

Intravitreal Ranibizumab versus Vitreous Lavage for Postoperative Vitreous Hemorrhage in Proliferative Diabetic Retinopathy: A Randomized Controlled Trial

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Background: Postoperative vitreous hemorrhage (POVH) after pars plana vitrectomy (PPV) for proliferative diabetic retinopathy (PDR) is a common complication that delays visual recovery. While vitreous lavage (VL) mechanically clears hemorrhages, intravitreal ranibizumab (IVR) targets VEGF-mediated neovascularization. We compared the efficacy and safety of IVR and VL for the management of POVH.

Objective: To compare the visual outcomes, hemorrhage clearance efficiency, and complications between IVR and VL over a 24-week follow-up period.

Methods: In this prospective randomized controlled trial, 26 patients with POVH for PDR were allocated to the VL (n=12) or IVR (n=14) groups. Follow-up evaluations at 1 day, 1 week, 2 weeks, and monthly for up to 6 months included best-corrected visual acuity (BCVA) and complications. Novel metrics that included Visual Acuity Recovery Rate (VARR), Time to 1.0 logMAR-Equivalent Improvement (T1EI), and time to peak BCVA ($T_{\text{peak BCVA}}$) quantified the recovery dynamics.

Results: At 24 weeks, BCVA improvement was comparable between groups (VL: 0.30 LogMAR vs IVR: 0.22 LogMAR, $p=0.47$). VL achieved immediate BCVA gains in one day (1.99 vs 0.91 LogMAR, $p<0.01$), whereas IVR demonstrated progressive improvement after 2 weeks. VARR was higher in VL at 1 day (0.76 vs 0.25, $p<0.001$) and 2 weeks (0.84 vs 0.61, $p=0.06$) but converged by 24 weeks ($p=0.86$). The complication rates (recurrent hemorrhage and neovascular glaucoma) were similar ($p>0.05$).

Conclusion: VL and IVR were both associated with improved visual outcomes in patients with POVH throughout the 24-week follow-up period. The VL group achieved immediate BCVA improvement, and IVR showed a progressive improvement pattern. The VL group showed superior short-term efficiency. IVR showed a trend towards sustained recovery over the 24-week study period. In our study, IVR showed a trend of higher recovery efficiency within the follow-up timeframe. The adverse treatment outcomes after the two treatments did not significantly differ. Thus, treatment selection should balance the urgency of visual rehabilitation and patient-specific factors.

Keywords: postoperative vitreous hemorrhage, intravitreal ranibizumab, vitreous lavage

Introduction

Diabetic retinopathy (DR) is a microvascular complication of diabetes and is a major cause of blindness among working-age individuals worldwide.¹ Proliferative diabetic retinopathy (PDR) can result in serious complications, such as vitreous hemorrhage and neovascular glaucoma, leading to irreversible visual impairment.¹

Pars plana vitrectomy (PPV) is a common treatment for PDR. Postoperative vitreous hemorrhage (POVH) is a common complication that can impair vision recovery and quality of life, despite its effectiveness in removing hemorrhage.² POVH incidence varies, with international reports ranging from 12% to 59.9% worldwide and studies from 4.6% to 37.8% in China.³ If left untreated, POVH can result in vision loss or blindness.

POVH is associated with factors such as neovascular exudation and fibrovascular tissue growth at the site of the scleral puncture. Although over 83% of cases spontaneously resolve within three months, more prolonged bleeding may necessitate further intervention.² Vitreous cavity lavage (VL) is a common POVH treatment method that effectively eliminates bleeding. It rapidly restores vision but carries risks such as increased intraocular pressure, infection, and choroidal detachment.⁴ VEGF is critical for PDR neovascularization and is increased in patients with diabetes, encouraging the formation of new blood vessels. Anti-VEGF agents improve visual function and structural recovery by decreasing complications, such as vitreous hemorrhage and diabetic macular edema. Ranibizumab, an anti-vascular endothelial growth factor monoclonal antibody, reduces the risk of rebleeding and enhances vision recovery.⁵ However, repeated injections are necessary, and their long-term safety requires further investigation. Thus, the priority of the treatment choice was controversial. And most studies focused on the effect of a single treatment,^{2,5} rather than a comparison of the effects of two treatments.

We hypothesized that IVR would be non-inferior to VL in improving best corrected visual acuity at 24 weeks post-treatment, while offering a comparable safety profile. This study aimed to directly compare the efficacy and safety of intravitreal ranibizumab (IVR) injections into the VL for POVH. Patients were randomly assigned to either group. This study aimed to assess the visual recovery and prognosis, potentially offering new treatment strategies for POVH.

