# Long-term visual outcome in inferior posterior staphyloma and efficacy of treatment for complicated choroidal neovascularization

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**Short title:**
Long-term visual outcome in inferior posterior staphyloma

## ABSTRACT

**Purpose:** To investigate long-term visual outcome in inferior posterior staphyloma (IPS) in each group classified based on macular complications and to examine the treatment effect for eyes with IPS with choroidal neovascularization (CNV)
**Design:** Prospective clinical cohort study
**Participants:** We analyzed 56 eyes of 43 consecutive patients with IPS who were followed for 4 years.
**Methods:** We classified eligible eyes into three groups based on baseline findings: eyes without CNV or retinal exudate (no-exudate group), eyes without CNV and with retinal exudate (exudate group), and eyes with CNV (CNV group). We investigated the best-corrected visual acuity (BCVA) and associated parameters for 4 years.
**Results:** BCVA declined during 4 years only in the exudate group ($P = 0.002$), whereas it was maintained for 4 years in the no-exudate and CNV groups ($P = 0.53$ and 0.20, respectively). Baseline BCVA was lower in the CNV group than in the exudate group ($P = 0.004$); however, the 4-year BCVA was not ($P = 0.84$). The 4-year BCVA was associated with baseline BCVA in all groups. Eyes in the CNV group required 9.0 ± 8.7 anti-vascular endothelial growth factor (VEGF) therapy in 4 years.
**Conclusions:** Better baseline BCVA in eyes with exudative IPS without CNV spontaneously declined in 4 years, whereas worse baseline BCVA in eyes with IPS with CNV did not, probably because of treatment for retinal exudate from CNV. Anti-VEGF therapy would be effective for long-term maintenance of BCVA in eyes with IPS with CNV, similar to other diseases with CNV.

## INTRODUCTION

Inferior posterior staphyloma (IPS) is a subtype of posterior staphyloma proposed by Curtin,[1] who reported that IPS was observed in only 12 eyes (2.6%) out of 453 eyes with myopic staphyloma, although the prevalence of IPS has not yet been reported. IPS is often accompanied by tilted disc syndrome, peripapillary crescent, and dysversion of retinal vessels.[2] When the upper-temporal border of the IPS lies across the macula, macular complications, including choroidal neovascularization (CNV, 25%), serous retinal detachment (SRD, 41%), and retinal pigment epithelium (RPE) atrophy (13%), often develop and lead to visual loss.[2, 3] Especially in eyes with IPS with CNV, best-corrected visual acuity (BCVA) has been reported to be worse than in eyes with IPS with other macular complications.[3] However, there is no longitudinal study to demonstrate long-term visual outcome in eyes with IPS.

The efficacy of intravitreal anti-vascular endothelial factor (VEGF) agent injections and photodynamic therapy (PDT) for various exudative macular diseases with CNV, including neovascular age-related macular degeneration (AMD), polypoidal choroidal vasculopathy, and myopic CNV, has been reported in long-term observation.[4-6] A previous multicenter study with >1-year observation period demonstrated that visual prognosis of SRD in eyes without CNV and with tilted disc syndrome, which is often accompanied by IPS, was better when SRD resolved but not influenced by anti-VEGF therapy or PDT.[7] The long-term effect of treatment for CNV with IPS eyes has not been identified.

In the present study, we classified eyes with IPS into three groups on the basis of macular complications, as previously reported,[2] and examined long-term visual outcome in eyes with IPS in each group and the effect of therapy for eyes with IPS with CNV.

## METHODS

The ethics committee of Kyoto University Graduate School of Medicine (Kyoto, Japan) approved this prospective clinical cohort study. All study protocols adhered to the tenets of the Declaration of Helsinki. We explained the nature of the study and the possible risks and benefits of participation were explained to all study candidates, who agreed to participate after providing written informed consent.

### Participants

This study included treatment-naïve eyes affected by IPS in consecutive patients who visited Kyoto University Hospital between January 2008 and May 2016. All eyes underwent a comprehensive ophthalmologic examination, including autorefractometry (ARK1; Nidek, Gamagori, Japan), BCVA measurements with a 5 m Landolt chart, measurement of intraocular pressure, indirect ophthalmoscopy, slit-

lamp biomicroscopy with contact lens, axial length (AL) measurement using partial coherence interferometry (IOLMaster; Carl Zeiss Meditec, Dublin, CA, USA), color fundus photography (TRC-NW8F; Topcon Corp., Tokyo, Japan), optical coherence tomography (OCT, Spectralis HRA+OCT, Heidelberg Engineering, Heidelberg, Germany; RS-3000 Advance, Nidek; or DRI OCT-1, Topcon, Tokyo, Japan), fundus fluorescein angiography (FA), and indocyanine green angiography (ICGA, Heidelberg Retina Angiography 2, Heidelberg Engineering).

