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Full-field Electroretinography in Age-related Macular Degeneration: can retinal electrophysiology predict the subjective visual outcome of cataract surgery?

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ABSTRACT.

Purpose: **Predicting the visual gain from cataract surgery when the main cause of vision loss is age-related macular degeneration may be difficult and warrants the need for an objective predictor of subjective outcome. Full-field electroretinography is an objective measure of overall retinal function. We therefore wanted to study if full-field electroretinography can predict subjective visual outcome using visual function questionnaire.**

Methods: **Thirty-one patients with age-related macular degeneration operated for bilateral cataract underwent full-field electroretinography preoperatively. Full-field electroretinography was performed according to International Society for the Clinical Electrophysiology of Vision standards using a Ganzfeld bowl (RETI-port/scan 21, Roland, Berlin) and Dawson–Trick–Litzkow fibre electrodes. Vision-related quality of life was measured using the National Eye Institute Visual Function Questionnaire-39 before first-eye surgery and 4.12 ± 2.11 months after second-eye surgery.**

Results: **Mean change in composite visual function questionnaire score after cataract surgery was 9.2 ± 11.9. The patients were divided into three groups: visual function questionnaire composite score increase > 10 (n = 17); no change (n = 8); and decrease (n = 6). In the dark-adapted full-field electroretinography responses, we found a significant difference between the three groups in the 0.01 b-wave amplitude (p = 0.05), the 10.0 b-wave amplitude (p = 0.04) and a near-significant difference in 3.0 a-wave amplitude (p = 0.09). Other dark-adapted responses (the 3.0 b-wave and 10.0 a-wave) did not show any significant differences between the three groups, and neither did the light-adapted responses.**

Conclusion: **Patients with low dark-adapted responses on full-field electroretinography preoperatively experience a decrease in subjective vision-related quality of life, suggesting that maintained rod function before cataract surgery may be important.**

Key words: age-related macular degeneration – cataract surgery – full-field electroretinography – visual function questionnaire

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Introduction

Age-related macular degeneration (AMD) is the most common cause of vision loss in the Western world (Wong et al. 2014), and cataract is the most common cause of blindness worldwide (World Health Organization 2002). Since these diseases often affect elderly people, many patients with AMD have coexisting cataract. Not only is there a growing prevalence of AMD in our ageing population (Sedeh et al. 2017), but the number of cataract operations is also expected to rise in the coming decades (Kessel 2011). The appropriate management of patients with AMD and cataract is therefore becoming increasingly relevant.

Cataract surgery improves vision-specific quality of life (Lamoureux

et al. 2011), but the decision to operate should not be taken lightly since a cataract operation is neither a risk- nor a cost-free procedure. Thorough consideration of the indication for surgery is warranted in each individual patient and it can be difficult to predict the visual gain from cataract surgery when the main cause of vision loss is macular disease. Visual acuity is a measure of macular function that is routinely used during preoperative assessment. According to the Danish national guidelines for the treatment of age-related cataract: 'Patients with age-related cataracts with a visual acuity greater than 0.5 should not be routinely offered surgery unless they are significantly symptomatic, as vision improvement will be modest and there is a risk of side-effects' (Sundhedsstyrelsen 2019). However, the routine use of preoperative visual acuity as sole criteria for surgical indication is not recommended as this method has low predictive value for the patient's satisfaction with their visual outcome (Taipale et al. 2018) and it is not cost-effective (Tuuminen 2020).

Despite the lack of an accurate visual prognosis, many patients with AMD and cataract are grateful for their surgery. They may report an improvement in their vision, even if this cannot be demonstrated by testing visual acuity alone (Lundström et al. 2002). This highlights the need for a subjective functional assessment, such as a visual function questionnaire, as an additional visual outcome measure in patients with AMD.

Full-field electroretinography (ffERG) is an objective measure of overall retinal function. Changes to ffERG in patients with AMD have been reported (Walter et al. 1999), and recent studies have shown an increased prevalence of peripheral retinal lesions in eyes with AMD-affected maculas compared with eyes with normal maculas: 82.7% and 33.3%, respectively (Forshaw et al. 2019). These findings suggest that ffERG as a marker of overall retinal function could be used as a prognostic indicator in patients with AMD undergoing cataract surgery. In this study, we wanted to find out if ffERG is predictive of the subjective visual outcome in patients with AMD undergoing bilateral cataract surgery. Additionally, we wanted to see how cataract surgery affects retinal function in patients with AMD.