Materials and Methods

Design

This was a prospective, randomized controlled trial. We treated postoperative vitreous hemorrhage (POVH) after pars plana vitrectomy (PPV) for PDR between January 2022 and June 2024. The patients were randomly assigned to the VL or IVR groups according to a randomized table.

A sample size was calculated as 42, assuming a difference of 0.1 logMAR in mean visual acuity over 24 weeks, a standard deviation of 0.2 logMAR visual acuity, 80% power, and an overall 2-sided type I error rate of 0.05. And assume a 20% loss to follow-up rate among patients. The sample size was designed as 42 to account for uncertainty in these assumptions.

POVH was defined as vitreous hemorrhage following vitrectomy. The time between POVH and vitrectomy was defined as the period from the initial vitrectomy to vitreous bleeding. The VH grades are as follows: Grade 1, the main details of the fundus are visible; however, examining the retinal nerve fiber layer and tiny blood vessels is challenging. Grade 2: able to observe the optic disc and main vessels, which is the lowest degree of retinopathy included in this study. Grade 3: only faint red reflections can be observed, fundus details are blurred, and the optic disc is discernible. Grade 4: no red reflex in the fundus, optic disc, or other fundus structures.⁶ Visual acuity was recorded as logMAR VA. Counting fingers had 2 logMAR, and hand motion had 3 logMAR.⁷

Patients in the VL group underwent vitreous lavage surgery. Patients in the IVR group were administered intravitreal ranibizumab injections. Other treatments were permitted in both groups. All patients were observed for at least 6 months. Baseline characteristics, including sex, age, duration of diabetes, body mass index, fasting blood glucose, glycosylated hemoglobin A1c, blood urea nitrogen, estimated glomerular filtration rate, and time between POVH and vitrectomy, were collected. Baseline ocular data included the best-corrected visual acuity (BCVA) of the logarithm of the minimum angle of resolution (logMAR), intraocular pressure, slit lamp, funduscopy examination, and ocular ultrasound.

In the IVR group, UVH and RVH lasting over 4 weeks were treated with another injection. VL could be performed if the bleeding failed to clear after 2 injections. IVR was treated soon after patients with NVG.

Follow-ups were performed at 1 day, 1 week, 2 weeks, 4 weeks, 8 weeks, 16 weeks, and 24 weeks postoperatively. The primary outcome was the BCVA of the operative eye at 24 weeks. Secondary outcomes were BCVA at follow-up, efficiency of vitreous hemorrhage clearance, and prognosis of complications following treatment.

Inclusion and Exclusion Criteria

Patients with non-resolving POVH after 4 weeks of conservative management for DR were included in the study. Patients who declined to participate in the study, those with neovascular glaucoma, those with long-acting gas or silicone oil in the eye with VH, and those with severe systemic comorbidities were excluded. [Figure 1](#) shows the flowchart of the study.

Procedure of the VL and IVR

Surgeries were performed by a single surgeon. In the VL group, after disinfection and draping, standard three-port 25G vitreous lavage surgery was performed with the microscope system (OPMI Lumera T; Carl Zeiss AG, Jena, Germany) under local anesthesia. The bleeding was removed using a vitrectomy system (Constellation, Alcon Laboratories, Inc., America). And perfusion fluid (B.S.S. solution) replaced the bleeding gradually. The Intraocular pressure was maintained from 20 to 30 mmHg. In the IVR group, after disinfection and draping, intravitreal ranibizumab (Lucentis, Novartis Pharma Schweiz A. G) injection (0.5 mg in 0.05 mL) was given.

Quantification of the Efficiency of the Vitreous Hemorrhage Clearance

We proposed several metrics to demonstrate the efficiency of vitreous hemorrhage clearance. The first metric is the Visual Acuity Recovery Rate (VARR), which was defined as the ratio of post-intervention BCVA to optimal BCVA following vitrectomy. This parameter quantitatively evaluates the visual rehabilitation efficacy after secondary interventions for persistent postoperative bleeding. Second, we propose the Time to 1.0 logMAR-Equivalent Improvement (TIEI). This metric is a normalized ratio designed to quantify the efficiency of visual recovery. It is calculated as the time (in weeks) required for a patient to achieve their peak postoperative BCVA, divided by the total magnitude of BCVA improvement. The resulting value represents the number of weeks needed to achieve a theoretical 1.0 logMAR unit of visual gain, thereby standardizing the recovery speed across patients with different maximum visual potential. A lower TIEI value indicates a faster visual recovery per unit of improvement. The third is the time to peak BCVA ($T_{\text{peak BCVA}}$), which was defined as the time interval required to achieve BCVA following treatment (in weeks).