Retinal specialists diagnosed IPS on the basis of fundus photography, dilated binocular indirect ophthalmoscopy, and slit-lamp biomicroscopy with contact lens. As previously reported, vertical scans of OCT were used to confirm that the border of the inferior staphyloma lay across the macula.[2] The inclusion criterion was IPS, of which the superior edge was lying across the macula, followed for 4 years. The exclusion criteria were as follows: the absence of baseline and 4-year BCVA and OCT image; poor OCT image quality for analysis at baseline; photocoagulation or PDT for eyes without CNV during the observation period; and other baseline macular diseases, including epiretinal membrane, vitreomacular traction syndrome, diabetic retinopathy, and macular hole.

**Classification**

We classified eligible eyes with IPS into three groups on the basis of macular complications at baseline (Figure 1), as previously reported[2]: (1) eyes without CNV or retinal exudate including SRD or retinal pigment epithelial detachment (no-exudate group), (2) eyes without CNV and with retinal exudate (exudate group), and (3) eyes with CNV (CNV group). We carefully determined the presence or absence of CNV on the basis of OCT, FA, and ICGA findings. We performed pro re nata (PRN) intravitreal anti-VEGF agent injections (Eylea, Bayer, Basel, Switzerland; Lucentis, Novartis, Basel, Switzerland) in eyes with exudate in the CNV group. When the poor effectiveness of anti-VEGF therapy was confirmed, we performed additional PDT. In the no-exudate and exudate groups, we confirmed CNV development in the 4-year observation period.

**Analysis of OCT images and color fundus photography images**

We measured the central retinal thickness (CRT), central choroidal thickness (CCT), subretinal fluid (SRF) height at the foveal center, and the distance between the upper border of the IPS and fovea (defined as “border–fovea distance”) on a vertical-scan OCT image through the fovea using the built-in software. We defined CRT as the distance between the vitreoretinal surface and the outer surface of the RPE. We defined CCT as the distance between the outer surface of Bruch’s membrane and the chorioscleral interface. We defined SRF height as the distance between the outer

surface of the sensory retina and the inner surface of RPE. In addition, we defined the border–fovea distance as the distance between the inner surface of the RPE at the fovea and that at the upper border, which we defined as the thinnest point of the choroid (Figure 2) because previous studies showed that eyes with IPS often have a belt-shaped area with the thinnest choroid being at the superior border of the staphyloma.[2, 8] Positive values of the border–fovea distance demonstrated that the fovea lies superior to the border. We confirmed tilted disc on the basis of color fundus photography images.

**Statistical analysis**

As applicable, we presented all data as mean ± standard deviation or number of eyes. We converted all BCVA values into the logarithm of the minimum angle of resolution (logMAR) values for statistical analysis. Among the three groups, we performed comparison analyses using one-way analysis of variance (ANOVA) and subsequent pairwise comparisons and chi-square trend test where applicable. Using repeated measures ANOVA in each group, we analyzed the change in logMAR BCVA values in 4 years (baseline, 6-month, 1-year, 2-year, 3-year, and 4-year BCVA values) were analyzed. Using Spearman's correlation coefficient, we performed univariate correlation analyses between the 4-year logMAR BCVA and baseline or treatment-associated parameters; and between the 4-year change in logMAR BCVA and those parameters. Multivariate correlation analyses were performed using the 4-year logMAR BCVA or 4-year change in logMAR BCVA as the dependent variable and baseline or treatment-associated parameters with *P*-values < 0.20 on Spearman's correlation test as independent variables. We conducted all statistical analyses using SPSS version 27 software (IBM Corp., Armonk, NY, USA).

**RESULTS**

In the present study, we included 56 eyes of 43 patients (mean age, 64.1 ± 10.5 years, Table 1). We classified 25, 21, and 10 eyes into no-exudate, exudate, and CNV groups, respectively. Thus, the prevalence of eyes with retinal exudate was 21 of 46 (46%) eyes without CNV, and that of eyes with CNV was 10 of 56 (18%) eyes with whole IPS. Comparing the three groups, significant differences were found in the baseline and 4-year logMAR BCVA ($P < 0.001$ and $P = 0.005$, respectively), 4-year change in logMAR BCVA ($P = 0.01$), baseline CRT ($P = 0.005$), 4-year change in CRT ($P = 0.04$), and the prevalence of tilted disc at baseline ($P = 0.04$). Among the three groups, the border–fovea distance was not different. In the CNV group, two eyes had no retinal exudate at baseline and developed retinal exudate 1 and 3 years after baseline. Taken together, all eyes in the CNV group underwent anti-VEGF therapy (9.0 ± 8.7 injections), and one eye underwent not only anti-VEGF therapy

but also PDT twice because of the poor effectiveness of anti-VEGF monotherapy. CNV did not develop in 4 years in either the no-exudate group or the exudate group.