Methods

Two groups of patients were studied prospectively: one group with age-related macular degeneration and a control group with healthy retina. All patients included in the study had bilateral age-related cataract. Patients were recruited consecutively from the outpatients' department of a university teaching hospital. An ophthalmologist performed a detailed ocular examination at the start of the study, assessing the visual significance of the cataract. All patients underwent cataract surgery using standard phacoemulsification technique with intraocular lens implantation. Criteria for exclusion were as follows: a retinal pathology other than AMD, amblyopia, glaucoma or any other intraocular disease affecting retinal function. Also excluded from the study, were patients with dementia who were unable to give their informed consent or fully participate in an interview.

One hundred and seventy-seven patients were studied pre- and postoperatively. Of these, twenty-nine were lost to follow-up. Seventeen patients were not interested in participating further in the study. Five patients died. Two patients declined the offer of cataract surgery. Three patients developed an intraocular pathology that warranted exclusion during the postoperative period, including one patient with central vein occlusion; one patient with retinal detachment and one patient from the healthy retina group who went on to develop neovascular AMD. Two patients were unable to participate in follow-up due to fall sequelae and cognitive decline. This left one hundred and forty-eight patients for analysis. Seventy-eight patients were diagnosed with AMD by fundus examination and retinal OCT, and seventy patients without vitreoretinal disease were included as a control group. If a patient had clinical evidence of AMD in one eye only, this was the eye included in our study. Of the patients with AMD, forty-six had neovascular AMD and thirty-two had the non-neovascular form of the disease.

Visual acuity

Visual acuity was measured after best monocular refraction pre- and postoperatively. It was not always possible to measure visual acuity and VFQ on the same day. In some cases, it was necessary to measure visual acuity at a separate visit. The mean visual acuity follow-up time after second-eye surgery was 4.07 ± 2.14 months. All visual acuity examinations were carried out according to departmental guidelines. The preferred method of measuring best-corrected visual acuity (BCVA) was the Early Treatment of Diabetic Retinopathy Study scale (ETDRS). In some patients, particularly those with healthy retina, BCVA had been recorded as a decimal. In these patients, decimal to ETDRS conversion was carried out using a decimal to ETDRS conversion table. Of the one hundred and forty-eight patients, seventy-five required decimal to ETDRS conversion: twenty-two with AMD and fifty-three with healthy retina. The eye with the highest ETDRS score was included in our analysis of visual acuity to better reflect overall visual function.

Visual function questionnaire-39

We measured vision-related quality of life using the National Eye Institute Visual Function Questionnaire-39 (VFQ-39) as a primary outcome measure. A validated Danish language version was used (Sørensen et al. 2011) The VFQ consists of thirty-nine items concerning the self-reported visual health status of an individual. One of the authors (T.R.J.F.) performed VFQ investigations prior to first-eye surgery and following second-eye surgery either in person or by telephone using a clear interview guide. The mean follow-up time after second-eye surgery was 4.12 ± 2.11 months. This follow-up time was 4.30 ± 2.46 months in the AMD group and 3.92 ± 1.66 months in the healthy retina group ($p = 0.258$, Independent samples *t*-test).

The questionnaire items regarding the self-perceived ability to perform a select activity used a scale to grade responses where: 1 = no difficulty at all; 2 = a small amount of difficulty; 3 = a moderate amount of difficulty; 4 = severe difficulty; and 5 = unable to perform the activity. The following sub-scores were generated: general health; general vision; ocular pain; near activities; distance activities; social functioning; vision-related mental health; vision-related role difficulties;

vision-related dependency; driving; colour vision; peripheral vision and an overall composite score. In this study, we included only the vision-specific sub-scores validated for use in patients with AMD (Sørensen et al. 2011). General health, peripheral vision and colour vision sub-scores were therefore excluded from our analysis and from the composite score calculation. After adjusting for the age difference between the two groups (Table 1) using linear regression, we found that ocular pain and driving were not independent of age and so these VFQ sub-scores were also excluded from our analysis.

