Visual Outcome of Non-traumatic Dense Vitreous Hemorrhage in Patients without Diabetes: Single Center Case Series

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Short Title: Non-traumatic Dense Vitreous Hemorrhage

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ABSTRACT

Purpose: Dense vitreous hemorrhage is a vision-threatening disease with varied clinical manifestations. Herein, we aimed to evaluate its causes and outcomes in patients without diabetes.

Methods: A retrospective cohort including 60 eyes from 60 patients with an initial diagnosis of non-traumatic fundus-obscuring dense vitreous hemorrhages and without diabetes was recruited. The relevant medical records from January 2013 to December 2019 were reviewed and analyzed. We classified patients into the following four groups, depending on the underlying cause of dense vitreous hemorrhage: eight cases in the age-related macular degeneration (AMD) group, four cases in the posterior vitreous detachment group, 20 cases in the Tear group, and 28 cases in the Vascular group.

Results: The most common cause of dense vitreous hemorrhage was retinal vascular obstructive disease (46.7%); the AMD group showed the worst prognosis. The extent of best corrected visual acuity change was significantly better in patients who underwent vitrectomy compared to those receiving conservative treatment; best corrected visual acuity change (logMAR) was 1.62±0.57 and 1.06±0.88 in the surgical and non-surgical groups, respectively (p=0.007, Student t-test).

Conclusions: Retinal vascular disease is the most common cause of vitreous hemorrhages, and surgical treatments have a better visual outcome than non-surgical treatments.

Keywords: Age-related macular degeneration, Visual acuity, Vitreous hemorrhage
INTRODUCTION

Vitreous hemorrhage is a vision-threatening disease with varied clinical manifestations and causes. The prognosis of vitreous hemorrhage depends on its underlying cause. The most common cause of vitreous hemorrhage is proliferative diabetic retinopathy [1,2]. However, trauma, posterior vitreous detachment (PVD), retinal breaks, and vascular occlusive disease can also cause vitreous hemorrhage [1–3]. Diabetic retinopathy is a leading cause of blindness in adults of the working age group worldwide [4]. Previous studies have reported the prognosis and visual outcomes of vitreous hemorrhage caused by proliferative diabetic retinopathy [4,5].

Diagnosis and treatment of acute, dense fundus obscuring vitreous hemorrhages in patients without diabetic retinopathy is challenging. In dense vitreous hemorrhage patients, fundus examination is usually impossible; therefore, ultrasonographic examinations are used. However, ultrasonography provides limited information. Ultrasonography can be useful in detecting retinal detachment and horseshoe tears, but tears can be missed when multiple tears are present [6]. Missed tears could progress to retinal detachment, leading to irreversible visual loss. The amount of time needed for vitreous hemorrhage to resolve is important because rapid subsiding of the hemorrhage allows fast examination of the fundus, facilitating the identification and treatment of the underlying cause of hemorrhage, including retinal tears. In contrast, prolonged hemorrhage can lead to retinal detachment and proliferative vitreoretinopathy [7].

If an apparent retinal detachment or choroid abnormality is observed on ultrasound examination in cases where a fundus examination is impossible due to dense vitreous bleeding, surgical treatment can be planned immediately. However, if there are no specific findings on ultrasound examination, it may be difficult to determine the cause of vitreous hemorrhage, potentially leading to delays in determining the direction of treatment. In this retrospective study, we report the cause, clinical manifestation, treatment, and prognosis of non-traumatic dense vitreous hemorrhage in patients without diabetes, with no findings of retinal detachment in the ultrasonographic examination.

MATERIALS AND METHODS

Setting

This institutional, retrospective cohort study was conducted at the Department of Ophthalmology at the Sanggye Paik Hospital of the Inje University of Korea, Seoul, Korea, from January 2013 to December 2019. The study protocol was approved by the Inje University Institutional Review Board (No. 2021-12-003). The informed
consent requirement was waived due to the study’s retrospective nature. This research adhered to the tenets outlined in the Declaration of Helsinki and all state laws in Korea.