**Comparison of BCVA**

Baseline logMAR BCVA of the no-exudate, exudate, and CNV groups was 0.08 ± 0.23, 0.18 ± 0.23, and 0.53 ± 0.41, respectively. Pairwise comparison demonstrated that baseline BCVA was better in the no-exudate and exudate groups than in the CNV groups ($P < 0.001$ and $P = 0.004$, respectively), whereas there was no difference in baseline BCVA between the no-exudate and exudate groups ($P = 0.41$). In the analysis of each group, BCVA declined only in the exudate group in 4 years ($P = 0.002$), whereas BCVA was maintained in the no-exudate and CNV groups in 4 years ($P = 0.53$ and $P = 0.20$, respectively; Figure 3). The 4-year logMAR BCVA values of the no-exudate, exudate, and CNV groups were 0.06 ± 0.19, 0.28 ± 0.34, and 0.35 ± 0.29, respectively. Pairwise comparison demonstrated that 4-year BCVA was better in the no-exudate group than in the exudate and CNV groups ($P = 0.03$ in both), whereas no significant difference in 4-year BCVA was found between the exudate and CNV groups ($P = 0.84$).

**Correlation between 4-year BCVA or change in BCVA and the studied parameters in each group**

In all groups, 4-year logMAR BCVA was significantly associated with baseline logMAR BCVA and was not associated with the border–fovea distance (detailed data shown in Table 2). In the no-exudate group, the 4-year logMAR BCVA was associated with age ($P < 0.001$; $r = 0.64$), AL ($P = 0.01$; $r = -0.54$), and CCT ($P = 0.03$; $r = 0.47$). In the exudate group, the 4-year logMAR BCVA was associated with SRF height ($P = 0.03$; $r = 0.47$). In the CNV group, the 4-year logMAR BCVA was associated with the presence of tilted disc ($P = 0.03$, $r = 0.67$) but not with age ($P = 0.69$), AL ($P = 0.80$), CCT ($P = 0.68$), SRF height ($P = 0.52$), or 4-year anti-VEGF injections ($P = 0.48$). The multivariate correlation analyses between 4-year logMAR BCVA and other studied parameters revealed no significant correlations in the no-exudate group; significant correlations of baseline logMAR BCVA ($P = 0.01$, $\beta = 0.52$) and SRF height ($P = 0.02$, $\beta = 0.41$) in the exudate group; and significant correlations of baseline logMAR BCVA ($P = 0.01$, $\beta = 0.62$) and tilted disc presence ($P = 0.02$, $\beta = 0.57$) in the CNV group. Furthermore, the 4-year change in logMAR BCVA was associated with the SRF height in the exudate ($P = 0.03$; $r = 0.48$) and CNV ($P = 0.03$; $r = 0.69$) groups (Table 3); however, the multivariate analyses revealed no significant correlations ($P = 0.08$ and 0.44, respectively).

**DISCUSSION**

In this study, we demonstrated a 4-year course of BCVA in eyes with IPS assigned into three groups based on baseline macular complication. Baseline BCVA was higher in eyes with IPS without CNV than in eyes with IPS with CNV. However, BCVA in eyes with exudate and without CNV spontaneously declined in the 4-year observation period, although that in eyes without exudate or CNV was maintained for 4 years. Long-term retinal exudate would induce retinal damage and subsequent BCVA decline even in eyes with IPS without CNV. Furthermore, the 4-year BCVA was significantly associated with baseline SRF height, only in the exudate group. SRF status would play an essential role in long-term visual outcome. By contrast, in eyes with IPS with CNV, lower baseline BCVA did not further decline in 4 years, probably because retinal exudates were under control due to treatments including anti-VEGF therapy.

Among eyes without CNV, the BCVA declined in eyes with retinal exudate but not in the eyes without retinal exudate in the present study, although baseline BCVA was at the high level without significant differences between them. Chronic central serous chorioretinopathy (CSC), in which retinal exudate remains during the long-term period, can be a vision-threatening disease, leading to legal blindness,[9] although its natural course is highly varied between individuals.[10] Prolonged separation of the photoreceptors from the RPE and choroid is associated with outer retinal damage.[11, 12] During the mean follow-up period of 11.3 ± 8.5 years in chronic CSC, logMAR BCVA changed from 0.43 ± 0.47 to 0.52 ± 0.55.[12] In the exudate group, it changed from 0.18 ± 0.23 to 0.28 ± 0.34 during the 4-year period ($P$ = 0.002), which is similar to the change in logMAR BCVA in the previous study with chronic CSC. Half-dose PDT for chronic CSC was effective in the improvement of logMAR BCVA from 0.21 ± 0.24 to 0.08 ± 0.16 at 3 years after treatment ($P$ < 0.001).[13] The treatment might also be effective in preventing eyes with IPS with retinal exudate without CNV from BCVA decline. However, the etiology of SRF in IPS may be not only RPE dysfunction but also choroidal perfusion anomalies at the upper border of the staphyloma.[14] Short-term choriocapillaris occlusion after PDT even with half dose has been reported.[15] Furthermore, marked choroidal thinning at the upper border of the staphyloma was reported.[2, 8] Therefore, the efficacy of PDT might be different between CSC and SRF with IPS. Further interventional study is required.

