

1 **Effect of vitrectomy for epiretinal membrane on visual function and**
2 **vision-related quality of life**

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23 Epiretinal membrane (ERM) is a non-vascular fibrocellular proliferation that
24 develops on the surface of the internal limiting membrane, resulting in retinal
25 wrinkling and distortion. The prevalence of ERM formation is 5.3% to 18.5% of
26 the population.¹⁻⁴ The first report of successful removal of ERM was published
27 by Machemer in 1978.⁵ Since then, favorable visual outcome has been
28 achieved in the majority of cases postoperatively.⁶⁻¹⁰ Visual acuity improves in
29 many patients after successful removal of ERM, whereas it has been reported
30 that metamorphopsia can still be present even if ERM was successfully
31 removed with improvement of visual acuity.¹¹ Metamorphopsia occurring in eyes
32 with ERM is one of the most common conditions responsible for deterioration in
33 vision-related quality of life (VR-QOL); however, relatively little attention has
34 been paid to the relationship between metamorphopsia and VR-QOL in patients
35 with ERM.

36 In ophthalmology, traditional objective clinical outcome measures such as
37 visual acuity are increasingly being complemented with assessment of patients'
38 perception of their visual function and quality of life. The National Eye Institute
39 25-Item Visual Function Questionnaire (VFQ-25) is a VR-QOL instrument
40 designed to assess patients' perception of their visual function and QOL.¹² The
41 VFQ-25 has been used to track the outcome of many ocular diseases such as
42 cataract, glaucoma, age-related macular degeneration, diabetic retinopathy,
43 macular hole, rhegmatogenous retinal detachment, and keratoconus.¹³⁻²²

44 A recent study using VFQ-25 demonstrated that vitrectomy for ERM had a
45 beneficial effect on patients' subjective perception of visual function, and the
46 VFQ-25 responses correlated with visual acuity, but not with contrast sensitivity
47 and metamorphopsia in patients with ERM.²³ This study used the Amsler charts,
48 which have been widely used to detect and evaluate metamorphopsia in
49 patients with macular diseases.²⁴⁻²⁵ With the Amsler charges, however, it is
50 difficult to quantify the severity of metamorphopsia because the patients have to
51 self describe the degree of image distortion. An M-CHARTS (Inami Co., Tokyo,
52 Japan) is an instrument which can easily and quantitatively evaluate the degree
53 of metamorphopsia associated with macular diseases, with the patients only to
54 answer whether the line is distorted or not.²⁶⁻²⁷ The purpose of this study was to
55 evaluate VR-QOL in patients with ERM, and to investigate the relationship
56 between VR-QOL and visual function including metamorphopsia.

57 **Methods**

58 **Patients**

59 We included 28 eyes of 28 consecutive patients with ERM who were
60 undergoing pars plana vitrectomy at Tsukuba University Hospital between July
61 28, 2005, and February 20, 2007. There were 13 males and 15 females, and their
62 age averaged 66.7 ± 8.5 years (mean \pm SD). Twenty-six age-matched subjects
63 served as normal controls (12 males and 14 females, age 64.1 ± 10.4 years).
64 This study was conducted in accordance with the tenets of the Declaration of
65 Helsinki, and the study protocol was approved by the institutional review
66 committees. Prior to inclusion in the study, the nature of the study was explained
67 to all patients, and their written informed consent was obtained. ERM was defined
68 as a translucent or semi-translucent membrane with macular thickening involving
69

70 the center of the macula, with or without distortion and wrinkling of the inner
71 retinal surface on biomicroscopy and optical coherence tomography (OCT).
72 Exclusion criteria included patients with a previous history of vitreoretinal surgery
73 and ophthalmic disorders, except for mild refractive errors and mild cataract.
74 Eyes with secondary ERM due to retinal vascular disease, uveitis, trauma, and
75 retinal breaks were also excluded from the study.

76 Data were collected for logMAR best-corrected visual acuity (BCVA), letter
77 contrast sensitivity, and metamorphopsia preoperatively and at 3 months
78 postoperatively. Letter contrast sensitivity was measured using the CSV-1000LV
79 chart (Vector Vision, Columbus, Ohio).