Full-field electroretinography

Based on previous studies (Pedersen et al. 2010; Ma et al. 2015; Pedersen et al. 2016) and with a given significance value of 0.05 and a power of 80%, we calculated that 34 patients with AMD group were required for ffERG. Due to the risk of dropout, this number was increased to 40. We were unable to include nine patients, for the following reasons. Three patients were found to have additional ocular comorbidities (two patients had glaucoma and one patient had central serous chorioretinopathy). Two patients were not interested in participating further in the study. Two patients had their cataract operation postponed indefinitely. One patient had memory problems and could not participate in a VFQ assessment, and one patient was operated for cataract at a different centre and was therefore lost to follow-up. We measured objective retina function in 31 patients with AMD using ffERG (RETI-port/scan 21, Roland, Berlin) and Dawson–Trick–Litzkow fibre electrodes. Population demographics for these patients are shown in Table 2. ffERG was performed binocularly according to the International Society for the Clinical Electrophysiology of Vision (ISCEV); standard protocol (McCulloch et al. 2015) and ERG responses from the right eye were used as standard. Regarding the two main classes of photoreceptors in the human retina, the components of the ffERG are either rod- or cone-specific. In practice, it is difficult to test the rod and cone systems independently of one another, so dark and light adaptation are used during the procedure. We used only the ERG responses that would provide information regarding retinal function in eyes with AMD. We did not include oscillatory potentials in our study as these are more useful in the management of diabetic retinopathy. A table of the ERG responses included in this study and their cellular origins is provided (Table 3).

In additional to the main aim of our study, we performed ffERG in fifteen patients with AMD preoperatively and postoperatively to see how cataract surgery affects retinal function in eyes with AMD. We performed follow-up ERG at a separate visit; therefore, the mean time to follow-up was 4.67 ± 1.99 months.

Table 1. Population demographics by patient group.

	AMD group	Healthy retina group	p-value
Participants	78	70	–
Mean age (years) ± SD	78.9 ± 6.2	73.2 ± 7.8	<0.001*
Age range (years)	67–90	48–92	–
Sex (males/females)	24/54	29/41	0.18†
AMD phenotype (neovascular/non-neovascular)	32/46	_	<0.001†

AMD = age-related macular degeneration, SD = standard deviation.
* Independent samples *t*-test.
† Chi-squared test.

Statistical analysis

Statistical analysis was performed using SPSS 25 (IBM Corporation, Armonk, NY). Data distribution was assessed using the Shapiro–Wilk test of normality. In the case of normal distribution, parametric tests (Pearson's coefficient; independent samples *t*-test) were used. In the absence of normal distribution, non-parametric tests were used (Spearman's rho coefficient; Mann–Whitney *U*-test). Linear regression was used to account for any difference in VFQ sub-scores between the two patient groups that might be attributable to age, and a Holm–Bonferroni correction was performed to allow for the multiple comparisons involved in ffERG testing. About 95% confidence intervals were used, and a p-value of <0.05 was considered statistically significant.

Ethical considerations

Informed consent was obtained from all individual participants included in the study. The research project was carried out in accordance with the ethical standards of the Region Zealand ethics committee (SJ-618) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Results

In both the AMD group and the healthy retina group, there was an overall improvement in vision-related quality of life after cataract surgery, as measured by the VFQ composite score. The median changes in VFQ composite scores were 7.13 interquartile range (IQR): 14.02 in the AMD group and 12.91 IQR: 19.08 in the healthy retina group (p = 0.27; Mann–Whitney *U*-test). Other VFQ sub-score results are shown in Table 4. Population demographics and best-corrected visual

Table 2. Population demographics for patients with AMD randomized for full-field electroretinography

	Preoperative ffERG only	Pre- and postoperative ffERG	p-value
Participants	16	15	–
Mean age (years) ± SD	77.6 ± 5.9	79.3 ± 7.8	0.44*
Age range (years)	63–86	69–87	–
Sex (males/females)	5/11	5/10	0.9†
AMD phenotype (neovascular/non-neovascular)	12/ 4	6/ 9	0.21†

AMD = age-related macular degeneration, ffERG = full-field electroretinography, SD = standard deviation.
* Independent samples *t*-test.
† Chi-squared test.