Anti-VEGF therapy appears to be effective in the maintenance of BCVA for up to 4 years in the eyes with IPS with CNV. Only one eye (10%) showed poor effectiveness of anti-VEGF monotherapy and needed additional PDT twice. A 5-year real-world observation study to investigate BCVA of neovascular AMD treated with anti-VEGF therapy, followed by PRN regimen, showed that BCVA improved at 1 year after the initial anti-VEGF therapy; however, it significantly declined since the third

year, followed by PRN regimen.[16] Another previous large-scale clinical trial of the SEVEN-UP study, in which monthly anti-VEGF therapy in the MARINA[17] and ANCHOR[18] studies and followed by PRN regimen, showed a decline of 8.6 ETDRS letters 7 years after the initial treatment compared with that at baseline in neovascular AMD.[19] In myopic CNV, BCVA was maintained for up to 4 years by anti-VEGF therapy in PRN regimen and marginally better in 4-year BCVA than in baseline BCVA ($P = 0.07$).[20] Furthermore, the mean number of anti-VEGF therapy was approximately twice annually in the present study. A 5-year comparison study of anti-VEGF therapy in PRN regimen showed four to six injections annually in neovascular AMD and zero to five injections annually in myopic CNV was needed in median.[6] The efficacy of anti-VEGF therapy in eyes with IPS with CNV may be between neovascular AMD and myopic CNV. Our findings suggest that anti-VEGF therapy should be performed for exudative IPS with CNV.

The multivariate correlation analyses between the 4-year logMAR BCVA and other studied baseline or treatment-associated parameters revealed that the baseline SRF height in the exudate group and the presence of tilted disc in the CNV group were associated with 4-year logMAR BCVA, except for baseline logMAR BCVA. The FLUID study showed that the 2-year BCVA in eyes with lower SRF height ($\leq 200$ $\mu$m) at the foveal center treated with a relaxed regimen of anti-VEGF therapy was similar to that in eyes without SRF treated with an intensive regimen for AMD.[21] This finding suggests that lower SRF height does not affect the BCVA for at least 2 years. In the present study, lower SRF height at baseline would have little effect on the 4-year BCVA in the exudate group. Furthermore, a case report showed that the BCVA decreased in three eyes with CNV complicated with tilted disc syndrome 3 or 6 months after intravitreal bevacizumab injection.[22] The results obtained in the present study was consistent with those from that previous study; that is, the presence of tilted disc has a negative effect on the 4-year BCVA in eyes with CNV complicated with IPS. However, its etiology remains unclear and further research is needed.

In contrast to our expectations, the border–fovea distance was not different among the three groups ($P = 0.32$) and had no association with 4-year logMAR BCVA in all groups. Marked choroidal thinning and upward convex of RPE line are observed at the superior border of IPS.[2, 8] The development of macular complication plays an essential role in the maintenance of long-term BCVA and was not associated with border–fovea distance.

This study had some limitations. First, the sample size was small. Eyes with IPS are rare. Although this 4-year longitudinal study included 56 eyes, previous cross-sectional studies included 4–42 eyes.[2, 3, 8] Second, the treatment regimen for exudative IPS with CNV has not been identified. We performed real-world anti-VEGF

therapy in the PRN regimen on the basis of neovascular AMD or myopic CNV. However, it is unclear which PRN or fixed regimen and which anti-VEGF therapy or PDT is effective for exudative IPS with CNV. Since PDT for myopic CNV has a risk of chorioretinal atrophy in comparison with anti-VEGF therapy, anti-VEGF therapy might be safer for IPS, which has marked choroidal thinning of the superior border of the staphyloma near the fovea.[23] Further study is required

In conclusion, relatively better baseline BCVA in exudative IPS eyes without CNV spontaneously declined in the 4-year observation period, whereas relatively worse baseline BCVA in eyes with IPS with CNV did not decline in 4 years probably because of PRN treatment for retinal exudate from CNV. Anti-VEGF therapy would be effective in the long-term maintenance of BCVA in eyes with IPS with CNV, similar to that for other diseases with CNV.

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**c. Other Acknowledgments**

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**FIGURE LEGENDS**

Figure 1. Representative vertical-scan optical coherence images used for classification based on macular complication

Eligible eyes with inferior posterior staphyloma were classified into three groups based on macular complication at baseline.

