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Author(s)	Hasegawa, Tomoko; Otani, Atsushi; Sasahara, Manabu; Gotoh, Norimoto; Ooto, Sotaro; Tamura, Hiroshi; Yamashiro, Kenji; Tsujikawa, Akitaka; Yoshimura, Nagahisa
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Title: Prognostic Factors of Vitreous Hemorrhage Secondary to Exudative Age-related Macular Degeneration

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Corresponding Author: Atsushi Otani, M.D. Ph.D.

Corresponding Author's Institution: Kyoto University

First Author: Hasegawa Tomoko, MD

Order of Authors: Hasegawa Tomoko, MD; Atsushi Otani, MD; Manabu Sasahara, MD; Norimoto Gotoh, MD; Sotaro Ooto, MD; Hiroshi Tamura, MD; Kenji Yamashiro, MD; Akitaka Tsujikawa, MD; Nagahisa Yoshimura, MD

ABSTRACT

PURPOSE: Vitreous hemorrhage (VH) is a rare but serious complication of the eyes with exudative age-related macular degeneration (AMD). This retrospective study was designed to evaluate various clinical factors that may affect the visual prognosis of patients with VH secondary to exudative AMD.

DESIGN: Retrospective case study.

METHODS: We intensively documented 31 cases of VH secondary to exudative AMD and retrospectively analyzed best-corrected visual acuity (BCVA). All eyes underwent standard pars plana vitrectomy (PPV) for treating VH. Three subgroups were created according to the clinical course and treatment history before the occurrence of VH: (1) Gas group (7 eyes), Pneumatic displacement with SF₆ gas performed to treat massive submacular hemorrhage; (2) PDT group (9 eyes), Photodynamic therapy performed to treat exudative AMD; (3) Untreated group (15 eyes), No treatment performed.

RESULTS: As a whole, BCVA before the occurrence of VH was 1.05 ± 0.59 (LogMAR). After the occurrence of VH, BCVA before PPV dropped to 2.61 ± 0.82 . After the operation, final BCVA significantly improved to 1.25 ± 0.73 ($P<10^{-8}$). In a subgroup analysis, no statistically significant difference was seen among the three subgroups at any time point. We found that the eyes whose fellow eye had exudative AMD showed significantly poor final BCVA compared to the unilateral cases (0.92 ± 0.57 and 1.49 ± 0.72 , P=0.02).

CONCLUSIONS: PPV can improve visual acuity in the eyes with VH secondary to AMD, although effectiveness is limited. Medical practitioners should be cautious of the visual prognosis, especially in the cases whose fellow eye has exudative AMD.

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TITLE PAGE

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<u>Authors:</u> Tomoko Hasegawa, Atsushi Otani, Manabu Sasahara, Norimoto Gotoh, Sotaro Ooto, Hiroshi Tamura, Kenji Yamashiro, Akitaka Tsujikawa, and Nagahisa Yoshimura

<u>Affiliation:</u> Department of Ophthalmology and Visual Sciences, Kyoto University Graduate School of Medicine, Japan

<u>Corresponding author:</u> Atsushi Otani, MD
Department of Ophthalmology and Visual Sciences
Kyoto University Graduate School of Medicine
54 Shogoin-Kawahara-cho, Sakyo-ku, Kyoto 606-8386, Japan
Fax: +81-75-752-0933; E-mail: <u>otan@kuhp.kyoto-u.ac.jp</u>

INTRODUCTION

Choroidal neovascularization (CNV) secondary to exudative age-related macular degeneration (AMD) has a poor visual prognosis due to fundus manifestations that include pigment epithelial detachment, retinal detachment, sub-retinal/macular hemorrhage, hard exudates, macular edema, and subretinal fibrosis. Vitreous hemorrhage (VH) is a rare but serious complication of exudative AMD.¹⁻³ VH itself contributes to vision loss in AMD and is considered a sign of AMD progression. Although unstable neovasculature may be related to VH, the precise mechanisms that lead to ocular VH with exudative AMD remain unclear. In some cases, VHs may be spontaneously absorbed over time; however, pars plana vitrectomy (PPV) is often required to remove the hemorrhage. PPV surgery provides a relatively good visual prognosis.^{4, 5}

In ocular VH with exudative AMD, submacular hemorrhage often precedes the occurrence of spontaneous VH.² VH can occur in cases of massive submacular hemorrhage following treatments such as pneumatic displacement.^{6, 7} Photodynamic therapy (PDT) for the treatment of exudative AMD can also cause VH.^{8, 9} However, there is little information about how the clinical course of the disease affects visual prognosis in eyes with VH due to exudative AMD.