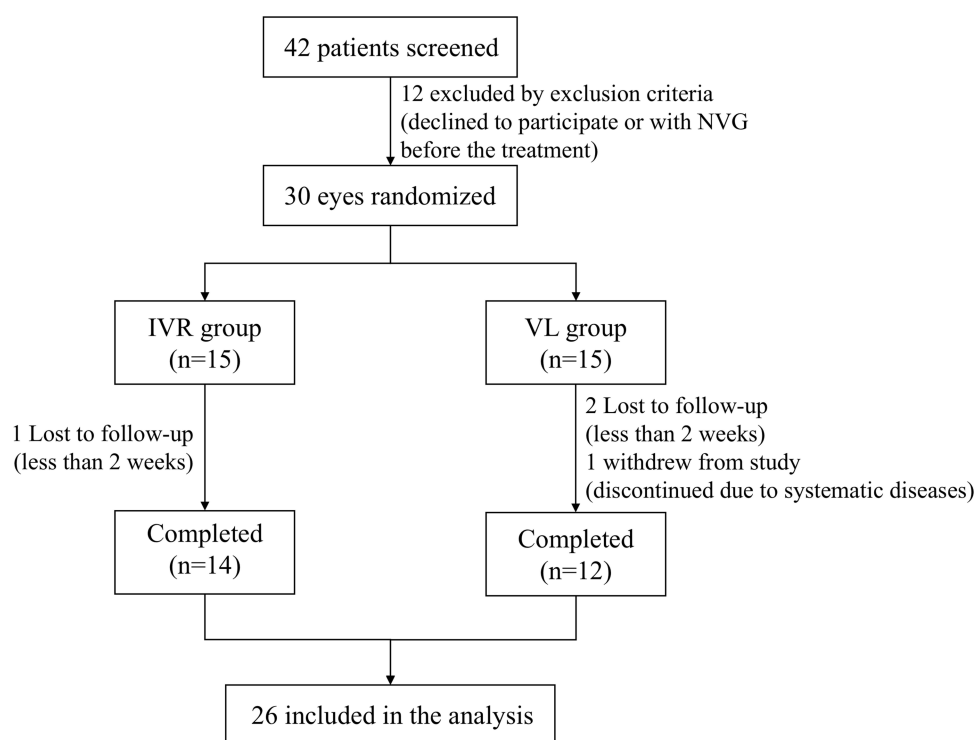


Figure 1 The flowchart of this study.

$$\text{Visual Acuity Recovery Rate} = \frac{3 - BCVA_{\text{after treatment}}}{3 - BCVA_{\text{after vitrectomy}}} \times 100\%$$

$$\text{Time to 1.0logMAR – Equivalent Improvement} = \frac{T_{\text{peak VA}}}{BCVA_{\text{baseline}} - BCVA_{\text{peak}}}$$

$T_{\text{peak VA}}$: time necessary to achieve the BCVA following treatment (in weeks)

$BCVA_{\text{baseline}}$: The recorded visual acuity before treatment

It is important to note that the parameters VARR, T1EI, and $T_{\text{peak VA}}$ are novel, investigator-proposed metrics designed to provide a more granular analysis of recovery dynamics in this specific clinical context. Potential biases should be considered in their interpretation. For instance, T1EI, as a ratio, may be disproportionately influenced by small changes in BCVA when the denominator (improvement magnitude) is small.

Statistical Methods

Statistical analyses were performed using SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, N.Y., USA). The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to assess the distribution of continuous variables, thereby guiding the selection of appropriate parametric or non-parametric testing methods. Results are presented as the mean and standard deviation (mean $\pm$ SD) for normally distributed data. The median and interquartile range (Median [IQR]) are reported for non-normally distributed data. An independent-sample *t*-test was conducted for normally distributed data when comparing continuous variables between groups, whereas the Mann–Whitney *U*-test was applied for non-normally distributed data. Categorical variables were compared using Fisher’s exact test. Spearman correlation analysis was utilized to determine the relationship between preoperative clinical indicators and BCVA six months following surgery. All the tests were performed bilaterally. The *p*-value for significance was set at *p* < 0.05.

Results

General Information and Baseline Characteristics

In this study, we collected 26 eyes of 26 patients (17 men, 9 women; age range 26–74 y, mean age = 51.15 $\pm$ 11.83 years) with POVH. Twelve patients underwent lavage surgery, and 14 were treated with ranibizumab injections. No significant differences were observed in the baseline characteristics, including age, sex, duration of diabetes mellitus, or complications of diabetes mellitus, between the two groups. When comparing patient characteristics of the initial PPV for PDR, no significant difference was observed between the two groups. (Table 1 shows the details of the baseline characteristics).

