severe metamorphopsia.

Remarkably, we found that horizontal metamorphopsia scores were higher than vertical metamorphopsia scores. This difference may be explained by unintentional downward displacement of the retina, which may occur after vitrectomy for RD. It has been suggested that the displacement is due to the force of gravity (Shiragami et al., 2010).

The relation between the change in retinal sensitivity and the distance to the RD border was assessed using a LOWESS curve. However, we must take into account that de LOWESS curve considered the measurements as independent. In fact, multiple measurements were paired with one patient, meaning the confidence interval may be higher than reported. Moreover, the confidence interval widened starting from 18 to 23 degrees as the number of measurements decreased. This decrease in measurements was due to the limited scanning field of the microperimetry as it is conventionally used to assess the central retina. Further research, preferably with a larger sample size and a microperimetry with a wider scanning field, is necessary to confirm our findings.

The strengths of current study are the following: first study to combine OCT and microperimetry to assess both detached and attached retina, preoperative OCT to confirm fovea-on RD and one investigator who performed the measurements on OCT and microperimetry.

As for limitations, we had a small sample size which was due to strict in- and exclusion criteria. Displacement of the RD border during posturing and interruption of posturing can be considered as a limitation of our study. Therefore, measures were taken to limit the displacement: The assessments were performed within 1 h after posturing, the duration of the assessments was less than 30 min and the patients were transported by wheelchair. Furthermore, the displacement of the RD border during posturing and the interruption of posturing was taken into account by using the velocity results of the study by De Jong et al., which was less than two degrees (576 μm) for both posturing and its interruption. We found that the loss of sensitivity extends four degrees beyond the RD border, so even if we take the two degrees displacement of the RD border into account, our results still show that the retinal damage extends beyond the RD border.

In conclusion, our study shows that retinal damage extends beyond the border of the detached retina in patients with fovea-on retinal detachment. Retinal sensitivity loss decreased drastically as the distance to the RD increased and reached a plateau starting at four degrees away from the RD. Postoperative recovery of retinal sensitivity occurred for both attached and detached retina, but was slightly better for the attached retina which was at least two degrees away from the RD border.

Postoperative visual function loss can be present despite no foveal detachment. A shorter RD-umbo distance results in more visual function loss shortly after surgery which can improve to healthy values during 6 months after surgery. However, metamorphopsia and aniseikonia can be perceived at 6 months after surgery, in which a RD closer to the fovea is associated with more severe metamorphopsia.

AUTHOR CONTRIBUTIONS

JvM, KV, ELH and HJN contributed to study the concept and design. HJN conducted the study. HJN and CK collected the data. HJN and KV analysed the data. HJN wrote the manuscript. JvM, KV and ELH critically revised the manuscript. All authors discussed the results and commented on the manuscript.

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ETHICAL APPROVAL

This study is registered in the Central Committee on Research Involving Human Subjects (NL72120.078.19). Ethical review of the study was performed by the Medical Research Ethics Committee Erasmus MC (MEC-2019-0756). All patients provided written informed consent prior to enrolment in the study.

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