80 The severity of metamorphopsia was evaluated by the M-Charts. M-Charts
81 consist of 19 dotted lines with dot intervals ranging from 0.2 degrees to 2.0
82 degrees of visual angle. If the straight line is substituted with a dotted line and the
83 dot interval is changed from fine to coarse, the distortion of the line decreases
84 with the increasing dot interval, until the dotted line appears straight.^{26,27} At first,
85 vertical straight lines (0 degrees) were shown to the patient. If the patient
86 recognized the straight line as straight, the metamorphopsia score was 0. If the
87 patient recognized the straight line as irregular or curved, then subsequent pages
88 of M-Charts, in which the dot intervals of the dotted line change from fine to
89 coarse, were shown one after another. When the patient recognized a dotted line
90 as being straight, the visual angle that separated the dots was considered to
91 represent his/her metamorphopsia score for vertical line. Also, the M-Charts were
92 rotated 90 degrees and the same test is performed using horizontal lines. The
93 examinations were repeated three times for each subject to evaluate the
94 reproducibility of the test, and their mean was used for data analyses. The
95 examination was performed at 30 cm and the refraction of the eye was exactly
96 corrected for this distance.

97 Central macular thickness was measured using OCT (Stratus OCT 3000,
98 Carl Zeiss Ophthalmic Systems-Humphrey Division, Dublin, CA, USA)
99 preoperatively and at 3 months postoperatively. OCT was performed with the fast
100 macular thickness map mode, and central macular thickness was obtained from
101 the retinal map analysis function.

102

103 ***Surgical procedures***

104 All surgeries were performed by a single surgeon (F.O.) under sub-Tenon
105 local anesthesia. The lens was removed by phacoemulsification and intraocular
106 lens implantation when required, following which vitrectomy was performed. The
107 surgical technique used was standard 20-gauge three-port pars plana vitrectomy.
108 With conventional contact lenses, posterior hyaloid separation and removal of the
109 posterior vitreous membrane were performed. The ERM was engaged and
110 removed from the macula with a pick and intraocular forceps. Peripheral retinal
111 examination with scleral depression was performed to search for a retinal tear or
112 dialysis. Air-fluid exchange was performed if iatrogenic retinal tear and/or
113 rhegmatogenous retinal detachment were identified intraoperatively.

114

115 ***VFQ-25***

116 The patients answered VFQ-25 preoperatively and 3 months

117 postoperatively. Preoperative VFQ-25 was administered 1-2 days before surgery.
118 The research staff explained the questionnaire to the patients, verbally
119 administered instructions, and provided assistance when required. The
120 completed questionnaires were reviewed for missing data by the research staff.
121 Prior to surgery, all the missing items were incorporated by the subjects
122 themselves.

123 The VFQ-25 comprises 25 items wherein patients are expected to assess
124 the level of difficulty of particular visual symptoms or day-to-day activities. Each
125 item is assigned to one of the 12 subscales, namely, general health, general
126 vision, ocular pain, near activities, distance activities, social functioning, mental
127 health, role difficulties, dependency, driving, color vision, and peripheral vision.
128 The subscales are scored on a 0- to 100-point scale, where 100 indicates the
129 highest possible function or the minimal subjective impairment. The VFQ-25
130 composite score is calculated as the unweighted average response to all items,
131 excluding the questions on general health.¹² The VFQ-25 used in this study was a
132 Japanese version, with modifications to suit the Japanese culture and lifestyle.
133 The modified NEI VFQ-25 questionnaire has been assessed for reliability and
134 validity, and it has been proven to accurately measure VR-QOL in Japanese
135 individuals.¹³

136

137 **Statistical analysis**

138 The mean scores and standard deviations were calculated for each VFQ-25
139 subscale as well as composite score, in patients with ERM and normal controls.
140 The Mann-Whitney *U* test was performed to compare each subscale score and
141 composite score between ERM patients and normal controls. The Wilcoxon
142 signed-ranks test was used to compare preoperative and postoperative results.
143 The relationship between the questionnaire scores and visual acuity, contrast
144 sensitivity, metamorphopsia, central macular thickness, and age were examined
145 by the Spearman rank correlation test. All tests of association were considered
146 statistically significant if $P < 0.05$. The analyses were carried out using StatView
147 (version 5.0, SAS Inc., Cary, NC, USA).