Study population

Sixty eyes of 60 consecutive patients with an initial diagnosis of non-traumatic dense fundus obscuring vitreous hemorrhage were identified retrospectively in a review of patients with vitreous hemorrhage seen at our department between January 2013 and December 2019. We included patients with grade 4 vitreous hemorrhage density grading based on the Lieberman scale, which indicates dense vitreous hemorrhage with no red reflex present [8]. All patients had undergone ophthalmic examination, including ultrasonography, to detect PVD or any retina abnormality. Patients with at least 12 months of follow-up after their initial visit were included in the study. Since the study aimed to examine the degree of visual improvement with and without surgery in dense vitreous hemorrhage and since hemorrhage resolution takes an amount of time, we decided that at least a 1-year follow-up period is required. We excluded cases with shorter follow-up periods to determine the long-term prognosis, as cases with <1 year were often lost to follow-up. After the first hospital visit, a monthly follow-up observation was performed. A vitrectomy was performed if there was no vitreous hemorrhage improvement within this period. Surgical treatment was decided when there was no sign of improvement in hemorrhage in the first 1–2 months of follow-up. In addition, a vitrectomy was performed when the patient complained of discomfort and strongly desired surgery. After vitrectomy, cataracts progress faster than before surgery. Therefore, in patients with a grade ≥3 cataract based on Lens Opacities Classification System (LOCS) III, vitrectomy and cataract surgery were performed simultaneously if the patient consented.

We excluded cases of vitreous hemorrhage caused by intraocular surgery, trauma, or diabetic retinopathy and patients diagnosed with diabetes or abnormal retinal findings in the non-affected eye, including hypertensive retinopathy. In addition, we excluded cases in which fundus examination by an experienced ophthalmologist revealed mild generalized retinal arteriolar narrowing according to the Keith-Wagener-Baker classification [9]. However, patients with well-controlled systemic hypertension without hypertensive retinopathy were not excluded. We applied the criteria from Korea, where hypertension is defined as a systolic blood pressure of ≥140 mmHg or a diastolic blood pressure of ≥90 mmHg. In ultrasonographic examination, patients with retinal detachment and abnormal choroid examinations were excluded. Patients with a history of retinal detachment surgery, including scleral buckling or vitreous surgery, and uveitis were also excluded.

We categorized patients into four groups depending on the underlying cause of vitreous hemorrhage: age-related
macular degeneration (AMD), PVD, Tear, and Vascular groups. Following the resolution of vitreous hemorrhage, patients exhibiting evidence of AMD, including choroidal neovascularization, large submacular hemorrhage, and polypoidal choroidal vasculopathy, were classified into the AMD group. Meanwhile, those with disc hemorrhage caused by PVD were classified into the PVD group. The Vascular group included branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), branch retinal artery occlusion (BRAO), and central retinal artery occlusion (CRAO).

Outcome analysis and variables

Data were collected for demographic and clinical manifestation and past medical history. The source of systemic infection and blood culture results were also reviewed. Ophthalmic examinations included slit-lamp examinations, initial and final best corrected visual acuity (BCVA), intraocular pressure (measured using Goldmann applanation tonometry), fundus examinations, and ultrasonography in every visit.

RESULTS

A total of 60 eyes from 60 patients were included in this study. Eight, four, 20, and 28 eyes were included in the AMD, PVD, Tear, and Vascular groups, respectively. In the Vascular group, 25 eyes were diagnosed as BRVO only, one eye had both BRVO and BRAO, and one case of CRAO and CRVO was diagnosed each.

The baseline characteristics of all groups are listed in Table 1. The average patient age was 66.03 ± 11.11 years, and there was no significant difference in the average age of patients in each group (p=0.101, one-way ANOVA). Hypertension was more frequent in the Vascular group compared to other groups (p<0.001, odds ratio 7.52, chi-square test). Moreover, there was no statistically significant difference in the prevalence of hypertension between the Vascular and AMD groups (p=0.286, chi-square test). The causes by age groups are shown in Table 2; no clear tendency was observed. Patients who received vitrectomy underwent surgery on an average of 37.6 days after the first visit.