(Top) No-exudate group. Eyes without choroidal neovascularization (CNV) or retinal exudate of subretinal detachment or retinal pigment epithelial detachment

(Middle) Exudate group. Eyes without CNV and with retinal exudate

(Bottom) CNV group. Eyes with CNV

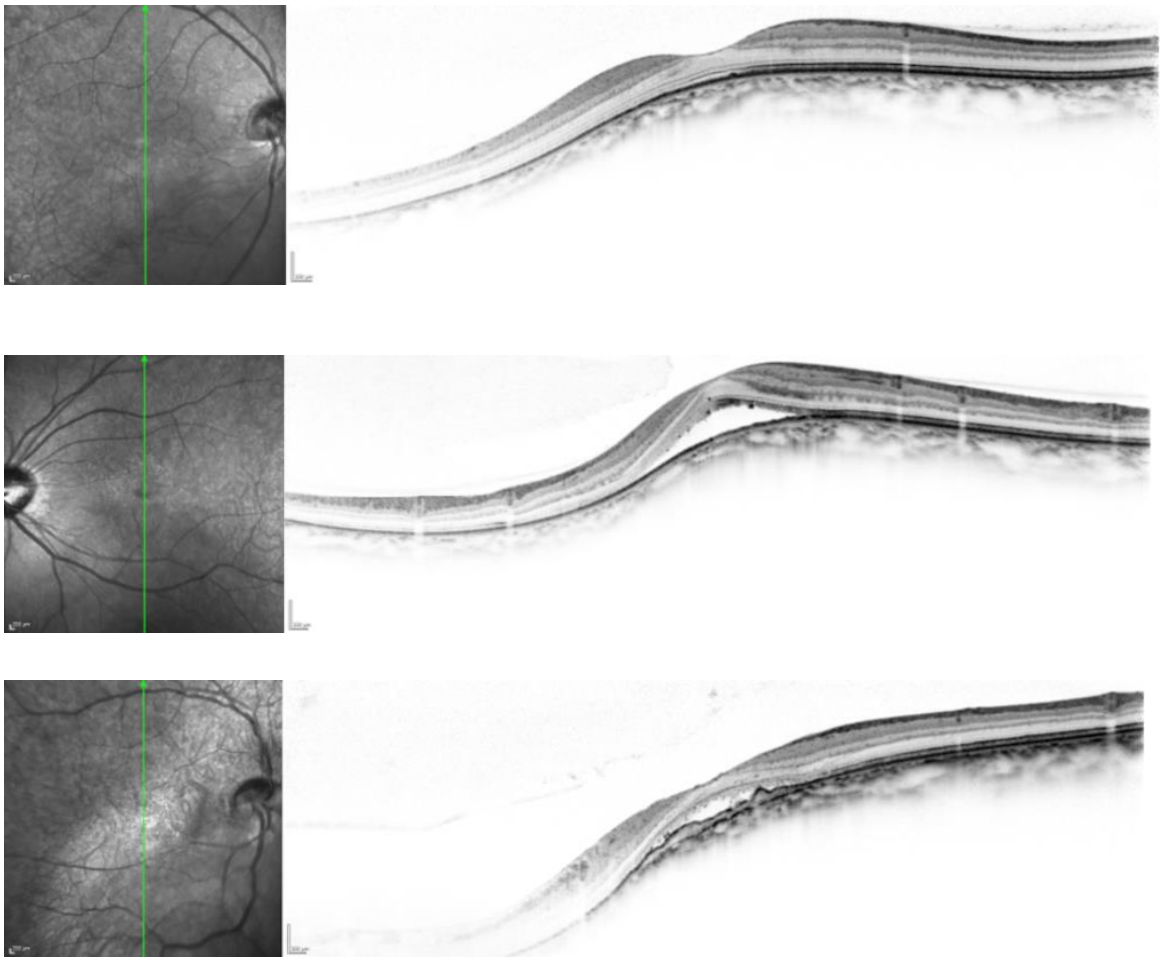

Figure 2. Measurement of the border–fovea distance
We defined the distance between the upper border of the staphyloma and fovea as the border–fovea distance. It was measured as the distance between the inner surface of the retinal pigment epithelium at the fovea (the right arrowhead) and that at the upper border which was defined as the thinnest point of the choroid (left arrowhead) on a vertical-scan OCT image through the fovea using built-in software.