Table 1 Baseline Characteristics of Patients

Characteristics	VL Group	IVR Group	p value
Gender (Male, %)	8(66.67)	9(64.29)	1.00
Age (x $\pm$ s, y)	49.50 $\pm$ 11.36	52.57 $\pm$ 12.46	0.52
DM duration [M(Q1,Q3), y]	15.60 (8.74, 18.19)	13.16 (10.58, 14.78)	
BMI (x $\pm$ s, kg/m ²)	24.79 $\pm$ 5.30	24.50 $\pm$ 3.21	0.87
Fast blood glucose (x $\pm$ s, mmol/L)	8.50 $\pm$ 2.62	7.923.14	0.61
HbA1c (x $\pm$ s, %)	7.88 $\pm$ 1.86	8.21 $\pm$ 2.90	0.73
BUN (x $\pm$ s, mmol/L)	6.91 $\pm$ 2.24	6.46 $\pm$ 2.94	0.66
eGFR (x $\pm$ s, mL/min/1.73m ²)	98.53 $\pm$ 21.76	97.85 $\pm$ 15.04	0.93

(Continued)

Table 1 (Continued).

Characteristics	VL Group	IVR Group	p value
Hypertension [n(%)]			1.00
Yes	8(66.67)	9(64.29)	
No	4(33.33)	5(35.71)	
Diabetic nephropathy [n(%)]			0.49
Yes	5(41.67)	3(21.43)	
No	7(58.33)	11(78.57)	
BCVA before treatment	2.75	2.50	0.63
[M(Q1,Q3), y]	(2.125, 3.00)	(2.00, 3.00)	
Time to POVH ($\bar{x} \pm s$, d)	131.75 $\pm$ 90.11	285.14 $\pm$ 422.33	0.21
IOL implantation [n(%)]			0.72
Yes	6(50.00)	8(57.14)	
No	6(50.00)	6(42.86)	
Silicone Oil injection [n(%)]			0.48
Yes	0(0)	2(14.29)	
No	12(100.00)	12(85.71)	
Anti-VEGF injection [n(%)]			0.47
Yes	6(50.00)	4(28.57)	
No	6(50.00)	10(71.43)	

Abbreviations: IVR group, Intravitreal injection of Ranibizumab; VL group, Vitreous cavity Lavage; DM, Diabetes Mellitus; BMI, Body Mass Index; HbA1c, Glycosylated Hemoglobin Type A1c; BUN, Blood Urea Nitrogen; eGFR, Estimated Glomerular Filtration Rate; BCVA, Best Corrected Visual Acuity; POVH, postoperative vitreous hemorrhage; IOL, Intraocular lens.

Primary Outcome

Vision Improvement

The primary outcome of the BCVA in logMAR over 24 weeks was 0.222 in the IVR group and 0.301 ($P = 0.473$) in the VL group. No difference was observed between the two groups at 24 weeks. During the 24-week follow-up period, BCVA trends improved in the VL and IVR groups. Significant differences were observed between the baseline BCVA and BCVA at follow-up in the VL group. [Figure 2](#) shows visual acuity through 24 weeks.

Secondary Outcome

BCVA During the Follow-up Period

Throughout the follow-up period, both groups showed improvements in visual acuity. The visual acuity of the IVR group (1.99 ± 0.69) was worse than that of the VL group (0.91 ± 0.43) one day following treatments ($p < 0.01$). Furthermore, the difference in visual acuity diminished one week after treatment. The mean visual acuities of the IVR and VL groups were similar at 4 weeks following treatment. At all other pre-specified follow-up intervals, no statistically significant differences were observed between the two groups ([Table 2](#) shows the visual acuity outcomes of this study).