The percentage of patients who underwent surgery and the initial BCVA, final BCVA, and the extent of BCVA change in each group are shown in Table 3. Five patients in the AMD group, all in the PVD group, 18 in the Tear group, and 19 in the Vascular group, underwent surgery. There was no significant difference in the initial BCVA among groups (p=0.812, Kruskal–Wallis test), but there was a significant difference in the final BCVA and in the extent of BCVA change (p=0.003 and p=0.006, respectively; Kruskal–Wallis test). In the post-hoc analysis, there
was a significant difference in the final BCVA between the AMD and PVD groups and between the AMD and Tear groups (p=0.004 and p=0.001, respectively; Mann–Whitney U test). In addition, the extent of BCVA change in the AMD group was significantly smaller compared to other groups (PVD, Tear, and Vascular; p=0.008, p=0.001, p=0.007, respectively; Mann–Whitney U test).

We compared the initial BCVA, final BCVA, and the extent of BCVA change according to the presence or absence of hypertension; all parameters showed no significant difference (p=0.574, p=0.601, p=0.769, respectively; Student t-test).

The initial BCVA, final BCVA, and the extent of BCVA change depending on whether or not surgery was performed are shown in Table 4. The initial BCVA was significantly better in the non-surgical group than in the surgical group (p=0.001, Student t-test). There was no significant difference in the final BCVA, but the extent of BCVA change was significantly better in the surgical group (p=0.007, Student t-test). Among patients who underwent surgery, there was no significant difference in initial BCVA, final BCVA, and BCVA change between the group that received vitrectomy with cataract surgery and the group that received vitrectomy only (p=0.295, p=0.158, and p=0.174, respectively; Student t-test).

As a result of reviewing the charts of patients with a final BCVA of >1.0, among 10 patients, four were in the AMD group, two in the Tear group, and four in the Vascular group. Macular-off rhegmatogenous retinal detachment was observed intraoperatively in the two patients in the Tear group. Among the patients in the Vascular group, the cause of vitreous hemorrhage was BRVO invading the macula in two patients, CRVO in one patient, and CRAO in the remaining patient.

DISCUSSION

In our study, vascular diseases, especially BRVO, were the most common causes of dense vitreous hemorrhage. Retinal neovascularization was observed in 18 patients, and eight cases of BRVO had as much vascular obstruction as hemi-CRVO. A previous prospective study has reported that vitreous detachment and traction to a retinal vessel were the most common causes of vitreous hemorrhage [10]. Pighin et al. reported that retinal tears were found in 65.8% of healthy patients with dense vitreous hemorrhage [11]. Although these findings differ from our result, the proportion of patients with well-controlled hypertension in these studies was 16% [10] and 21.7% [11], respectively. In the present report, 44% of patients had systemic hypertension, a well-known, classic risk factor of BRVO [12]. Moreover, in the present study, hypertension was significantly more frequent in the Vascular group.
compared to other groups. Zhang et al. reported retinal vein occlusion as the most common cause (58.1%) of dense vitreous hemorrhage in patients with non-traumatic and non-diabetic retinopathy in China [13]. This aligns with our findings and suggests that the variations in the prevalence of systemic hypertension among different races may contribute to these results.

Visual outcomes of dense vitreous hemorrhage depended on the underlying cause of the hemorrhage. Vitreous hemorrhage caused by macular degeneration was significantly associated with worse visual outcomes in this study, as shown in previous reports [10,14,15]. In our study, choroidal neovascularization rupture, large submacular hemorrhage, and polypoidal choroidal vasculopathy-related vitreous hemorrhage were observed. As the prevalence of AMD has increased with the aging population, the proportion of macular degeneration as a cause of spontaneous vitreous hemorrhage has also increased. Therefore, macular degeneration has become a more important cause of vitreous hemorrhage.

Rhegmatogenous retinal detachment is the most severe complication of vitreous hemorrhage in patients without diabetes. In the present study, retinal tears were the second most common cause of vitreous hemorrhage and showed favorable visual outcomes compared with the other groups. We excluded patients with abnormal ultrasonographic examination, such as retinal detachment and large tears. Therefore, only patients with small retinal tears undetectable by ultrasonographic examination were included. This selection bias may underlie the favorable visual outcomes observed in the Tear group.