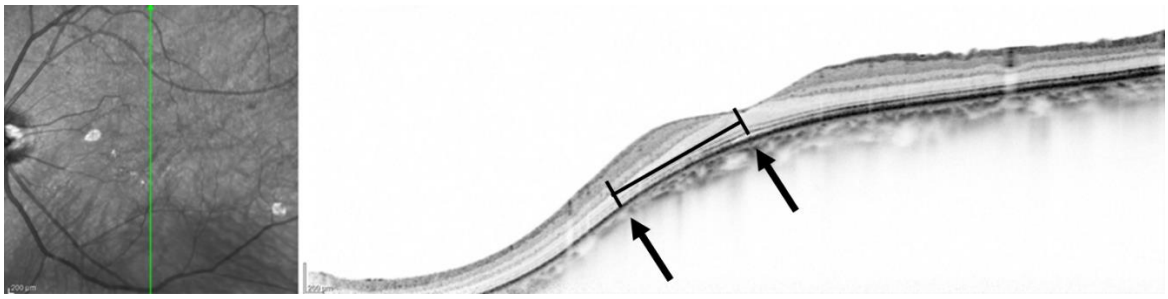

Figure 3. Four-year course of best-corrected visual acuity (BCVA) in each group. In the analysis of each group, BCVA declined only in the exudate group in 4 years ($P$ = 0.002), whereas BCVA was maintained in the no-exudate and CNV groups in 4 years ($P$ = 0.53 and $P$ = 0.20, respectively). Comparing the three groups, baseline BCVA was better in the no-exudate and exudate groups than in the CNV groups ($P$ < 0.001 and $P$ = 0.004, respectively); whereas, no difference in baseline BCVA was found between the no-exudate and exudate groups ($P$ = 0.41). Four-year BCVA was better in the no-exudate group than in the exudate and CNV groups ($P$ = 0.03 and $P$ = 0.03), whereas there was no difference in 4-year BCVA between the exudate and CNV groups ($P$ = 0.84). Six-month, 1-year, 2-year, and 3-year data are missing in 7, 5, 5, and 2 eyes, respectively; however, the CNV group had no missing data. Bars represent standard errors.