To clarify the factors that affect the prognosis of VH secondary to exudative AMD, we documented the clinical courses of patients with exudative AMD that underwent PPV to remove VH. Clinical factors likely to influence visual prognosis were investigated. We additionally evaluated the efficacy of pars plana vitrectomy (PPV) for treating VH due to exudative AMD.

METHODS

For this interventional case study, we retrospectively reviewed the medical records of 979 consecutive patients with exudative AMD who were treated at the Macula Service, Department of Ophthalmology, Kyoto University Hospital, from January 2004 to September 2008. Inclusion criteria were as follows: (1) the occurrence of VH during the follow-up period in the clinic, (2) a diagnosis of exudative AMD during followup, (3) treatment with PPV for VH, and (4) a postoperative follow-up period greater than three months. Patients were divided into 3 subgroups depending on their clinical course before the occurrence of VH: (1) gas group: pneumatic displacement with SF_6 gas was used to treat massive submacular hemorrhage before the occurrence of VH; (2) PDT group: PDT was used to treat exudative AMD before the occurrence of VH; and (3) untreated group: no treatment was performed before the occurrence of VH. For the purposes of this study, patients with polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP) were considered to have exudative AMD and were included in the study. We use the term AMD to mean exudative AMD that could not be diagnosed as PCV or RAP. Patients with other types of CNV, i.e. pathologic myopia, angioid streaks, RAP, idiopathic CNV, presumed ocular histoplasmosis syndrome, and other secondary CNV were excluded from this study. Patients with other retinal/macular abnormalities, i.e., retinal macroaneurysm, diabetic retinopathy, retinal vein occlusion, or uveitis, were also excluded from the study.

A PCV diagnosis was based on an indocyanine green (ICG) angiogram that showed polypoidal structures along the border of the branching vascular network. A polypoidal lesion can appear as a single polyp or as a cluster of polyps. In most PCV cases, reddish-orange subretinal nodules were seen under ophthalmoscopic examination that corresponded to the polypoidal lesions seen by ICG angiography. All patients had comprehensive ophthalmologic examinations, including best-corrected visual acuity (BCVA) measurements, binocular ophthalmoscopy, slit-lamp biomicroscopy with a contact lens, color fundus photography, fluorescein angiography, ICG angiography, and optical coherence tomography (OCT). Fluorescein angiography and ICG angiography were performed simultaneously using a confocal laser scanning system (HRA-2; Heidelberg Engineering, Dossenheim, Germany). Four types of OCT instruments were used (Stratus OCT, Carl Zeiss, Dublin, CA; OCT-ophthalmoscope, Nidek, Gamagori, Japan; 3D OCT-1000, Topcon, Tokyo, Japan; RTVue, Optovue Corp., San Francisco, CA). All patients were assessed carefully at baseline and then

every 3 months. In addition, patients were advised to visit the clinic if they felt their vision was worsening.

To treat VH, standard three-port PPV was performed on all patients in the study using a 20-gauge or 23-gauge system. Six experienced surgeons in our macular clinic performed all surgeries. Phacoemulsification and intraocular lens implantation was combined in all phakic eyes because of the expected progressive nuclear sclerosis. Fluid-air exchange and sulfur hexafluoride (SF₆) gas tamponade was performed in some cases.

To treat massive submacular hemorrhage, pneumatic displacement was performed using 0.5 ml of 100% SF₆ gas injected into the vitreous cavity with a 30gauge needle. Patients were instructed to maintain a prone position at least 4 days. PDT with verteporfin to treat exudative AMD was performed according to standard procedures. A 689-nm laser system (Carl Zeiss, Dublin, CA) was used, and 50-J/mm² energy was delivered with an 83-second exposure time.