Table 3. Median full-field electroretinography responses in patients with age-related macular degeneration pre- and postcataract surgery. After: McCulloch DL, et al. (2015) ISCEV Standard for full-field clinical electroretinography (2015 update). Doc Ophthalmol 130:1–12

					(n = 15)		
ERG test	Dark-adapted?	Light intensity (range) cd.s/m^{-2}	Background light intensity (range) cd/m^2	Type of response	Precataract surgery	Postcataract surgery	p-value
0.01 b-wave implicit time (ms)	Yes	0.01 (0.0063–0.016)	0.025 (0.02–0.03)	rod-initiated on pathways	98.30 IQR 7.00	100.50 IQR 11.40	0.23
0.01 b-wave amplitude (μV)	Yes	0.01 (0.0063–0.016)	0.025 (0.02–0.03)	rod-initiated on pathways	122.70 IQR 113.30	145.30 IQR 44.10	0.94
3.0 a-wave implicit time (ms)	Yes	3.0 (2.7–3.4)	7.5 (6.7–8.4)	photoreceptors & postreceptoral on pathways	24.40 IQR 5.80	20.80 IQR 5.90	0.57
3.0 a-wave amplitude (μV)	Yes	3.0 (2.7–3.4)	7.5 (6.7–8.4)	photoreceptors & postreceptoral on pathways	136.60 IQR 71.30	127.80 IQR: 70.20	0.37
3.0 b-wave implicit time (ms)	Yes	3.0 (2.7–3.4)	7.5 (6.7–8.4)	on & off bipolar cells	49.90 IQR 0.30	53.60 IQR 7.00	0.02
3.0 b-wave amplitude (μV)	Yes	3.0 (2.7–3.4)	7.5 (6.7–8.4)	on & off bipolar cells	241.40 IQR 166.30	224.20 IQR 118.20	0.65
10.0 a-wave implicit time (ms)	Yes	10 (8.9–11.2)	25 (18–34)	photoreceptors & postreceptoral on pathways	19.00 IQR 2.10	18.80 IQR 2.00	0.87
10.0 a-wave amplitude (μV)	Yes	10.0 (8.9–11.2)	25 (18–34)	photoreceptors & postreceptoral on pathways	155.60 IQR 67.30	140.20 IQR 102.90	0.49
10.0 b-wave implicit time (ms)	Yes	10 (8.9–11.2)	25 (18–34)	predominantly rod bipolar cells (on pathways)	49.90 IQR 3.20	57.10 IQR 7.40	<0.001*
10.0 b-wave amplitude (μV)	Yes	10 (8.9–11.2)	25 (18–34)	predominantly rod bipolar cells (on pathways)	211.10 IQR 161.60	239.70 IQR 138.30	0.84
3.0 a-wave implicit time (ms)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	cones with postreceptoral on & off pathways	18.50 IQR 4.20	18.20 IQR 1.80	0.81
3.0 a-wave amplitude (μV)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	cones with postreceptoral on & off pathways	24.70 IQR 6.50	18.30 IQR 13.20	0.23
3.0 b-wave implicit time (ms)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	on & off bipolar cells	35.50 IQR 3.00	34.30 IQR 2.90	0.02
3.0 b-wave amplitude (μV)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	on & off bipolar cells	71.10 IQR 29.7	87.40 IQR 28.30	0.51
30 Hz flicker implicit time (ms)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	cone systems with postreceptoral on & off pathways	31.90 IQR 3.80	32.20 IQR 3.50	0.87
30 Hz flicker amplitude (μV)	No	3.0 (2.7–3.4)	7.5 (6.7–8.4)	cone systems with postreceptoral on & off pathways	60.30 IQR 19.40	63.60 IQR 32.20	0.54

Median values for both groups provided.
cd/m^2 = candela per metre squared, cd.s/m^2 = candela-seconds per metre squared, Hz = Hertz, IQR = interquartile range, ms = milliseconds, μV = microvolts.
* Indicates difference is significant at the 0.05 level after Holm–Bonferroni correction.

acuities are shown in Tables 1 and 5, respectively.