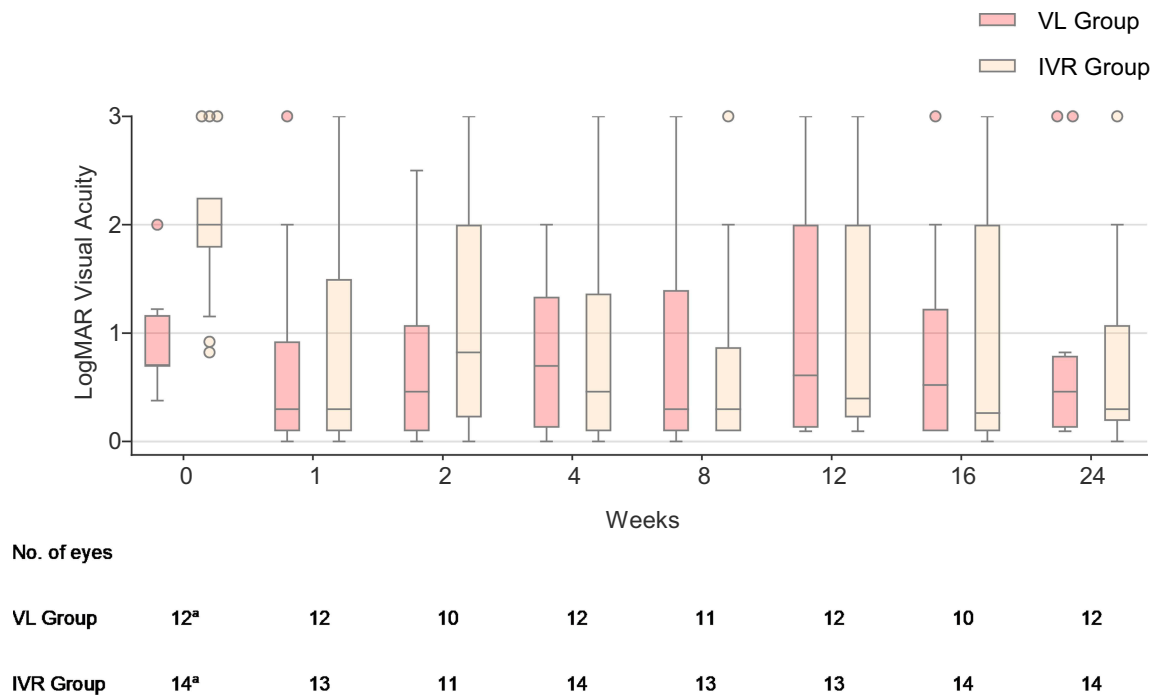
Efficiency of Vitreous Hemorrhage Clearance

In this study, we proposed metrics for quantifying the efficiency of vitreous hemorrhage clearance. $T_{\text{peak VA}}$ was defined as the time interval required to achieve BCVA following treatment (weeks).

Patients in the VL group reached their peak visual acuity more rapidly than those in the IVR group throughout the follow-up, although the differences between the two groups were statistically insignificant (3.18 ± 3.58 w in the VL group vs 5.71 ± 3.97 w in the IVR group, $p = 0.10$).

T1EI was calculated as the ratio of the time necessary to achieve BCVA following treatment (weeks) to the magnitude of BCVA improvement. The VL group (3.64 ± 7.37 w) demonstrated a higher T1EI than the IVR group (0.90 ± 8.24). No significant difference was observed in the T1EI between the two groups ($p = 0.38$).

Visual Acuity through 24 weeks



Abbreviations: VL, Vitreous cavity lavage; IVR, intravitreal ranibizumab.

The box plot shows the visual acuity within the follow-up for 24 weeks.

^aThis reveals the first day following treatment.

Figure 2 Visual Acuity through 24 weeks of the two groups.

The VARR was defined as the ratio of post-intervention BCVA to optimal BCVA following vitrectomy. The VARR in the VL group was significantly higher one day following the treatments (difference is 0.41, 95% confidence interval [CI] 0.24 to 0.57, $p < 0.01$). The VARR was similar at 24 weeks between the two groups (difference is -0.02 , 95% CI -0.30 to 0.25 , $p = 0.86$), and this difference started to diminish at 1 week. The VARR of the VL group remained more stable than that of the IVR group, and the range (0.17) was lower than that of the IVR group (0.56). Table 3 shows the detailed results of the efficiency of vitreous hemorrhage clearance between the two groups.

The POVH Treatment Outcomes

We recorded four adverse outcomes of POVH following treatment, and no significant difference was observed between the two groups. Two patients were observed with Unclear Vitreous Hemorrhage (UVH) in the IVR group ($p=0.48$). The two patients received another injection at 4 weeks and 12 weeks, respectively. The number of patients with Recurrent Vitreous Hemorrhage (RVH) was similar between the two groups ($p=1.00$). Furthermore, the Early Recurrent Vitreous Hemorrhage (ERVH) was the main prognosis (5 eyes in the VL group and 5 eyes in the IVR group). With observation, another injection or lavage surgery, bleeding was absorbed in both groups. Delayed Recurrent Vitreous Hemorrhage (DRVH) was recorded in the VL and IVR group. The VL group consisted of three patients with Neovascular Glaucoma (NVG) ($p=0.20$) and one with Diabetic Macular Edema (DME) ($p=0.46$). Table 4 shows the adverse outcomes following the treatment of POVH between the two groups. 5 patients received 2 injections. And 2 patients received VL for unclear vitreous in the IVR groups. Table S1 shows the Intraocular