For statistical analysis, counting fingers (CF), hand motion (HM) and light perception (LP) were considered to indicate decimal visual acuity of 0.005, 0.001 and 0.0005, respectively. The BCVA was determined using the Landolt ring test and converted into the logarithm of the minimum angle of resolution (logMAR). All values are reported as the mean ± standard deviation. Continuous variables between two groups were compared using the Student's t-test (two-tailed). Continuous variables between three groups were compared by one-way analysis of variance. Multivariate linear regression analysis was performed to correlate final visual acuity with other clinical parameters. All analyses were performed using a commercial software program (SPSS v.13.0; SPSS, Chicago, IL). A difference was considered statistically significant when the *P* value was less than 0.05.

RESULTS

This study included 31 patients, each with one eye with VH due to exudative AMD (3.2% of the 979 age-related exudative AMD patients) (Table 1). The patients ranged in age from 55 to 86 years (mean \pm standard deviation, 73.8 \pm 7.7 years). The mean postoperative follow-up period was 19.9 \pm 14.2 months (range, 5–52 months). Of the 31 eyes, 22 (71%) were diagnosed as PCV by angiographic analysis; the other 9 were diagnosed as AMD. Patient characteristics are summarized in Table 1. Submacular hemorrhage and hemorrhagic pigment epithelial detachment was detected prior to VH in 14 and 15 eyes, respectively. Seven patients presented with VH at their initial visit to the clinic. The CNV lesion was located parafoveally in patients 2, 12, 13, 14, 15, 17, 18, and 21 (n = 8) (Table 1).

Vitreous hemorrhage was observed after pneumatic displacement of submacular hemorrhage using intravitreal injection of SF₆ gas in 7 eyes (the gas group); the mean period from gas injection to the occurrence of VH was 51 \pm 102 days (range, 3–300 days). Before VH, PDT was performed in 9 eyes (the PDT group). In the PDT group, the mean period from the last PDT to the occurrence of VH was 14 \pm 12 months (range, 0.5–31 months). In the other 15 eyes (the untreated group), no treatment was performed before VH was detected. PPV was performed in all cases to remove the VH and was performed in conjunction with phacoemulsification in 25 eyes (81%).

The mean BCVA (at the last documentation for each eye) before VH in the 25 patients who were seen in the clinic before the VH occurred was 1.05 ± 0.59 LogMAR units. After the occurrence of VH, the mean BCVA decreased to 2.61 ± 0.82 and then showed significant improvement 3 months after PPV surgery ($P < 10^{-8}$); improvements in BCVA were maintained during the follow-up period (Figure 1, top). The mean BCVA 6 months after surgery was 1.23 ± 0.78 and was 1.12 ± 0.82 12 months after surgery ($P < 10^{-8}$). Although the improvement in BCVA after surgery was more than 0.3 LogMAR units in 26 eyes (84%), the final BCVA was not satisfactory in most cases. Only 8 eyes (26%) had a final BCVA ≥ 1.0 LogMAR units. When analyzing the five cases with relatively good visual prognosis (less than LogMAR 0.6, cases 4, 7, 12, 18, and 21), we found that all cases were PCV and that four patients (80%) were unilaterally affected. In addition, all five cases had polypoidal lesions, pigment epithelial detachment, or submacular hemorrhage that was para- or extrafoveal. Three of the 5 eyes (60%) showed branching vascular networks under the fovea (cases 7, 18, and 21).

In the subgroup analysis, BCVA before the occurrence of VH was 0.82 ± 0.30 in the gas group, 0.97 ± 0.26 in the PDT group, and 1.08 ± 0.65 in the untreated group.