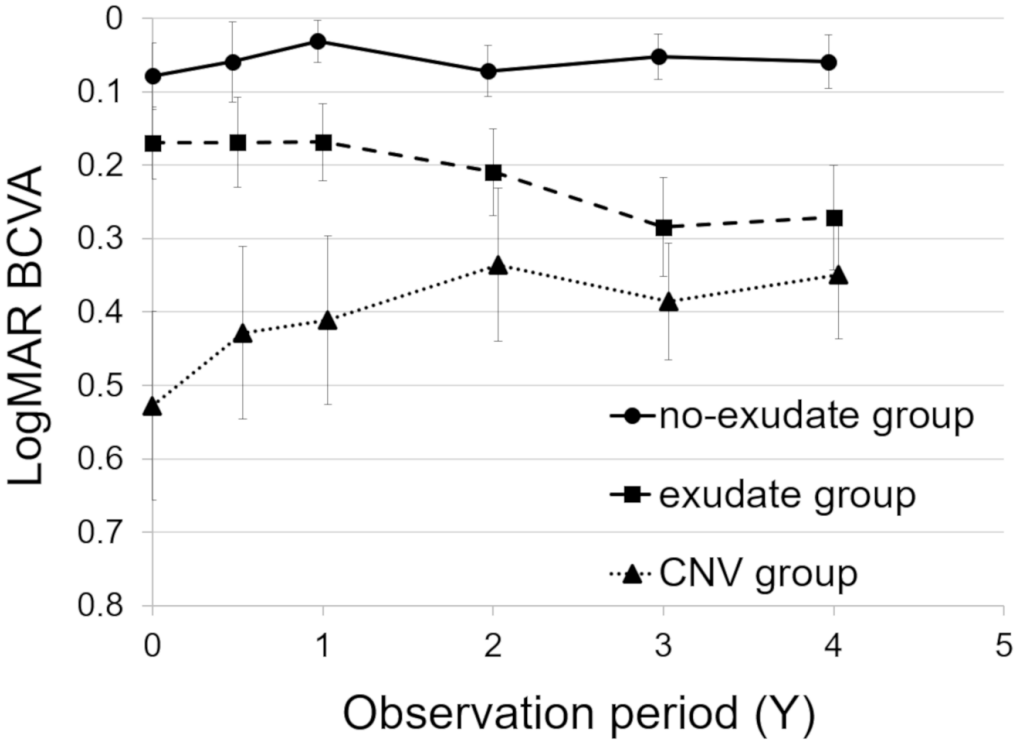

**Table 1. Comparison of the studied parameters among the three groups**

| | | Whole group | No-exudate Group (G1) | Exudate group (G2) | CNV group (G3) | *P* values among the three groups | *P* values of pairwise comparisons | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | G1 vs. G2 | G1 vs. G3 | G2 vs. G3 |
| Eyes (patient), n | | 56 (43) | 25 (25) | 21 (17) | 10 (9) | | | | |
| Age, years (range) | | 64.1 ± 10.5 (42–83) | 64.4 ± 11.2 (42–83) | 61.3 ± 9.7 (42–77) | 69.0 ± 9.6 (48–83) | 0.16 | | | |
| Sex (M/F), n | | 6/37 | 5/20 | 2/15 | 2/7 | 0.21† | | | |
| Tilted disc (%), n | | 35 (63) | 12 (48) | 15 (71) | 8 (80) | 0.04*† | 0.06 | 0.04* | 0.31 |
| Axial length, mm (range) | | 25.12 ± 1.35 (22.11–28.60) | 25.25 ± 1.36 (22.48–28.60) | 24.95 ± 1.52 (22.11–28.46) | 25.15 ± 0.95 (23.73–26.86) | 0.75 | | | |
| LogMAR BCVA (range) | Baseline | 0.19 ± 0.31 | 0.08 ± 0.23 | 0.18 ± 0.23 | 0.53 ± 0.41 | < 0.001* | 0.41 | <0.001* | 0.004* |
| | 4-year | 0.20 ± 0.29 | 0.06 ± 0.19 | 0.28 ± 0.34 | 0.35 ± 0.29 | 0.005* | 0.03* | 0.03* | 0.84 |
| | Change | 0.002 ± 0.26 | −0.01 ± 0.22 | 0.11 ± 0.24 | −0.18 ± 0.30 | 0.01* | 0.22 | 0.17 | 0.009* |
| Central retinal thickness, μm | Baseline | 274.3 ± 120.2 | 219.5 ± 36.9 | 286.7 ± 97.1 | 385.0 ± 203.4 | 0.005* | 0.02* | 0.07 | 0.35 |
| | 4-year | 215.3 ± 48.5 | 213.2 ± 39.4 | 225.1 ± 41.8 | 200.2 ± 76.7 | 0.40 | | | |
| | Change | −59.6 ± 127.5 | −13.2 ± 28.4 | −55.3 ± 100.0 | −184.8 ± 227.0 | 0.04* | 0.17 | 0.09 | 0.24 |
| Central choroidal thickness, μm | Baseline | 127.9 ± 72.1 | 115.2 ± 75.8 | 148.9 ± 66.3 | 115.9 ± 70.9 | 0.25 | | | |
| | 4-year | 114.1 ± 56.8 | 110.0 ± 57.7 | 127.9 ± 54.1 | 95.7 ± 58.9 | 0.30 | | | |
| | Change | −9.0 ± 104.4 | −10.5 ± 31.3 | 15.4 ± 136.9 | −56.8 ± 135.6 | 0.20 | | | |
| Border-fovea distance, μm (+, the fovea superior to the border) | Baseline | 148.3 ± 602.0 | 183.1 ± 662.2 | 230.5 ± 511.7 | −111.7 ± 607.4 | 0.32 | | | |
| | 4-year | 175.2 ± 620.3 | 219.4 ± 670.5 | 274.2 ± 503.9 | −143.3 ± 668.7 | 0.19 | | | |
| | Change | 26.9 ± 115.7 | 36.3 ± 99.8 | 43.67 ± 129.9 | −31.6 ± 114.1 | 0.21 | | | |
| SRF height at the foveal center, μm | | | 0 | 66.0 ± 76.8 | 27.7 ± 64.8 | | | | |
| Anti-VEGF injections in 4 years, n | | | 0 | 0 | 9.0 ± 8.7 | | | | |
| Photodynamic therapy in 4 years, n | | | 0 | 0 | 0.2 ± 0.6 | | | | |
| CNV development in 4 years, n | | | 0 | 0 | - | | | | |

Data are presented as mean ± standard deviation.

logMAR BCVA, logarithm of the minimum angle of resolution of best-corrected visual acuity; SRF, subretinal fluid; VEGF, vascular endothelial growth factor; CNV, choroidal neovascularization

No-exudate group = eyes without CNV or exudate of subretinal detachment (SRD) or retinal pigment epithelial detachment at baseline; Exudate group = eyes without CNV and with exudate at baseline; CNV group = eyes with CNV at baseline

†Chi-square trend test was performed. Others tests for comparison of the three groups using an analysis of variance and subsequent pairwise comparisons were performed.

