

1 **Vision-related quality of life and visual function following vitrectomy for**  
2 **proliferative diabetic retinopathy**

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24 Diabetic retinopathy is one of the most common causes of blindness in  
25 industrialized countries.<sup>1</sup> It can lead to severe visual loss by causing retinal  
26 detachment, macular edema, vitreous hemorrhage, and neovascular glaucoma.  
27 Pars plana vitrectomy is known to be effective in preserving and restoring visual  
28 function in patients with proliferative diabetic retinopathy (PDR).<sup>2-6</sup> Despite the  
29 large body of published material regarding the visual outcome of vitrectomy for  
30 PDR, the impact of this surgical intervention on patients' quality of life (QOL) has  
31 not been reported in literature.

32 In ophthalmology, traditional objective clinical outcome measures such as  
33 visual acuity are increasingly being complemented with assessment of patients'  
34 perception of their visual function and quality of life. The National Eye Institute  
35 25-Item Visual Function Questionnaire (VFQ-25) is a vision-related QOL  
36 (VR-QOL) instrument designed to assess patients' perception of their visual  
37 function and QOL.<sup>7</sup> Prior studies have reported the influence of vitrectomy on  
38 VR-QOL in patients with macular hole,<sup>8-10</sup> epiretinal membrane,<sup>11</sup> and  
39 age-related macular degeneration.<sup>12,13</sup> The purpose of this study was to evaluate  
40 the VR-QOL and visual function following vitrectomy for PDR by using VFQ-25.

41

## 42 **Methods**

43 We analyzed 51 eyes of 51 patients with PDR who were scheduled to  
44 undergo pars plana vitrectomy. Their age averaged  $55.8 \pm 12.1$  years (mean  $\pm$   
45 SD), and there were 21 males and 30 females. Forty-six eyes of 46 age-matched  
46 subjects served as normal controls. The current study was a prospective,  
47 interventional, consecutive, comparative case series, and was conducted in  
48 accordance with the Declaration of Helsinki, and the study protocol was approved  
49 by the Institutional Review Committee of Tsukuba University Hospital. Prior to  
50 inclusion in the study, all patients provided written informed consent after the  
51 nature of the study was explained to them.

52 The surgery was performed in our clinic by an experienced vitreoretinal  
53 surgeon from June 2005 through September 2006. The indications for vitrectomy  
54 included recurrent or persistent nonclearing vitreous hemorrhage (11 eyes),  
55 traction or combined traction/rhegmatogenous retinal detachment (17 eyes), and  
56 adherent posterior hyaloid causing excessive macular traction (23 eyes).  
57 Exclusion criteria included patients with previous history of ocular surgery and  
58 ophthalmic disorders, except for mild refractive errors and mild cataract. Patients  
59 who had undergone vitrectomy for bilateral eyes within at least three months were  
60 also excluded. The presence and severity of cataract were graded using the lens  
61 opacities classification system III (LOCS III) reference standards.<sup>14</sup> The following  
62 preoperative information was obtained for each patient: age, gender, duration of  
63 diabetes mellitus (DM), serum HbA1c, and fasting plasma glucose. Data on the  
64 patients' characteristics are presented in Table 1.

65 LogMAR best-corrected visual acuity (BCVA), letter contrast sensitivity, and  
66 the severity of metamorphopsia were obtained preoperatively and at 3 months  
67 postoperatively. Letter contrast sensitivity was measured using the CSV-1000LV  
68 chart (Vector Vision, Columbus, Ohio). Metamorphopsia was evaluated using  
69 M-CHARTS (Inami Co., Tokyo, Japan), which enable quantitative evaluation of  
70 the degree of metamorphopsia in patients with macular diseases.<sup>15,16</sup>

71

## 72 **Surgical procedures**

73 All surgeries were performed by a single surgeon (F.O.) under sub-Tenon  
74 local anesthesia. The crystalline lens was removed by phacoemulsification and  
75 intraocular lens implantation when required, following by 20-gauge three-port  
76 pars plana vitrectomy. Using contact lenses, posterior hyaloid separation and  
77 removal of the posterior vitreous membrane were performed, and then bimanual  
78 delamination, en bloc dissection, and segmentation techniques were used to  
79 remove proliferative tissues. Membrane dissection and segmentation were  
80 performed when necessary to eliminate all tangential tractions. Peripheral  
81 vitrectomy and panretinal endophotocoagulation were routinely performed.  
82 Air-fluid exchange was performed when an iatrogenic retinal tear and/or  
83 rhegmatogenous retinal detachment were identified intraoperatively.