Treatment of vitreous hemorrhage in healthy patients poses a dilemma to the ophthalmologist. Many ophthalmologists favor a conservative treatment if the hemorrhage is minimal and does not obscure fundus details. Almost all the hemorrhages of this scale spontaneously resolve with conservative treatment.

However, in patients presenting with dense vitreous hemorrhage, the presence of a retinal tear cannot be ruled out solely by ultrasonographic examination. In the present study, there were retinal breaks not detected by ultrasonographic examination in 20 eyes. However, the small retinal breaks did not rapidly progress to retinal detachment. Therefore, the visual prognosis of patients in the Tear group did not differ from that of the other groups, except for the AMD group.

Longstanding dense vitreous hemorrhage may cause visual distortion due to the toxic effect of the hemorrhage on the retina and the formation of epiretinal membranes [13]. In addition, delayed surgery can be associated with poor visual outcomes due to proliferative vitreoretinopathy. In the present study, 78% of patients underwent trans pars plana vitrectomy. The initial BCVA was better in the non-surgical group than in the surgical group, whereas the final BCVA was not significantly different between the two groups. The extent of BCVA improvement between
the initial and final visit was significantly better in the surgical group. However, 54% of the patients in the surgical treatment group underwent cataract surgery with vitrectomy; this may have influenced the better visual outcomes of the surgical group.

The causes of vitreous hemorrhage were not significantly different between the surgical and non-surgical groups. However, the surgery rate is lower in the AMD and Vascular groups than in the PVD and Tear groups. While hemorrhage caused by AMD or vascular causes usually continues in the initial hemorrhage, the hemorrhage in the PVD and Tear groups tends to gradually increase as it progresses and is difficult to resolve even with a long period of follow-up. This may account for the higher rate of surgical treatment decisions in the PVD and Tear groups.

There were no differences in the final BCVA between the surgical and non-surgical groups. The final BCVA is significantly worse in the AMD group, and the BCVA change is also significantly the lowest in the AMD group, as shown in Table 3. In the AMD group, it is estimated that the difference in BCVA is less due to the poor visual prognosis because of macular lesions, which may not have been significantly affected by the improvement in vitreous hemorrhage. In the AMD group, five patients underwent vitrectomy, while three did not, which seems to make no significant difference to the final BCVA (as shown in Table 4), as the AMD patients with poor final BCVA were classified into the surgical or non-surgical group at similar rates.

The study had some limitations. First, its small sample size makes statistical analyses difficult. Second, only small retinal breaks not detected on ultrasound were included; therefore, it does not represent the overall visual prognosis of vitreous hemorrhage with retinal breaks or retinal detachments. Third, cases of vitrectomy and cataract surgery were mixed. Although no severe cataract was above grade 5 based on LOCS III, the possibility that cataract surgery affected vision prognosis cannot be ruled out. Finally, since we included only patients with a 12-month follow-up period to track long-term prognosis, it may introduce selection bias.

In conclusion, the most common cause of vitreous hemorrhage was BRVO, and surgical treatment may be a good option for improving visual acuity in patients with severe vitreous hemorrhage that does not improve with initial observation.

ACKNOWLEDGMENTS

Statement of Ethics

Study approval statement: The study was conducted per the Declaration of Helsinki and approved by the Institutional Review Board of the Sanggye Paik Hospital (approval number: SGPAIK 202112003).
Consent to publish statement: Patient consent was waived because of the retrospective nature of the study, and the analysis used anonymous clinical data.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

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Author Contributions
Substantial contributions to the conception or design of the work: J.S.K; Acquisition of data for the work: J.S.K, Y.R.L and Drafting the work: Y.R.L

Data Availability Statement
All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.
REFERENCES


Table 1. Baseline characteristics of the groups

<table>
<thead>
<tr>
<th></th>
<th>AMD</th>
<th>PVD</th>
<th>Tear</th>
<th>Vascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.75 ± 12.65</td>
<td>69.00 ± 9.09</td>
<td>61.20 ±8.04</td>
<td>67.71 ± 12.06</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>6/2</td>
<td>4/0</td>
<td>14/6</td>
<td>12/16</td>
</tr>
<tr>
<td></td>
<td>(75.0%/25.0%)</td>
<td>(100.0%/0%)</td>
<td>(70.0%/30.0%)</td>
<td>(42.9%/57.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>4 (50.0%)</td>
<td>0 (0.0%)</td>
<td>3 (15.0%)</td>
<td>19 (67.9%)</td>
</tr>
</tbody>
</table>

AMD; Age-related Macular Degeneration, PVD; Posterior Vitreous Detachment.