148

149 **Results**

150 Among the 28 patients with ERM, 8 were pseudophakic and 20 were phakic.
151 Eighteen of 20 patients who had slight or moderate lens opacity underwent
152 combined cataract surgery and vitrectomy to avoid cataract formation following
153 vitrectomy. No significant intraoperative and postoperative complications were
154 observed, such as retinal detachment, choroidal detachment, subretinal
155 hemorrhage, cataract formation, and infection. Air-fluid exchange was performed
156 in 7 patients because of intraoperative identification of retinal tears. In 2 patients,
157 intraocular pressure elevated above than 25 mmHg, and antihypertensive agent
158 was administered. These patients responded to treatment, and antihypertensive
159 agent was discontinued within 3 days.

160 Vitrectomy significantly improved logMAR BCVA from 0.495 ± 0.293
161 preoperatively to 0.245 ± 0.294 postoperatively ($P < 0.0001$). Sixteen patients
162 (57.1%) gained 2 or more early treatment diabetic retinopathy study (ETDRS)
163 lines. No change in logMAR BCVA was observed in 11 eyes (39.3%), and vision

164 decreased by 1 or more lines in 1 patient (3.6%). The postoperative reduction in
165 visual acuity was attributed to retinal atrophy of the macula. Twenty-seven
166 (96.4%) patients underwent ERM surgery in their worse-seeing eye. LogMAR
167 BCVA in the fellow eye was 0.062 ± 0.191 . The letter contrast sensitivity
168 significantly increased from 14.6 ± 5.3 preoperatively to 18.6 ± 5.5
169 postoperatively ($P < 0.0001$). The severity of metamorphopsia also significantly
170 improved from 0.79 ± 0.47 preoperatively to 0.33 ± 0.44 postoperatively ($P =$
171 0.0005). Central macular thickness also significantly improved from 440 ± 106
172 μm to $315 \pm 89 \mu\text{m}$ ($P < 0.0001$).

173 The results of VFQ-25 questionnaire pre- and postoperatively are
174 summarized in Table 1. The preoperative VFQ-25 composite score was
175 significantly lower in the ERM patients than in the normal controls ($P < 0.0001$).
176 The preoperative subscale scores were significantly lower in the ERM patients
177 than in the normal controls in all subscales, except for general health and ocular
178 pain. Membrane peeling surgery significantly improved VFQ-25 composite score
179 ($P < 0.0001$) and the scores in 10 out of 12 subscales, except for general health
180 and peripheral vision. However, postoperative VFQ-25 composite score still
181 remained significantly lower in the ERM patients than in the normal controls ($P <$
182 0.0001).

183 The preoperative VFQ-25 composite score exhibited significant correlation
184 with the severity of preoperative metamorphopsia ($r = -0.411$, $P < 0.05$, Fig 1). No
185 correlation was observed between preoperative VFQ-25 composite score and
186 preoperative logMAR BCVA ($r = 0.018$, $P = 0.928$), letter contrast sensitivity ($r =$
187 0.092 , $P = 0.659$), central macular thickness ($r = 0.162$, $P = 0.415$), and age ($r =$
188 -0.010 , $P = 0.960$).

189 The postoperative VFQ-25 composite score exhibited significant correlation
190 with the severity of postoperative metamorphopsia ($r = -0.393$, $P < 0.05$, Fig 2)
191 and postoperative logMAR BCVA ($r = -0.373$, $P < 0.05$), but not with letter
192 contrast sensitivity ($r = 0.170$, $P = 0.411$). The correlation between the
193 postoperative VFQ-25 composite score and central macular thickness was
194 borderline significance ($r = -0.372$, $P = 0.051$).