84

## 85 **Questionnaire (VFQ-25)**

86 The patients were requested to answer VFQ-25 preoperatively and 3  
87 months postoperatively to assess VR-QOL. Preoperative VFQ-25 was examined  
88 the day before or two days before operation. The research staff explained the  
89 questionnaire to the patients, verbally administered instruction, and provided  
90 assistance when required. The completed questionnaires were reviewed for  
91 missing data by the research staff. Prior to surgery, all the missing items were  
92 incorporated by the subjects themselves.

93 The VFQ-25 comprises 25 items wherein patients are expected to assess the  
94 level of difficulty of particular visual symptoms or day-to-day activities. Each item  
95 is assigned to one of the 12 subscales, namely, general health, general vision,  
96 ocular pain, near activities, distance activities, social functioning, mental health,  
97 role difficulties, dependency, driving, color vision, and peripheral vision. The  
98 subscales are scored on a 0 to 100-point scale, where 100 indicates the highest  
99 possible function or the minimal subjective impairment. The VFQ-25 composite  
100 score is calculated as the unweighted average response to all items, excluding  
101 the questions regarding general health.

102 The VFQ-25 used in this study was a Japanese version, with modifications  
103 to suit the Japanese culture and way of life. The modified NEI VFQ-25  
104 questionnaire has been assessed for reliability and validity, and it has been  
105 proven to accurately measure VR-QOL in Japanese individuals.<sup>17</sup>

106

## 107 **Statistical analysis**

108 The mean scores and standard deviations were calculated for each VFQ-25  
109 subscale result as well as for the VFQ-25 composite score in patients with PDR  
110 and normal controls. A Mann-Whitney *U* test was performed to compare each  
111 subscale score and composite score between the PDR patients and normal  
112 controls. The Wilcoxon signed-ranks test was used for variables that were  
113 present both pre- and postoperatively. The relationships of the questionnaire  
114 scores with visual acuity, contrast sensitivity, metamorphopsia, age, duration of  
115 DM, serum HbA1c, and fasting plasma glucose were examined by the Spearman  
116 rank correlation test. To correlate visual acuity with the questionnaire score, the  
117 Snellen visual acuity was converted to its logMAR equivalent. Approximations for

118 visual acuity worse than 20/400 were as follows: counter fingers, 20/2000; hand  
119 motions, 20/4000; and light perception, 20/8000.<sup>18,19</sup> All tests of association were  
120 considered statistically significant if  $P < 0.05$ . The analyses were carried out  
121 using StatView (version 5.0, SAS Inc., Cary, NC).

122

## 123 **Results**

124 The logMAR BCVA ranged from 2.30 to 0.00 preoperatively (mean, 1.24;  
125 median, 1.30) and from 2.60 to -0.08 postoperatively (mean, 0.46; median, 0.30).  
126 The vitrectomy significantly improved visual acuity ( $p < 0.0001$ ), with 39 patients  
127 (75.0%) gaining 2 or more ETDRS lines. No change was observed in 9 eyes  
128 (17.3%), and vision decreased by 1 or more lines in 4 patients (7.6%). The  
129 postoperative reduction in visual acuity was attributed to neovascular glaucoma  
130 (2 patients) and optic disc atrophy (2 patients). These patients did not have  
131 neovascular glaucoma and optic disc atrophy preoperatively. The mean letter  
132 contrast sensitivity significantly improved from 7.5 preoperatively to 15.0  
133 postoperatively ( $p < 0.001$ ).

134 All patients underwent PDR surgery for their worse-seeing eye. The  
135 logMAR BCVA in the fellow eye ranged from 1.20 to 0.00 (mean, 0.62; median,  
136 0.60).

137 Preoperative and postoperative mean logMAR BCVA on the type of PDR  
138 were vitreous hemorrhage (pre 1.34, post 0.25), tractional retinal detachment  
139 (pre 1.31, post 0.24), and excessive macular traction (pre 1.22, post 0.74).  
140 Further, preoperative and postoperative mean VFQ-25 composite scores on the  
141 type of PDR were vitreous hemorrhage (pre 51.2, post 62.3), tractional retinal  
142 detachment (pre 61.1, post 70.3), and excessive macular traction (pre 55.2, post  
143 59.4).