*Statistically significant ($P < 0.05$)

**Table 2. Correlation between 4-Year logMAR BCVA and other studied baseline or treatment-associated parameters in each group**

| | No-exudate group | | Exudate group | | CNV group | |
|---|---|---|---|---|---|---|
| | Univariate | Multivariate | Univariate | Multivariate | Univariate | Multivariate |
| | *P*-value (r) | *P*-value (β) | *P*-value (r) | *P*-value (β) | *P*-value (r) | *P*-value (β) |
| Age | < 0.001* (0.64) | 0.08 (0.45) | 0.19 (0.30) | 0.38 (0.16) | 0.69 (0.15) | N/A |
| Sex (1, male; 2, female) | 0.27 (0.23) | N/A | 0.69 (0.09) | N/A | 0.81 (0.09) | N/A |
| Tilted disc (0, absent; 1, present) | 0.91 (−0.02) | N/A | 1.00 (0) | N/A | 0.03* (0.67) | 0.02* (0.57) |
| Axial length | 0.01* (−0.50) | 0.052 (−0.42) | 0.53 (−0.15) | N/A | 0.80 (0.09) | N/A |
| LogMAR BCVA (baseline) | < 0.001* (0.81) | 0.91 (0.03) | < 0.001* (0.81) | 0.01* (0.52) | 0.04* (0.67) | 0.01* (0.62) |
| Central retinal thickness | 0.69 (−0.08) | N/A | 0.46 (−0.17) | N/A | 0.50 (0.24) | N/A |
| Central choroidal thickness | 0.03* (−0.43) | 0.70 (0.09) | 0.89 (−0.03) | N/A | 0.68 (0.15) | N/A |
| Border-fovea distance (+, the fovea superior to the border) | 0.14 (−0.30) | 0.33 (−0.20) | 0.44 (−0.18) | N/A | 0.29 (−0.37) | N/A |
| SRF height at the foveal center | N/A | N/A | 0.03* (0.47) | 0.02* (0.41) | 0.52 (0.23) | N/A |
| Anti-VEGF injections in 4 years | N/A | N/A | N/A | N/A | 0.48 (0.25) | N/A |

LogMAR BCVA, logarithm of the minimum angle of resolution of best-corrected visual acuity; CNV, choroidal neovascularization; SRF, subretinal fluid; VEGF, vascular endothelial growth factor

no-Exudate group = eyes without CNV or exudate of subretinal detachment (SRD) or retinal pigment epithelial detachment at baseline; Exudate group = eyes without CNV and with exudate at baseline; CNV group = eyes with CNV at baseline; N/A = not applicable

Statistical analysis in photodynamic therapy could not be performed because of the small sample size.

*Statistically significant ($P < 0.05$)

**Table 3. Correlation between 4-Year Change of logMAR BCVA and other studied baseline or treatment-associated parameters in each group**

| | No-exudate group | | Exudate group | | CNV group | |
|---|---|---|---|---|---|---|
| | Univariate | Multivariate | Univariate | Multivariate | Univariate | Multivariate |
| | *P*-value (r) | *P*-value (β) | *P*-value (r) | *P*-value (β) | *P*-value (r) | *P*-value (β) |
| Age | 0.73 (−0.07) | N/A | 0.65 (−0.11) | N/A | 0.92 (−0.04) | N/A |
| Sex (1, male; 2, female) | 0.73 (−0.07) | N/A | 0.17 (0.31) | 0.81 (−0.05) | 0.32 (0.35) | N/A |
| Tilted disc (0, absent; 1, present) | 0.44 (0.16) | N/A | 0.82 (−0.05) | N/A | 0.12 (0.52) | 0.01* (0.52) |
| Axial length | 0.78 (−0.06) | N/A | 0.41 (−0.19) | N/A | 0.71 (−0.13) | N/A |
| LogMAR BCVA (baseline) | 0.18 (−0.28) | < 0.001* (−0.65) | 0.39 (0.20) | N/A | 0.06 (−0.61) | 0.17 (−0.35) |
| Central retinal thickness | 0.44 (0.16) | N/A | 0.94 (−0.02) | N/A | 0.93 (−0.03) | N/A |
| Central choroidal thickness | 0.27 (0.23) | N/A | 0.70 (0.09) | N/A | 0.65 (0.17) | N/A |
| Border-fovea distance (+, the fovea superior to the border) | 0.60 (0.11) | N/A | 0.15 (−0.32) | 0.46 (−0.17) | 0.16 (0.48) | 0.08 (0.50) |
| SRF height | N/A | N/A | 0.03* (0.48) | 0.08 (0.42) | 0.03* (0.69) | 0.44 (0.12) |
| Anti-VEGF injections in 4 years | N/A | N/A | N/A | N/A | 0.83 (−0.08) | N/A |

LogMAR BCVA, logarithm of the minimum angle of resolutionof best-corrected visual acuity; CNV, choroidal neovascularization; SRF, subretinal fluid; VEGF, vascular endothelial growth factor

No-Exudate group = eyes without CNV or exudate of subretinal detachment (SRD) or retinal pigment epithelial detachment at baseline; Exudate group = eyes without CNV and with exudate at baseline; CNV group = eyes with CNV at baseline; N/A = not applicable

Statistical analysis in photodynamic therapy could not be performed because ofthe small sample size.

*Statistically significant ($P < 0.05$)