Table 2 The Visual Acuity Outcomes of This Study

	VL Group	IVR Group	Difference (95% CI)	p
Mean visual acuity in logMAR at 24w ($\bar{x} \pm s$)	0.81 $\pm$ 1.05 ^a	0.70 $\pm$ 0.87 ^{abcdef}	0.10 (−0.69 to 0.90)	0.79
Median visual acuity in logMAR at 24w (Q1, Q3)	0.46 (0.13, 0.79)	0.30 (0.19, 1.08)		
Mean visual acuity in logMAR at 1d ($\bar{x} \pm s$)	0.91 $\pm$ 0.43 ^a	1.99 $\pm$ 0.69	−1.08 (−1.54 to −0.62)	< 0.01
Median visual acuity in logMAR at 1d (Q1, Q3)	0.70 (0.70, 1.17)	2.00 (1.79, 2.25)		
Mean visual acuity in logMAR at 1w ($\bar{x} \pm s$)	0.70 $\pm$ 0.92 ^a	0.87 $\pm$ 1.05 ^a	−0.17 (−0.97 to 0.63)	0.66
Median visual acuity in logMAR at 1w (Q1, Q3)	0.30 (0.10, 0.92)	0.50 (0.10, 1.25)		
Mean visual acuity in logMAR at 2w ($\bar{x} \pm s$)	0.69 $\pm$ 0.60 ^a	1.24 $\pm$ 1.00 ^{ab}	−0.54 (−1.23 to 0.14)	0.11
Median visual acuity in logMAR at 2w (Q1, Q3)	0.70 (0.13, 1.00)	0.99 (0.45, 2.00)		
Mean visual acuity in logMAR at 4w ($\bar{x} \pm s$)	0.86 $\pm$ 0.83 ^a	0.91 $\pm$ 1.01 ^{ac}	−0.05 (−0.84 to 0.73)	0.89
Median visual acuity in logMAR at 4w (Q1, Q3)	0.70 (0.13, 1.34)	0.46 (0.10, 1.49)		
Mean visual acuity in logMAR at 8w ($\bar{x} \pm s$)	0.77 $\pm$ 0.93 ^a	0.68 $\pm$ 0.84 ^{abcd}	0.09 (−0.63 to 0.82)	0.79
Median visual acuity in logMAR at 8w (Q1, Q3)	0.35 (0.13, 1.23)	0.35 (0.10, 0.85)		
Mean visual acuity in logMAR at 12w ($\bar{x} \pm s$)	1.14 $\pm$ 1.12 ^a	0.99 $\pm$ 1.06 ^{abcde}	0.15 (−0.74 to 1.04)	0.73
Median visual acuity in logMAR at 12w (Q1, Q3)	0.61 (0.13, 2.00)	0.40 (0.22, 2.00)		
Mean visual acuity in logMAR at 16w ($\bar{x} \pm s$)	0.83 $\pm$ 0.87 ^a	0.88 $\pm$ 1.11 ^{abcdef}	−0.05 (−0.86 to 0.75)	0.89
Median visual acuity in logMAR at 16w (Q1, Q3)	0.61 (0.13, 0.94)	0.26 (0.10, 2.00)		

Notes: ^{a-f}There was no statistical difference between the VA labeled with the same letter in multiple comparisons. $F_{VL} = 5.995$, $p < 0.001$, $F_{IVR} = 8.249$, $p < 0.001$.

Abbreviations: VL, Vitreous cavity lavage; IVR, intravitreal ranibizumab.

Table 3 The Efficiency of the Vitreous Hemorrhage Clearance of the Two Groups

	VL Group	IVR Group	Difference (95% CI)	p
Visual acuity recovery rate, VARR				
VARR at 1d	0.76 $\pm$ 0.15	0.25 $\pm$ 0.25	0.41 (0.24 to 0.57)	< 0.001
VARR at 1w	0.82 $\pm$ 0.31	0.75 $\pm$ 0.37	0.08 (−0.20 to 0.35)	0.57
VARR at 2w	0.84 $\pm$ 0.19	0.61 $\pm$ 0.36	0.23 (−0.01 to 0.47)	0.06
VARR at 4w	0.77 $\pm$ 0.28	0.73 $\pm$ 0.38	0.06 (−0.22 to 0.31)	0.73
VARR at 8w	0.80 $\pm$ 0.31	0.81 $\pm$ 0.29	−0.01 (−0.26 to 0.23)	0.90
VARR at 12w	0.67 $\pm$ 0.39	0.70 $\pm$ 0.37	−0.04 (−0.35 to 0.27)	0.81
VARR at 16w	0.78 $\pm$ 0.30	0.73 $\pm$ 0.38	0.05 (−0.23 to 0.33)	0.73
VARR at 24w	0.77 $\pm$ 0.37	0.80 $\pm$ 0.30	−0.02 (−0.30 to 0.25)	0.86
Time to 1.0 logMAR-Equivalent Improvement, TIEI (w)	3.64 $\pm$ 7.37	0.90 $\pm$ 8.24	2.74 (−3.58 to 9.06)	0.38
Time to peak BCVA, T _{peak} VA (w)	3.18 $\pm$ 3.58	5.71 $\pm$ 3.97	−2.54 (−5.59 to 0.52)	0.10