After the occurrence of VH, BCVA before PPV was 2.46 ± 0.87 in the gas group, 2.54 ± 0.92 in the PDT group, and 2.71 ± 0.79 in the untreated group. The final BCVA was 0.90 ± 0.56 in the gas group, 1.35 ± 0.72 in the PDT group, and 1.34 ± 0.79 in the untreated group. There seemed to be a trend for the gas group to have a better visual prognosis compared to other groups; however, no statistically significant difference was seen in the three subgroups at any time point (Figure 1, middle). In our series, 7 of the 9 PDT cases that developed VH had only one PDT session. In the other 2 cases (cases 9 and 16), the patient received multiple PDT sessions before VH. In most of the PDT cases, the lesion was stabilized after PDT, and VH occurred with the recurrence of AMD. In 2 cases (cases 9 and 11 in Table 1), PDT did not stabilize the lesion; subsequently, VH occurred.

Interestingly, the percentage of bilaterally affected exudative AMD patients was high for the VH cases (16 eyes, 52%) compared to all the exudative AMD cases in our clinic (21%). Therefore, we compared unilaterally (n = 15) and bilaterally (n = 16) affected patients. BCVA before the occurrence of VH was 1.01 ± 0.72 in the unilateral group and 1.07 ± 0.48 in the bilateral group, while BCVA before PPV was 2.69 ± 0.62 and 2.55 ± 0.96 , respectively. There were significant differences in BCVA between the two groups at 3 months (0.95 ± 0.54 vs 1.56 ± 0.82 ; P = 0.02), 6 months (0.87 ± 0.56 vs 1.55 ± 0.83 ; P = 0.01), 12 months (0.71 ± 0.58 vs 1.53 ± 0.84 ; P = 0.02), and at the final end point (P = 0.02) (Figure 1, bottom).

Using multivariate regression analysis, we also examined other factors that might have influenced the 6-month BCVA (Table 2). Explanatory variables were age, sex, hypertension, diabetes mellitus, anticoagulant medication, history of smoking, angiographic subtype, submacular hemorrhage before VH, phacoemulsification and intraocular lens implantation combined vitrectomy, logMAR before VH, logMAR before PPV, and logMAR of the fellow eye. None of these factors showed statistical significance.

Avastin injection was used in cases 1, 6, 28, and 30. In all of these cases, the injection was performed once in the period after VH and surgery.

5	9
6	0
6	1
б	2
б	3
б	4
6	5

DISCUSSION

In our series of 31 eyes with VH secondary to CNV, PCV occurred in a high percentage of cases (71%). PCV is a subtype of exudative AMD, and the first published case of PCV was reported as posterior uveal bleeding syndrome.¹⁰ Subsequent to that report, there have been numerous studies of PCV. As detected by ICG angiography, polypoidal vasculature rather than massive bleeding is now considered a common and distinctive angiographic feature of the disease. Bleeding is still an important characteristic of PCV, and the rate of hemorrhagic complications, including hemorrhagic pigment epithelial detachment in PCV, is higher than in other types of AMD.^{11, 12}

VH is a hemorrhagic complication of exudative AMD that can cause severe vision loss. Although the incidence of VH in exudative AMD is not high (3.2% of 979 cases in our case series), the incidence of PCV among the VH cases was higher (71%) than the incidence of PCV among all exudative AMD cases (47% in our clinic). PCV should thus be considered when patients with exudative AMD present with VH.

Anticoagulant medications can contribute to the incidence of hemorrhagic complications in exudative AMD, for example in submacular hemorrhage or VH.^{1, 13} In the current study, only 16% of the 31 patients were on anticoagulants, and in our previous report on hemorrhagic complications in PCV cases after PDT, anticoagulants did not affect the incidence of complications.⁹ Larger case series are needed to fully explore this issue. During the observation period in this study, medications were not related to changes in BCVA.

In this study, the clinical courses leading to VH did not affect the significant differences we observed in BCVA (3-month mean BCVA: gas group 0.94 ± 0.59 , PDT group 1.36 ± 0.65 , untreated group 1.36 ± 0.86 ; 6-month mean BCVA: gas group 0.79 ± 0.55 , PDT group 1.35 ± 0.78 , untreated group 1.38 ± 0.85 ; 12-month mean BCVA: gas group 0.70 ± 0.57 , PDT group 1.28 ± 0.90 , untreated group 1.19 ± 0.86). Although the difference was not statistically significant (*P*=), eyes affected by VH in the six months after PDT tended to have a lower final BCVA than other eyes in the PDT group. There is no evidence that PDT itself triggers VH, but we previously found that 6.6% of PVC resulted in VH following PDT.⁹ It is possible that VH after PDT may result from incomplete tissue and vascular repair, indicating a poor prognosis. Further studies are required to clarify this issue; in the meantime, clinicians should focus on cases in which VH occurs immediately after PDT.