195 Changes in VFQ-25 composite score significantly correlated with changes
196 in the severity of metamorphopsia ($r = -0.411$, $P < 0.05$, Fig 3). There was no
197 significant correlation between changes in VFQ-25 composite score and changes
198 in logMAR BCVA ($r = -0.076$, $P = 0.705$), letter contrast sensitivity ($r = 0.267$, $P =$
199 0.189), and central macular thickness ($r = 0.05$, $P = 0.804$).

200 LogMAR BCVA in the fellow eye did not show any significant relationship
201 with preoperative VFQ-25 composite score ($r = 0.115$, $p = 0.563$), postoperative
202 VFQ-25 composite score ($r = 0.156$, $p = 0.432$), and changes in VFQ-25
203 composite score ($r = -0.178$, $p = 0.369$).

204 205 Discussion

206 In the present study, VFQ-25 composite score and all subscale scores,
207 except for general health and ocular pain, were significantly deteriorated in
208 patients with ERM compared to the normal controls. Vitrectomy to remove ERM
209 significantly improved not only visual acuity, contrast sensitivity, and central
210 macular thickness, but also VFQ-25 scores. Previous studies have reported that

211 the mean VFQ-25 composite scores after vitreoretinal surgery in patients with
212 macular hole, rhegmatogenous retinal detachment, proliferative diabetic
213 retinopathy, and age-related macular degeneration were 82.4,¹⁸ 80.3,²¹ 68.5,²⁰
214 and 54.4,¹⁷ respectively. The mean VFQ-25 composite score after ERM surgery
215 in this study (77.9) was similar to those after macular hole and rhegmatogenous
216 retinal detachment surgery and higher than those after vitrectomy for proliferative
217 diabetic retinopathy and age-related macular degeneration.

218 ERM surgery significantly improved the mean VFQ-25 composite score
219 from 66.2 preoperatively to 77.9 postoperatively. This improvement of VR-QOL in
220 patients with ERM was higher than these in macular hole and age-related
221 macular degeneration.¹⁷⁻¹⁸ Gupta OP et al. demonstrated that ERM surgery was
222 a very cost-effective procedure using quality-adjusted-life-years (QALYs)
223 methods.²⁸ The cost-effectiveness ratio for ERM surgery was higher than
224 macular hole surgery. Thus, ERM surgery improved VR-QOL and was
225 cost-effective intervention compared other vitreoretinal surgeries.

226 As shown in the results, even after successful membrane peeling surgery in
227 patients with ERM, VR-QOL remained at a lower level than the normal controls.
228 This finding is consistent with the results of previous case-control studies on
229 VR-QOL for retinal disorders such as rhegmatogenous retinal detachment and
230 proliferative diabetic retinopathy.^{20,21}

231 In our study, VR-QOL was significantly associated with the severity of
232 metamorphopsia before and after surgery. In addition, changes in VR-QOL were
233 associated with changes in metamorphopsia. This observation is not consistent
234 with the results of previous studies in patients with ERM and macular hole.^{23,24}
235 Ghazi-Nouri et al. showed that VFQ-25 responses correlated with visual acuity
236 but not with contrast sensitivity and metamorphopsia in patients with ERM.²³
237 Tranos et al. investigated VR-QOL in patients with macular hole and observed
238 that postoperative VFQ-25 responses significantly correlated with postoperative
239 metamorphopsia, whereas preoperative and change in VFQ-25 composite score
240 by surgery were not associated with the degree of metamorphopsia.²⁴ Such
241 discrepancy between our and previous studies may be attributable to the different
242 methods of evaluating metamorphopsia. In previous studies, the severity of
243 metamorphopsia was graded using the Amsler charts, which have been widely
244 used to detect metamorphopsia in macular diseases.^{24,25} As the methods of
245 evaluating metamorphopsia are numbered distorted squares on the Amsler chart,
246 the result indicates mainly extent of central metamorphopsia. On the other hand,
247 the M-Charts have been used to quantify severity of metamorphopsia in patients
248 with ERM and macular hole.^{26,27,29} The M-Charts can evaluate frequency
249 components of distortion in metamorphopsia. The fine high frequency component
250 of metamorphopsia which is usually observed in mild ERM is detect by fine dotted
251 lines, however, it is not detected by coarse dotted lines. In severe ERM, the large
252 amplitude and low frequency components of metamorphopsia increase, so it is
253 easy to detect by all kinds of lines, including coarse dotted lines. Thus, VR-QOL
254 seems to be associated with the frequency components of distortion in
255 metamorphopsia, but not with extent of central metamorphopsia.