There were two statistically significant correlations between the VFQ composite score and ffERG in patients with AMD. These were the dark-adapted 3.0 a-wave implicit time, a marker of rod and dark-adapted cone function (rho 0.417; p = 0.02) and the light-adapted 3.0 b-wave amplitude, a marker of the cone-driven response (rho 0.373; p = 0.04). However, these results were no longer significant after we performed a Holm–Bonferroni correction to allow for multiple comparisons.

In order to study the predictive ability of ffERG, we divided the patients with AMD into three subgroups: VFQ composite increase >10 (n = 17); no change (n = 8); and decrease (n = 6). In the dark-adapted ffERG responses, we found a significant difference between the three groups in the 0.01 b-wave amplitude (p = 0.05) and 10.0 b-wave amplitude (p = 0.04) and a near-significant difference in 3.0 a-wave amplitude (p = 0.09). Other dark-adapted responses (the 3.0 b-wave and 10.0 a-wave) did not show any significant differences between the three groups, and neither did the light-adapted responses. The differences in the 0.01 b-wave amplitude and the 10.0 b-wave amplitude between the AMD subgroups and are shown in Fig. 1 and 2. Additional figures representing linear regression between these ffERG

Table 4. Median visual function questionnaire sub-scores by patient group.

VFQ sub-score	Patient group: AMD (n = 78)	Patient group: Healthy retina (n = 70)	p-value
preoperative composite	76.55 (IQR 20.42)	89.85 (IQR 22.38)	0.17
postoperative composite	89.35 (IQR 24.98)	103.96 (IQR 11.49)	0.004*
Δ composite	7.13 (IQR 14.02)	12.91 (IQR 19.08)	0.27
preoperative general vision	55.00 (IQR 25.00)	60.00 (IQR 25.00)	0.25
postoperative general vision	80.00 (IQR 21.25)	85.00 (IQR 15.00)	<0.001*
Δ general vision	15.00 (IQR 26.25)	25.00 (IQR 20.00)	0.05*
preoperative near activities	62.50 (IQR 25.00)	70.80 (IQR 27.08)	0.02*
postoperative near activities	87.50 (IQR 33.33)	87.50 (12.50)	0.002*
Δ near activities	12.50 (IQR 23.75)	16.70 (IQR 25.00)	0.4
preoperative distance activities	70.80 (IQR 37.50)	81.30 (IQR 25.00)	0.07
postoperative distance activities	87.50 (IQR 34.37)	93.75 (IQR 12.50)	<0.001*
Δ distance activities	8.30 (IQR 20.43)	12.50 (IQR 26.23)	0.18
preoperative vision-specific mental health	65.00 (IQR 32.19)	75.00 (IQR 31.25)	0.09
postoperative vision-specific mental health	85.00 (IQR 30.00)	90.00 (IQR 11.25)	0.01*
Δ vision-specific mental health	14.40 (26.25)	15.00 (25.00)	0.6
preoperative social functioning	96.00 (IQR 19.00)	100.00 (IQR 19.00)	0.27
postoperative social functioning	100.00 (IQR 16.67)	100.00 (IQR 0.00)	0.009*
Δ social functioning	0.00 (IQR 8.00)	0.00 (IQR 17.00)	0.51
preoperative vision-related role difficulties	81.00 (IQR 37.75)	81.00 (IQR 37.81)	0.24
postoperative vision-related role difficulties	96.88 (IQR 31.25)	100.00 (IQR 12.50)	0.08
Δ vision-related role difficulties	13.00 (25.00)	13.00 (IQR 19.00)	0.84
preoperative vision-related dependency	94.00 (IQR 19.00)	100.00 (IQR 9.00)	0.21
postoperative vision-related dependency	100.00 (IQR 12.50)	100.00 (IQR 1.56)	0.01
Δ vision-related dependency	0.00 (IQR 9.25)	0.00 (IQR 6.00)	0.86

AMD = age-related macular degeneration; IQR = interquartile range; Δ = change in VFQ sub-score.
* Indicates difference is significant at the $p < 0.05$ level.

responses and the change in VFQ composite score in patients with AMD have been created. These are available as Figures S1 and S2.