In our series of 979 patients, there were 15 patients who were treated with pneumatic displacement for submacular hemorrhage. Of these, 7 developed VH and

were included in this study. The final mean visual acuity for these 7 cases was $0.90 \pm 0.56 \log$ MAR, whereas that of the other 8 cases who did not develop VH was 0.88 ± 0.6 . Because there was no significant difference between the two groups, it seems that development of VH after gas injection may have little effect on the prognosis of submacular hemorrhage. As shown in Figure 1, there was a tendency for the gas group to have better visual acuity compared to the untreated group. Gas injection should be considered for submacular hemorrhage, even if the treatment is a risk factor for VH. We calculated the risks associated with several factors that might affect the incidence of VH after pneumatic displacement. However, intra-ocular lens implantation, hypertension (HT), diabetes mellitus (DM), history of smoking, PDT, and anticoagulant medication were not correlated with the incidence of VH.

We found that cases that were bilaterally affected by exudative AMD had very poor visual prognosis after VH compared to unilateral cases. We previously reported a bilaterally affected case with a different a biological response to PDT treatment that had a worse visual prognosis compared to a unilaterally affected case.¹⁴ In addition, there is a loss of control of pathological vessels and tissues by circulating hematopoietic stem/progenitor cells in bilaterally affected cases.¹⁵ We noted a high percentage of bilaterally affected cases (52%) in our VH case series (this study). In general, the incidence of bilateral exudative AMD in Japanese patients is ~10-20%.^{16, 17} This extremely high rate of bilateral exudative AMD in VH cases suggests a relationship between susceptibility to VH and bilateral affection. In genomic studies, patients with high-risk homozygous ARMS2 polymorphisms tend to have bilateral AMD,^{18, 19} and this high-risk homozygous polymorphism is frequently seen in patients with VH.²⁰ These data suggest a common genetic background that that increases susceptibility to VH and bilateral exudative AMD. These reports, along with the data in the current study, raise the possibility that different biological responses or pathological causes may underlie the differences between bilateral and unilateral exudative AMD cases. Further investigations should clarify the relationship between susceptibility to VH and bilateral exudative AMD.

In conclusion, the current study searched for prognostic factors of VH secondary to exudative AMD. We found that (1) there is a high susceptibility to PCV in cases with VH secondary to exudative AMD, (2) PPV can restore visual acuity to a pre-VH level, although relatively good visual prognosis can only be obtained in limited cases, and (3) visual prognosis in bilaterally affected patients is poor. Although we included more patients in this study than were included in previous studies, an even larger case series

is necessary for clarify the prognosis of VH in exudative AMD cases. Further efforts should focus on the biological responses and background of bilateral exudative AMD cases.

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- e) Other acknowledgements: None.

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FIGURE LEGENDS

Figure 1. Changes in visual acuity before and after pars plana vitrectomy (PPV) for vitreous hemorrhage (VH) secondary to age-related macular degeneration (AMD). (Top) LogMAR units before VH (pre-VH), after VH (pre-PPV), and final visual acuity after PPV (final). *: $P < 10^{-6}$, compared to pre-PPV. (Middle) Comparison of LogMAR changes among the three subgroups. Gas = patients treated by intravitreal injection of SF₆ gas for displacing submacular hemorrhage before the occurrence of VH. PDT = patients treated by photodynamic therapy for exudative AMD before the occurrence of VH. Untreated = patients without any treatment before the occurrence of VH. (Bottom) Comparison of LogMAR changes between patients with unilateral and bilateral exudative AMD. *: P < 0.05.