144 The results of VFQ-25 questionnaire pre- and postoperatively are shown in  
145 table 2. The preoperative VFQ-25 composite score was significantly lower in the  
146 PDR patients than in the normal controls ( $p < 0.0001$ ). The preoperative  
147 subscales were significantly lower in the PDR patients than in the normal controls,  
148 except for ocular pain ( $p < 0.0001$ ). Vitrectomy significantly improved VFQ-25  
149 composite score ( $p < 0.005$ ) and subscales such as general vision, near activities,  
150 distance activities, social functioning, mental health, role difficulties, driving, and  
151 peripheral vision. However, postoperative VFQ-25 composite score still remained  
152 significantly lower in the PDR patients than in the normal controls ( $p < 0.0001$ ).

153 The preoperative VFQ-25 composite score exhibited significant correlation  
154 with the preoperative logMAR BCVA in the better-seeing eye but not in the  
155 worse-seeing eye (Figure 1). Significant correlation was also observed between  
156 the preoperative VFQ-25 composite score and letter contrast sensitivity (Figure  
157 1). The preoperative VFQ-25 composite score did not correlate with age ( $r =$   
158  $0.138$ ,  $p = 0.496$ ), duration of DM ( $r = 0.122$ ,  $p = 0.523$ ), serum HbA1c ( $r = 0.136$ ,  
159  $p = 0.400$ ), and fasting plasma glucose ( $r = 0.051$ ,  $p = 0.750$ ). At 3 months  
160 postoperatively, the VFQ-25 composite score exhibited significant correlation  
161 with the logMAR BCVA in the worse-seeing eye as well as the better-seeing eye  
162 (Figure 2). Similar significant correlation was observed between the VFQ-25  
163 composite score and letter contrast sensitivity (Figure 2). However, there was no  
164 significant relationship between the postoperative VFQ-25 composite score and

165 the severity of metamorphopsia ( $r = -0.390$ ,  $p = 0.081$ ). Further, there was no  
166 significant correlation between changes in VFQ-25 composite score by surgery  
167 and changes in logMAR BCVA ( $r = -0.212$ ,  $p = 0.148$ ) and letter contrast  
168 sensitivity ( $r = 0.307$ ,  $p = 0.093$ ).

169

## 170 Discussion

171 In the present study, VFQ-25 composite score and all subscale scores,  
172 except for color vision, were significantly reduced in patients with PDR, indicating  
173 that those patients were suffering from a wide range of functional vision  
174 difficulties as compared to the normal controls. The preoperative VFQ-25  
175 composite score significantly correlated with visual acuity and contrast sensitivity  
176 in the better-seeing eye. Postoperatively, VFQ-25 composite score significantly  
177 correlated with the condition of the worse-seeing eye as well as the better-seeing  
178 eye. Previous studies reported that VR-QOL significantly improved following  
179 vitreous for age-related macular degeneration,<sup>12,13</sup> macular hole,<sup>8-10</sup> and  
180 epiretinal membrane peeling.<sup>11</sup> The current study represents the first report that  
181 VR-QOL significantly improved following vitreous surgery for PDR. In patients  
182 with macular hole,<sup>8</sup> 4 of 12 subscales improved significantly with surgery, such as  
183 general vision, near activities, mental health, and role difficulties. Vitrectomy for  
184 epiretinal membrane significantly improved 2 of 12 subscales, including general  
185 vision and distance activities.<sup>11</sup> Vitrectomy for PDR significantly improved 8 of 12  
186 subscales (general vision, near activities, distance activities, social functioning,  
187 mental health, role difficulties, driving, and peripheral vision) in this case series.  
188 Based on these previous and current findings, it is suggested that vitrectomy for  
189 PDR offers greater subjective improvement in VR-QOL than that for other  
190 macular disorders.

191 The preoperative VFQ-25 composite score significantly correlated with  
192 preoperative visual acuity and contrast sensitivity in the better-seeing eye. These  
193 results are consistent with several previous reports. Miskala et al investigated  
194 VR-QOL in patients with subfoveal choroidal neovascularization by using the  
195 VFQ-25, and demonstrated that changes in the overall and subscale scores were  
196 linearly related to changes in visual acuity of the better-seeing eye but are not  
197 associated with changes in the worse-seeing eye.<sup>12</sup> Deramo et al investigated  
198 VR-QOL in patients with unilateral central retinal vein occlusion and observed  
199 that VFQ-25 responses significantly correlated with visual acuity in the  
200 better-seeing eye.<sup>19</sup> In other studies, VFQ-25 responses significantly correlated  
201 with binocular visual acuity in patients with macular hole and epiretinal  
202 membrane.<sup>8,11</sup> In our study, VR-QOL was significantly associated with contrast  
203 sensitivity as well as visual acuity in the better-seeing eye.