Correlations between pre- and postoperative visual acuity and change in VFQ composite score were not significant in either the AMD group or the group with healthy retina, as follows: healthy retina group: preoperative visual acuity (rho −0.135, p = 0.27) and postoperative visual acuity (rho 0.167, p = 0.18); AMD group: preoperative visual acuity (rho 0.103, p = 0.37) and postoperative visual acuity (rho 0.219, p = 0.06).

With regard to the secondary aim of our study, which was to see how cataract surgery affects retinal function in patients with AMD, the postoperative 10.0 b-wave implicit time was prolonged compared to baseline (p = 0.001) (Table 3; Fig. 3). This finding suggests that cataract surgery in patients with AMD may affect rod system function.

Table 5. Mean visual acuities in ETDRS letters by patient group

	Patient group: AMD (n = 78)	Patient group: Healthy retina (n = 70)	p-value (Independent Samples *t*-test)
Best-seeing eye at baseline ± SD	67.90 ± 14.78 Range: 20 to 87	79.01 ± 7.00 Range: 60 to 90	<0.001*
Follow-up ± SD	71.50 ± 14.84 Range: 21 to 90	82.09 ± 5.56 Range: 60 to 90	<0.001*
Gain ± SD	3.75 ± 11.67 Range: −29 to 39	2.97 ± 8.17 Range: −17 to 35	0.65
Mean follow-up time (months) ± SD	4.28 ± 2.46 Range: 1 to 15	3.84 ± 1.68 Range: 1 to 10	0.2

AMD = age-related macular degeneration; ETDRS = Early Treatment of Diabetic Retinopathy Study; SD = standard deviation. *Indicates difference is significant at the $p < 0.05$ level.

Discussion

Age-related macular degeneration (AMD) and cataract can both lead to a loss of visual acuity that can cause a deterioration in quality of life (Lamoureux et al. 2011). It can therefore be difficult to predict the visual outcome of cataract surgery in patients with AMD and patients' visual outcomes may not meet their expectations. However, many patients with AMD and cataract are grateful for having the chance of surgery and may even say that their vision has improved, even though visual acuity testing cannot demonstrate this (Lundström et al. 2002). In these patients, 'Cataract surgery is offered if it is the ophthalmologist's best clinical judgement that this will produce a significant subjective visual improvement, providing that the patient does not have unrealistically high expectations of the outcome of the operation' (Sundhedsstyrelsen 2019). Patient-reported subjective outcomes are therefore a highly relevant source of information when monitoring the effect of cataract surgery in patients with AMD.

Much has been written about the risks and benefits of cataract surgery in patients with AMD (Casparis et al. 2017). In particular, there is evidence to show that cataract surgery may be associated with increased choroidal neovascular membrane activity in exudative AMD (Daien et al. 2018). It is therefore recommended that cataract surgery should be performed after a sufficiently long exudative-free period to prevent the recurrence of exudation (Grixti et al. 2014).

Although improvement in visual functioning is more likely in cases of severe cataract, it is recommended cataract surgery be performed early in patients with AMD (Lamoureux et al. 2007; Pham et al. 2007) before there is significant loss of visual acuity due to retinal disease (Lamoureux et al. 2011). In such instances when there has not been such timely intervention, patients with AMD may have such low preoperative visual acuities that cataract