Figure 2. A case of vitreous hemorrhage (VH) secondary to exudative age-related macular degeneration resulting in relatively good visual prognosis (case 7). (Top left) The right eye is normal, with decimal visual acuity of 1.2. (Top right) The left eye showed massive submacular hemorrhage and hemorrhagic pigment epithelial detachment (PED) before the occurrence of VH. (Bottom left) Indocyanine green angiogram showed a branching vascular network and polypoidal structure at the border of the network. Fluorescence is blocked at the PED lesions. (Bottom right) Pars plana vitrectomy (PPV) was performed after VH developed. Macular hemorrhage was absorbed and the decimal visual acuity of the left eye improved to 1.0 nine months after PPV.

Figure 3. A case of vitreous hemorrhage (VH) secondary to exudative age-related macular degeneration (AMD) resulting in poor visual prognosis (case 15). (Top left) A fundus photograph of the right eye before the occurrence of VH. Large hemorrhagic pigment epithelial detachment (PED) can be seen beyond the vascular arcade. Orange subretinal lesions were observed at the border of the PED. The decimal visual acuity was 0.2. (Top right) The left eye showed fibrovascular scar formation secondary to old exudative AMD. (Bottom left) Indocyanine green angiogram of the right eye showed a large vascular network at the macula and aneurismal structures at the border of the network. (Bottom right) After the occurrence of VH, the patient underwent PPV. A huge choroidal neovascular membrane was seen at the macula. Ten months after PPV, the decimal visual acuity was 0.02.

case	Age case Sex HT DM (y)	Age	Sex	ex HT D	, IT DM	DM	HT DM	HT DM	HT DM	HT DM	HT DM	Anticoagulant	History of	Laterality	ality Diagnosis	Submacular Hemorrhage	Treatment before VH	Contents of	VA before	VA before	VA	Postoperative Follow-up
				Medication	Smoking	of CNV		before VH	(day)	Surgery	VH	PPV	Final	Periods (m)								
1	71	М	No	No	Yes	No	Unilateral	PCV	Yes	Gas (7)	PPV+PEA+IOL	0.3	N/A	0.1	29							
2	71	м	No	No	No	Yes	Bilateral	PCV	Yes	Gas (10)	PPV+PEA+IOL	0.2	0.1	0.1	6							
3	78	м	No	No	No	Yes	Unilateral	PCV	Yes	Gas (19)	PPV+PEA+IOL	0.1	нм	0.04	5							
4	70	м	No	No	No	Yes	Bilateral	AMD	Yes	Gas (7)	PPV+PEA+IOL	0.08	CF	0.3	24							
5	68	м	No	No	No	No	Unilateral	AMD	Yes	Gas (300)	PPV+PEA+IOL	0.06	нм	0.02	52							
6	68	м	Yes	Yes	Yes	No	Bilateral	AMD	Yes	Gas (10)	PPV+PEA+IOL	0.15	нм	0.2	48							
7	71	м	Yes	No	No	No	Unilateral	PCV	Yes	Gas (6)	PPV+PEA+IOL	0.4	N/A	1.0	13							
8	81	м	Yes	No	No	No	Bilateral	AMD	No	PDT (360)	PPV	0.04	CF	0.07	15							
9	73	м	Yes	No	No	Yes	Bilateral	PCV	No	PDT (45)	PPV+PEA+IOL	0.1	LP	нм	13							
10	78	м	Yes	No	No	Yes	Bilateral	PCV	No	PDT (180)	PPV	0.15	0.07	0.06	37							
11	81	м	No	No	No	Yes	Bilateral	PCV	Yes	PDT (15)	PPV	0.07	0.07	0.05	8							
12	70	м	No	No	No	No	Unilateral	PCV	No	PDT (930)	PPV+PEA+IOL	0.3	0.01	0.5	12							
13	76	м	No	No	No	Yes	Unilateral	PCV	No	PDT (810)	PPV+PEA+IOL	0.1	нм	0.07	11							
14	85	м	Yes	No	Yes	No	Bilateral	PCV	No	PDT (870)	PPV+PEA+IOL	0.07	LP	0.08	8							
15	68	м	No	No	No	Yes	Bilateral	PCV	No	PDT (420)	PPV+PEA+IOL	0.2	LP	0.02	10							
16	55	F	No	No	No	No	Unilateral	PCV	No	PDT (60)	PPV+PEA+IOL	0.1	LP	0.06	23							
17	80	м	Yes	No	No	Yes	Unilateral	PCV	Unknown	Untreated	PPV+PEA+IOL	N/A	нм	0.2	25							
18	77	F	Yes	No	No	No	Unilateral	PCV	Yes	Untreated	PPV+PEA+IOL	0.3	нм	1.0	29							
19	58	м	Yes	No	No	Yes	Unilateral	PCV	Yes	Untreated	PPV+PEA+IOL	0.06	НМ	0.02	20							
20	78	м	No	No	No	Yes	Bilateral	PCV	Yes	Untreated	PPV+PEA+IOL	0.04	LP	0.03	11							
21	65	м	Yes	No	No	Yes	Unilateral	PCV	Unknown	Untreated	PPV+PEA+IOL	N/A	CF	0.4	12							
22	58	м	No	No	No	Yes	Unilateral	PCV	Unknown	Untreated	PPV+PEA+IOL	N/A	0.09	0.2	8							
23	80	м	Yes	Yes	Yes	No	Bilateral	PCV	Unknown	Untreated	PPV	N/A	LP	НМ	6							
24	75	F	Yes	No	No	No	Unilateral	PCV	Unknown	Untreated	PPV+PEA+IOL	N/A	CF	0.08	8							