256 The preoperative VFQ-25 composite score significantly correlated with the
257 severity of preoperative metamorphopsia, but not with preoperative visual acuity.

258 In addition, changes in VFQ-25 composite score correlated with changes in
259 metamorphopsia, but not with changes in visual acuity. Many studies have shown
260 that visual acuity correlates with VR-QOL in patients with vitreoretinal disorders
261 such as ERM, macular hole, proliferative diabetic retinopathy, age-related
262 macular degeneration, and central retinal vein occlusion.^{18,20,23,30-32} The
263 preoperative visual acuities in this study were relatively good with a mean
264 preoperative logMAR BCVA of 0.495 and a mean postoperative logMAR BCVA
265 of 0.295. These good preoperative visual acuities may also explain why VFQ-25
266 did not correlate with visual acuity since patients had not lost that much vision
267 before they had surgery. Wong JG et al. interviewed 91 patients with ERM to
268 assess the influence of surgery on functional vision.³³ They reported that
269 frequency of patients with ERM complained of moderate to severe distortion
270 decreased from 80% to 30% by surgery. On the other hand, the frequency of
271 patients complained of visual disturbance decreased from 55% to 30% by
272 surgery. Bouwens MD et al. quantitatively evaluated the severity of
273 metamorphopsia in patients undergoing ERM using Sine Amsler Chart and
274 observed that metamorphopsia improved in 82% patients, while visual acuity
275 improved only in 48% by surgery.¹¹ Judging from these previous and our findings,
276 it seems that ERM peeling surgery is highly effective in improving
277 metamorphopsia, but significant improvement of visual acuity may not be
278 expected in many cases. In practice, surgical indication and outcome measures
279 are judged mainly based on visual acuity parameters.⁶⁻¹⁰ Postoperatively,
280 however, many patients complain of significant symptoms other than blurred
281 vision, especially distortion, which is not adequately reflected by visual acuity
282 assessment. In light of VR-QOL, we must pay more attention to the degree of and
283 changes in metamorphopsia in patients with ERM.

284 Our study has several limitations. First, there may be some placebo effect
285 for taking the VFQ-25 before and after surgery. The patients obviously know they
286 had surgery and may have answered the VFQ-25 questions more positively
287 following surgery due to an expectation that they would benefit from the surgery.
288 This cannot be avoided by the study design, but could account for some of the
289 improvements in the VFQ-25. Second, the sample size in our study was rather
290 small, and that may have influenced the relationship between visual function and
291 VFQ-25 scores. Third, postoperative follow-up was short. We evaluated the
292 patients at 3 months postoperatively. A long-term follow-up study in vitrectomy for
293 ERM reported that visual improvement was archived in 43% of eyes at 6 to 12
294 months, in 54% at 1 to 2 years, and 60% at 2 to 3 years.¹⁰ Future studies with a
295 larger sample size and longer follow-up period will further facilitate our
296 understanding of the relationship between VR-QOL and visual function in patients
297 undergoing surgery for ERM.

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299
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305 review of the manuscript (T.O.); and approval of the manuscript (F.O., Y.O., T.H.,
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307 University Hospital and was in adherence to the tenets of the Declaration of
308 Helsinki.
309

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408

409 **Figure legends**

410 Figure 1. Preoperative National Eye Institute 25-Item Visual Function
411 Questionnaire (VFQ-25) composite score vs. severity of preoperative
412 metamorphopsia in patients with epiretinal membrane.

413
414 Figure 2. Postoperative National Eye Institute 25-Item Visual Function
415 Questionnaire (VFQ-25) composite score vs. severity of postoperative
416 metamorphopsia in patients with epiretinal membrane.

417
418 Figure 3. Changes in National Eye Institute 25-Item Visual Function
419 Questionnaire (VFQ-25) composite score vs. changes in severity of
420 metamorphopsia after epiretinal membrane peeling surgery.

421