Table 4 The Adverse Outcomes Following the Treatment of the Two Groups

	VL Group	IVR Group	p
Unclear Vitreous Hemorrhage, UVH	0	2	0.48
Recurrent Vitreous Hemorrhage, RVH	6	7	1.00
Early Recurrent Vitreous Hemorrhage, ERVH	5	5	0.76
Delayed Recurrent Vitreous Hemorrhage, DRVH	1	2	0.72
Neovascular Glaucoma, NVG	3	1	0.20
Diabetic Macular Edema, DME	1	0	0.46

pressure of the patients following the treatment in the [Supplementary Files. Table S2](#) shows the re-treatment condition for the adverse prognosis in the [Supplementary Files](#).

Discussions

General Interpretation

POVH is one of the most vision-threatening postoperative complications. The primary methods used to clear bleeding are VL surgery and intravitreal injection of anti-VEGF agents. Several previous studies have revealed improved visual outcomes with the two treatments.^{8–10} However, few studies have compared the effects of these two treatments. In this prospective randomized controlled trial, we observed the BCVA and complications in patients with POVH following treatment for up to 24 weeks. We compared visual acuity, vitreous hemorrhage clearance efficiency, and complication outcomes between the VL and IVR groups.

Visual Acuity Outcomes

Diffuse bleeding in the vitreous cavity leads to poor visualization. In POVH without intervention, bleeding may occur on more than one occasion during blood reabsorption.¹¹ Thus, removing the standing hemorrhage and stopping new bleeding is necessary to improve visual acuity outcomes. VL, based on the fluid-fluid exchange technique, is the direct method to clear bleeding vitreous. *Chen et al* reported a fluid-fluid exchange device to resolve bleeding, and patients kept clearing vitreous after the treatment shortly.¹² And the rate of RVH in these patients after VL was low reported (19.3%).⁹ Furthermore, patients after VL obtained an average clear vitreous interval of 3 months in their study.⁹ Herein, we concluded that the lavage group exhibited immediate improvement in BCVA. Blocking VEGF may reduce the requirement for repeated vitrectomy for POVH.¹⁰ With intravitreal anti-VEGF agents, neovascularization regresses; thus, the repeated inflow of blood into the vitreous may be stopped.¹⁰ PPV, along with anti-VEGF agents injection, reduces early POVH incidence.⁶ However, few studies have compared VL and intravitreal injections for POVH treatment. Previously, patients with VH who underwent vitrectomy and intravitreal aflibercept injection achieved improved visual acuity outcomes over 24 weeks (20/63 in both).¹³ In our study, no significant difference was observed in the BCVA at 24 weeks between the two groups. The BCVA of both groups showed a significant difference 1 day following treatment only. Lavage surgery is an effective method for removing vitreous bleeding.¹⁴ Intravitreal anti-VEGF agent injection was previously shown to be a meaningful method.⁵ This is critical for intravitreal hemorrhage absorption and vision restoration. Decreasing the biological activity of VEGF-A enhances intraocular metabolism and promotes the natural absorption of intravitreal bleeding, thereby contributing to BCVA.¹⁵ The optimistic findings of this study revealed a VEGF-blocking effect on bleeding absorption.

Efficiency Outcomes

VL is considered to be more efficient owing to its short-term vision benefits.⁹ However, this comparison is partial, because it does not consider the patient's best visual acuity before treatment, the best visual acuity that can be achieved at post-treatment follow-up, or the time to recovery. We introduced some concepts, such as Visual Acuity Recovery Rate (VARR), Time to 1.0 logMAR-Equivalent Improvement (TIEI), and Time to peak BCVA ($T_{\text{peak VA}}$), to compare the efficiency of the vitreous hemorrhage clearance. These three concepts assist in quantifying the efficiency. $T_{\text{peak VA}}$ was easily acquired during follow-up. The VARR and TIEI values were calculated using the BCVA data during follow-up. Furthermore, a short $T_{\text{peak VA}}$ indicated a high recovery speed. The VL group revealed a higher recovery rate, although the difference was not statistically significant. VL surgery rapidly removed bleeding via fluid-fluid exchange.¹⁶ Thus, patients with POVH who underwent VL surgery achieved peak VA more quickly than those who received intravitreal injections. This rapid recovery may be attributed to the ability of the lavage procedure to directly eliminate intravitreal bleeding. However, the peak VA was not equal to the optimal VA. The TIEI in the VL group was higher than that in the IVR group, although the difference was not statistically significant. TIEI was considered the best VA before POVH and $T_{\text{peak VA}}$. The higher the TIEI, the lower the benefit of VA recovery. Furthermore, the VARR is a ratio that represents the degree of vision recovery. In the short term, the VL group showed a higher VARR; however, no differences were

observed in the 24-week follow-up. Thus, IVR manifested an acceptable efficiency outcome throughout the 24-week follow-up.