TABLE 1. Clinical Profile of 31 patients with Vitreous Hemorrhage Secondary to Age-related Macular Degeneration Treated by Pars Plana Vitrectomy.

25	82	м	No	No	Yes	Yes	Bilateral	PCV	No	Untreated	PPV	0.02	LP	CF	17
26	74	М	Yes	No	No	Yes	Bilateral	AMD	Yes	Untreated	PPV+PEA+IOL	0.08	нм	0.09	52
27	73	F	No	No	No	Yes	Unilateral	AMD	Yes	Untreated	PPV	0.2	нм	0.1	7
28	77	М	Yes	No	No	Yes	Bilateral	AMD	Yes	Untreated	PPV+PEA+IOL	0.01	LP	0.01	34
29	86	F	Yes	No	No	Yes	Unilateral	AMD	Unknown	Untreated	PPV+PEA+IOL	нм	нм	0.02	8
30	79	М	Yes	Yes	Νο	No	Bilateral	PCV	Unknown	Untreated	PPV+PEA+IOL	N/A	0.15	0.1	43
31	81	м	No	No	No	No	Bilateral	AMD	No	Untreated	PPV+PEA+IOL	1.0	нм	0.01	22

CNV=choroidal neovascularization; HT=hypertension; DM=diabetes mellitus: AMD = age-related macular degeneration; CF = counting finger; Gas = Intravitreal injection of SF_6 gas; HM = hand motion; IOL = intraocular lens implantation; LP = light perception; m = months; PCV = polypoidal choroidal vasculopathy; PDT = photodynamic therapy; PEA = phacoemulsification and aspiration; PPV = pars plana vitrectomy; VH = vitreous hemorrhage; VA=visual acuity; y = years. The numbers in the "Treatment before VH" column indicated the months between the treatment and VH

Independent Variable	β coefficient	P value		
Age	-0.20	0.47		
Sex	-0.45	0.11		
Hypertension	0.04	0.90		
Diabetes mellitus	-0.29	0.34		
Medication of anticoagulant	0.19	0.53		
History of smoking	0.25	0.42		
Angiographic subtype of PCV	-0.01	0.98		
Submacular hemorrhage before VH	-0.11	0.72		
PEA+IOL combined	-0.20	0.52		
LogMAR of pre VH	-0.06	0.86		
LogMAR of pre PPV	0.43	0.14		
LogMAR of fellow eye	-0.07	0.81		

TABLE 2. Multivariate analysis of the factors which might have influenced the BCVA

IOL = intraocular lens implantation; PCV = polypoidal choroidal vasculopathy; PEA = phacoemulsification and aspiration; PPV = pars plana vitrectomy; VH = vitreous hemorrhage.