204 Interestingly, postoperative VFQ-25 composite score significantly correlated  
205 with postoperative visual acuity and contrast sensitivity in both the worse-seeing  
206 and better-seeing eyes. Until now, there has been no previous report that showed  
207 significant relationship between VR-QOL and visual function of the worse-seeing  
208 eye in patients with vitreoretinal diseases. In PDR, however, bilateral eyes are  
209 usually affected to a rather similar extent, while other vitreoretinal diseases such  
210 as macular hole and epiretinal membrane are generally unilateral. In our study,  
211 mean visual acuity in the better-seeing eye was considerably deteriorated (0.62

212 logMAR BCVA), and the difference between the better-seeing and worse-seeing  
213 eyes was small. This seems to be the reason why VFQ-25 score correlated with  
214 the visual function not only in the better-seeing eye but also in the worse-seeing  
215 eye.

216 In several studies investigated quality of life outcomes following ocular  
217 surgery, only weak or absent correlation between increase in quality of life and  
218 improvement of visual acuity was observed.<sup>10,20</sup> In this study, there was no  
219 significant correlation between changes in VFQ-25 composite score and changes  
220 in visual acuity. This finding suggests visual acuity is only one aspect of visual  
221 function, which explains why despite increased visual acuity and letter contrast  
222 sensitivity in several cases VFQ-25 values decrease in our series.

223 There was no association between the severity of metamorphopsia and  
224 VFQ-25 composite score. This observation is consistent with the results of  
225 previous studies in patients with macular hole and epiretinal membrane.<sup>8,11</sup> Thus,  
226 it seems that visual acuity and contrast sensitivity are more suitable indicators for  
227 patients' VR-QOL than the degree of metamorphopsia.

228 This study has certain limitations, including small sample size and  
229 short-term follow-up. The VFQ-25 score in patients with macular hole was more  
230 improved at 1 year postoperatively than at 3 months postoperatively.<sup>11</sup> Thus,  
231 longer-term investigations of patients after vitrectomy for PDR might give  
232 somehow different results regarding VR-QOL and visual function. Future studies  
233 with a larger sample size and longer follow-up will further facilitate our  
234 understanding of the relation between VR-QOL and visual function in patients  
235 undergoing vitrectomy for PDR.

236  
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241 interpretation of the data (Y.O., S.H.); preparation of the manuscript (F.O.);  
242 review of the manuscript (T.O.); and approval of the manuscript (F.O., Y.O., S.F.,  
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244 Tsukuba University Hospital and was in adherence to the tenets of the  
245 Declaration of Helsinki.

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311 **Figure legends**

312

313 Figure 1. Preoperative National Eye Institute 25-Item Visual Function  
314 Questionnaire (VFQ-25) composite score vs. preoperative logMAR  
315 best-corrected visual acuity (BCVA) and preoperative letter contrast sensitivity in  
316 patients with proliferative diabetic retinopathy.  
317 (Top left) VFQ-25 composite score vs. logMAR BCVA in the better-seeing eye:  $r =$   
318  $-0.446$ ,  $p < 0.001$ . (Top right) VFQ-25 composite score vs. logMAR BCVA in the  
319 worse-seeing eye:  $r = -0.354$ ,  $p = 0.072$ . (Bottom left) VFQ-25 composite score vs.  
320 letter contrast sensitivity in the better-seeing eye:  $r = 0.407$ ,  $p = 0.016$ . (Bottom  
321 right) VFQ-25 composite score vs. letter contrast sensitivity in the worse-seeing  
322 eye:  $r = 0.255$ ,  $p < 0.153$ .

323

324 Figure 2. Postoperative National Eye Institute 25-Item Visual Function  
325 Questionnaire (VFQ-25) composite score vs. postoperative logMAR  
326 best-corrected visual acuity (BCVA) and postoperative letter contrast sensitivity in  
327 patients with proliferative diabetic retinopathy.  
328 (Top left) VFQ-25 composite score vs. logMAR BCVA in the better-seeing eye:  $r =$   
329  $-0.520$ ,  $p < 0.0001$ . (Top right) VFQ-25 composite score vs. logMAR BCVA in the  
330 worse-seeing eye:  $r = -0.632$ ,  $p < 0.0001$ . (Bottom left) VFQ-25 composite score  
331 vs. letter contrast sensitivity in the better-seeing eye:  $r = 0.323$ ,  $p = 0.041$ .  
332 (Bottom right) VFQ-25 composite score vs. letter contrast sensitivity in the  
333 worse-seeing eye:  $r = 0.374$ ,  $p = 0.014$ .

334

335