The POVH Treatment Outcomes

The outcomes of POVH after treatment were ideal in previous studies.^{5,8} However, some adverse outcomes still exist after positive interventions. The most common adverse outcome is RVH.⁵ Moreover, the mechanisms of the early and delayed RVH are different.^{17,18} RVH does not always require treatment. After treatment or follow-up observation, patients typically achieve good vision.⁹ In our study, no significant difference was observed in the RVH between the two groups. UVH is suspected to be a type of RVH.¹⁰ Bleeding and absorption are dynamic processes. With intravitreal anti-VEGF agents, neovascularization regresses; thus, the repeated inflow of blood into the vitreous may stop.¹⁰ NVG has a vision-threatening prognosis in both PDR and POVH. NVG demonstrated the progression of retinal microcirculatory hypoxia in these patients. The VL and IVR release their hypoxic course by diminishing VEGF agents. Additionally, lavage surgery removed the bleeding and VEGF agents from the vitreous cavity. The intravitreal injection of anti-VEGF agents inhibits VEGF in a targeted and permanent manner. Thus, intravitreal injection of anti-VEGF agents could have a potential advantage over lavage surgery in relieving the hypoxic course. In our study, there were more eyes with NVG in the VL group than in the IVR group, although the difference was not statistically significant.

Individual variations, including differences in the intraocular microenvironment and drug sensitivity, also markedly affect treatment outcomes.¹⁹ Furthermore, conditions such as inflammation and increased vascular fragility may reduce ranibizumab's efficacy. Thus, when treating POVH, considering these factors and potentially combining treatments is necessary because intravitreal injections alone may not be sufficient in some patients.

Limitations

The interpretation of our findings must be considered in the context of several important limitations. Limited enrollment reduced the statistical power to detect subtle intergroup differences. The study included only 26 patients, which substantially limits the generalizability of the findings. The low number reduces the statistical power to detect subtle but clinically relevant differences between groups. Furthermore, the 24-week follow-up period, while sufficient to assess the primary outcome of early visual recovery and short-term complication rates, may not be long enough to capture late complications such as delayed recurrent vitreous hemorrhage. This is particularly relevant for evaluating the true durability of IVR treatment and the potential for late NVG development. And the single-center design and exclusion of silicone oil-filled eyes limit broader applicability. And the novel efficiency parameters (VARR, T1EI) introduced in this study, while providing initial quantitative insights into the recovery procedure, are exploratory and require validation in larger, prospective cohorts to establish their clinical utility and generalizability. Unadjusted variables (eg, glycemic control variability and surgical technique differences) may have influenced the outcomes. These factors may affect the generalizability of our findings regarding the long-term comparative efficacy and safety profile of the two interventions. Future studies with larger cohorts and extended follow-up durations are warranted to confirm our preliminary conclusions and to establish the optimal long-term management strategy for POVH.

Conclusions

In this preliminary randomized trial, VL and IVR were both associated with improved visual outcomes in patients with POVH, with no significant differences in the primary outcome observed within the 24-week follow-up period. The VL group achieved immediate BCVA improvement, and IVR showed a progressive improvement pattern, suggesting a different mechanism of action. The VL group showed superior short-term efficiency; however, both modalities achieved similar results at 24 weeks. IVR showed a trend towards sustained recovery over the 24-week study period. In our study, IVR showed a trend of higher recovery efficiency for lower T1EI than VL within the follow-up timeframe. The advert prognosis after the two treatments did not significantly differ, supporting both treatments as viable options. These results support personalized treatment strategies, prioritizing VL for rapid intervention. And IVR may be beneficial for short-term and medium-term neovascular control, though its long-term durability requires further investigation.

Abbreviations

VL, Vitreous cavity lavage; POVH, postoperative vitreous hemorrhage; PDR, proliferative diabetic retinopathy; DR, diabetic retinopathy.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article and its supplementary files.

Ethics Approval and Informed Consent

This study was approved by the Ethics Committee of the Tianjin Medical University Eye Hospital. The committee's reference number: 2021KY-32 and registered in the ClinicalTrials.gov (registration number: NCT05248334). Before enrolling the patients, they or their legal guardians were informed about the study's purpose and methods in accordance with the Declaration of Helsinki. An ophthalmologist trained interpreted and answered the questions of the study for parents. Then the patients or legal guardians completed a questionnaire and signed an informed consent form.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there is no conflict of interest.

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