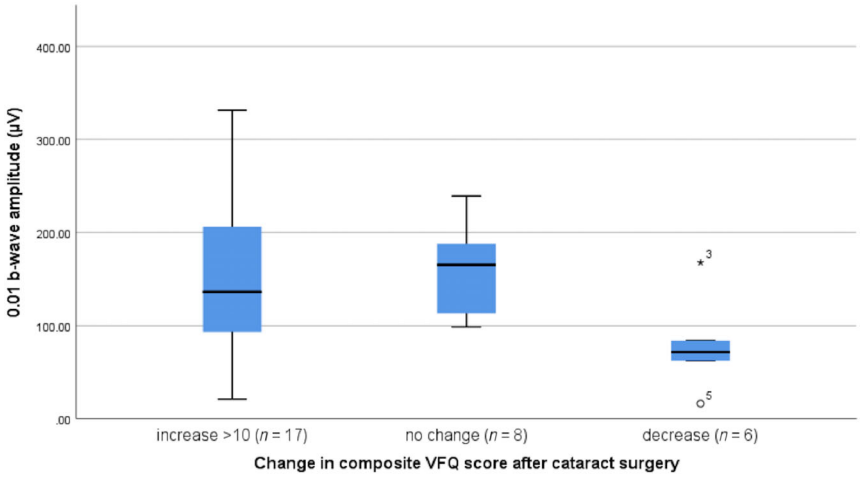

Fig. 1. Boxplot showing preoperative 0.01 b-wave amplitude in patients with AMD and change in composite VFQ score after cataract surgery.

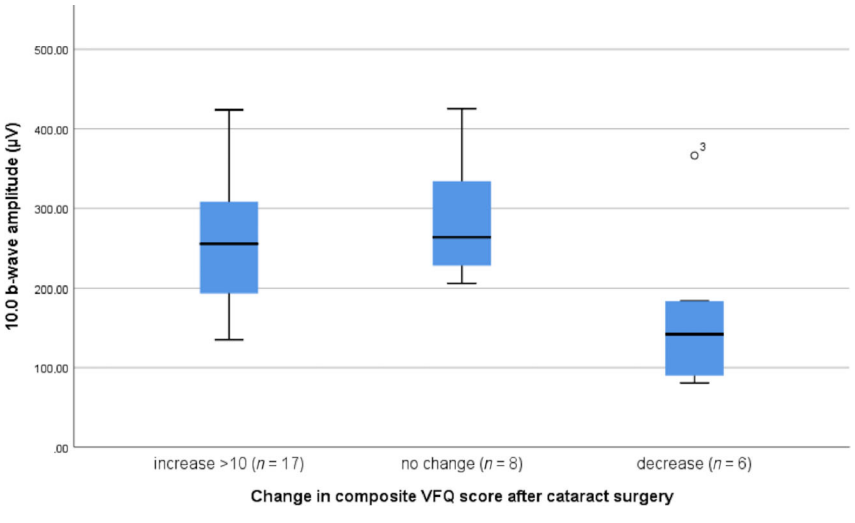

Fig. 2. Boxplot showing preoperative 10.0 b-wave amplitude in patients with AMD and change in composite VFQ score after cataract surgery.

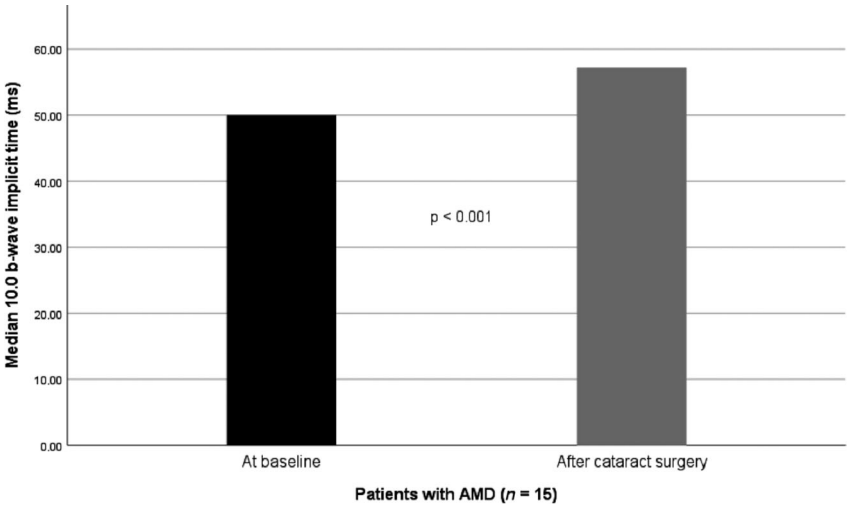

Fig. 3. Bar chart showing the difference in median 10.0 b-wave implicit time after cataract surgery in patients with AMD compared with baseline.

surgery is offered as an attempt to help improve other areas of visual function, including colour and contrast (Kessel et al. 2016).