* Mean ± Standard deviation

Table 2. Causes of vitreous hemorrhage according to age group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>AMD (%)</th>
<th>PVD (%)</th>
<th>Tear (%)</th>
<th>Vascular (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>2 (50.00%)</td>
<td>2 (50.00%)</td>
</tr>
<tr>
<td>50–59</td>
<td>1 (6.25%)</td>
<td>1 (6.25%)</td>
<td>7 (43.75%)</td>
<td>7 (43.75%)</td>
</tr>
<tr>
<td>60–69</td>
<td>2 (15.38%)</td>
<td>1 (7.69%)</td>
<td>7 (53.85%)</td>
<td>3 (23.08%)</td>
</tr>
<tr>
<td>70–79</td>
<td>4 (20.00%)</td>
<td>2 (10.00%)</td>
<td>3 (15.00%)</td>
<td>11 (55.00%)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>1 (14.29%)</td>
<td>0 (0.00%)</td>
<td>1 (14.29%)</td>
<td>5 (71.43%)</td>
</tr>
</tbody>
</table>

AMD: Age-related Macular Degeneration, PVD: Posterior Vitreous Detachment.
Table 3. Percentage of patients who underwent surgery, initial BCVA, final BCVA, and extent of BCVA change for each group

<table>
<thead>
<tr>
<th></th>
<th>AMD</th>
<th>PVD</th>
<th>Tear</th>
<th>Vascular</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery rate</td>
<td>5/8 (62.5%)</td>
<td>4/4 (100.0%)</td>
<td>18/20 (90.0%)</td>
<td>19/28 (67.9%)</td>
<td>0.095†</td>
</tr>
<tr>
<td>Initial BCVA (logMAR)</td>
<td>2.30 [2.08–2.30]</td>
<td>2.00 [1.68–2.30]</td>
<td>2.30 [1.85–2.30]</td>
<td>2.30 [1.85–2.30]</td>
<td>0.812*</td>
</tr>
<tr>
<td>Final BCVA (logMAR)</td>
<td>1.50 [0.73–2.23]</td>
<td>0.15 [0.08–0.23]</td>
<td>0.20 [0.10–0.55]</td>
<td>0.50 [0.20–0.93]</td>
<td>0.003*</td>
</tr>
<tr>
<td>BCVA change (logMAR)</td>
<td>0.50 [0.08–1.35]</td>
<td>1.80 [1.55–2.08]</td>
<td>1.70 [1.45–2.20]</td>
<td>1.60 [1.30–1.95]</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

AMD: Age-related Macular Degeneration, BCVA: Best Corrected Visual Acuity, PVD: Posterior Vitreous Detachment. Median [interquartile range]

†Chi-square test, *Kruskal–Wallis test

Table 4. Comparing BCVA based on whether or not surgery was performed

<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>Non-surgery</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial BCVA (logMAR)</td>
<td>2.18 ± 0.22</td>
<td>1.94 ± 0.23</td>
<td>0.001</td>
</tr>
<tr>
<td>Final BCVA (logMAR)</td>
<td>0.55 ± 0.58</td>
<td>0.88 ± 0.82</td>
<td>0.187</td>
</tr>
<tr>
<td>BCVA change (logMAR)</td>
<td>1.62 ± 0.57</td>
<td>1.06 ± 0.88</td>
<td>0.007</td>
</tr>
</tbody>
</table>

BCVA: Best Corrected Visual Acuity.

Final BCVA was measured 12 months postoperatively.

*Student t-test