Visual acuity is a measure of central macular function and therefore does not correlate well with the subjective outcome of cataract surgery in patients with AMD (Taipale et al. 2018), a finding that is supported by our results. Furthermore, visual acuity does not provide any information regarding peripheral retinal function and the quality of life benefits this provides. Peripheral function is especially important in patients with AMD who rely on their retinal periphery for mobility and other activities of daily living (Sunness et al. 1985). ffERG is a similarly clinic-based objective test of visual function that is non-invasive and acceptable to the patient. Moreover, it is a measure of overall retinal response. ffERG is therefore useful in assessing retinal function in AMD (Gerth 2009).

There are approximately 100 million rod photoreceptors and only 4.6–6.0 million cones in the human retina (Quinn et al. 2019). Rods are affected earlier and more severely than cones in AMD (Curcio et al. 1996) and although the macula is rod-rich, particularly in the area of perifovea, the vast majority of rods are found in the peripheral retina. The peripheral retina has been shown to contribute towards vision-related quality of life in terms of locomotion (Marigold 2008), mobility (Nakayama, 1985; Vargas-Martin & Peli 2006) and postural stability (Black et al. 2008). Peripheral retinal function is also a better predictor for driving ability amongst elderly persons than visual acuity (Huestegge & Bockler 2016; Peli et al. 2016).

Our results show that the AMD subgroup with the most improvement in their vision-related quality of life had better responses in the 0.01 and 10.0 ffERG preoperatively, while the subgroup that experienced a worsening of their vision-related quality of life had poor dark-adapted ffERG responses. Moreover, the 10.0 b-wave implicit time marker of mainly rod system function worsened significantly from baseline in patients with AMD following cataract surgery ($p < 0.001$).

The reason for this difference in 10.0 b-wave implicit time is unclear. However, we do know that increased levels of inflammatory immune mediators are

found in pseudophakic eyes for an extended period of time (Jakobsson et al. 2015). These sustained elevated levels are believed to be related to the pseudophakic status of the eye itself, and not only as residuals of an inflammatory reaction induced by the surgical procedure. Elevated levels of immune mediators in the vitreous may lead to a local inflammatory response that can contribute to AMD (Whitcup et al. 2013). These findings support the assertion that the decision to offer cataract surgery to patients with AMD should be a considered one; however, any potential risk to rod function must also be weighed up against the overall improvement in vision-related quality of life that is likely to benefit these patients.

Limitations of this study should be considered. We did not perform formal grading of AMD; therefore, our results reflect the heterogeneous nature of the disease. Likewise, we did not include information about the grade or morphology of cataract in our study. Lens opacities can be of mixed morphology and a good deal of inter-assessor variability exists with regard cataract grading (World Health Organization 2002). Moreover, the VFQ-39 does not address the issue of visual aids. Questions regarding the use of a hand lens or similar magnifying devices would provide more information regarding visual disability and could potentially reveal benefits of cataract surgery that are not addressed by the questionnaire in its current form (Lundström et al. 2002). ffERG also has its disadvantages. The equipment is expensive and it requires a trained operator. Furthermore, ffERG is time-consuming as dark adaptation alone takes at least twenty minutes. Abbreviated ffERG protocols are under development, but more research studies using these protocols are required.

In conclusion, ffERG appears to be predictive of overall subjective visual outcome of bilateral cataract surgery in patients with AMD. We therefore suggest that ffERG be considered in patients with late AMD and cataract, in whom the visual outcome of cataract surgery can be unreliable. In addition, rod function in patients with AMD seems to be vulnerable to the effects of cataract surgery, but longer-term follow-up is recommended.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Scatter plot showing linear regression between preoperative 0.01 b-wave amplitude in patients with AMD and change in VFQ composite score after cataract surgery.

Figure S2. Scatter plot showing linear regression between preoperative 10.0 b-wave amplitude in patients with AMD and change in VFQ composite score after cataract surgery.