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Risk Factors for Recurrent Vitreous Hemorrhage After 25-Gauge Pars Plana Vitrectomy in Patients With Proliferative Diabetic Retinopathy

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Abstract

Purpose: To report the incidence of and risk factors associated with recurrent vitreous hemorrhage (VH) in eyes that had 25-gauge pars plana vitrectomy (PPV) for proliferative diabetic retinopathy (PDR). **Methods:** This study included 220 eyes of 185 patients who were 21 years old or older and who had PPV for PDR and a minimum postoperative follow-up of 3 months. For patients who had bilateral PPV, data were gathered from both eyes. If surgery was performed in only 1 eye, data were collected from that eye alone. **Results:** The incidence of recurrent VH was 34.5% (76 eyes). The VH was categorized as early in 46 eyes (60.5%), delayed in 8 eyes (10.5%), or late in 22 eyes (28.9%). Sixty-eight eyes (89.5%) had mild/moderate recurrent VH and 8 (10.5%) had severe recurrent VH. The mean preoperative fasting blood glucose level was 147.7 mg/dL in eyes without recurrent VH and 176.7 mg/dL in eyes with recurrent VH ($P = .020$). Younger age ($P = .027$) and higher diastolic blood pressure at the time of surgery ($P = .005$) also significantly affected recurrent VH. **Conclusions:** Younger age, preoperative fasting blood glucose levels, and diastolic blood pressure were significantly associated with recurrent VH after PPV in patients with PDR.

Keywords

vitreoretinal disease, vitrectomy, vitreous hemorrhage, 25 gauge, pars plana approach, proliferative diabetic retinopathy, urban population

Introduction

Diabetes mellitus (DM) is a chronic disease that leads to vasculopathy in many organ systems, including the eyes, where it can cause numerous sequelae, such as diabetic retinopathy (DR). More than 1 in 10 individuals in the United States have DM, and approximately 4.1 million have DR, making it the most common microvascular complication of DM.[1] Proliferative diabetic retinopathy (PDR) remains a leading cause of blindness in the US and leads to vitreous hemorrhage (VH) in up to 75% of cases and tractional retinal detachment (TRD) in 20% to 40% of cases.[2–5] Pars plana vitrectomy (PPV) is a common surgical procedure to treat the vision-threatening sequelae of PDR and can be complicated by recurrent vitreous hemorrhage (VH).

Recurrent VH is a common vision-threatening complication of PPV for PDR, occurring in 12% to 40% of cases.[6–8] Approximately 5% to 13% of recurrent VH cases require reoperation, resulting in additional risks associated with multiple retinal surgeries.[6,7,9] Previous retrospective studies have identified risk factors for recurrent VH to better understand this common surgical complication.[6–8] Ding et al[7] found younger age, a shorter duration of DM, and higher serum creatinine levels to be significantly associated with recurrent VH. Khuthaila et al[6] also identified younger age to be a significant risk factor, in addition to incomplete scatter photocoagulation and phakia before PPV. Mahalingam et al[8] found intraoperative panretinal photocoagulation (PRP) and poor glycemic blood pressure control to be significant risks for rebleed. Baget-Bernaldiz et al[10] determined that a longer duration of diabetes, anemia, an attached hyaloid, the presence of TRD, the lack of PRP, and previous cardiovascular events increase the risk for recurrent VH. These studies were limited by their sample sizes, varied PPV instrument gauge and technique, and differing patient populations.

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The current study sought to identify risk factors specific to the patient population at the University of Illinois Hospital in Chicago, which primarily serves a minority population with higher levels of unemployment, poverty, and violence.[11] A 2023 survey of community needs indicated that 35% of patients in the University of Illinois Hospital service areas are Hispanic and 29% are Black.[11] Thirty-nine percent of patients had an income below $50,000, and 35% had only completed high school or less.[11] Low-income minority populations, such as those represented in the University of Illinois Hospital's population, may experience unique social determinants of health burdens that lead to worse posttreatment outcomes.

The relationship between social determinants of health and a worse presentation of DR has been well established through the presentation of social determinants of health as barriers to care. Patients who have a lower income, public insurance, or a primary language other than English have been found to experience more severe DR.[12,13] Moreover, these patients are more likely to be lost to follow-up or miss more appointments because of inadequate access to transportation, which can contribute to worsening disease severity.[14,15] Given the well-established link between these barriers to care and a worse presentation of DR, these factors may also have an impact on the postoperative outcomes after PPV, including recurrent VH.

Identifying risk factors for recurrent VH in a low-income minority population in a large urban city is the first step in addressing barriers to care, emphasizing modifiable risk factors during the preoperative, intraoperative, and postoperative stages of care. Any significant nonmodifiable risk factors may prompt further discussion regarding the socioeconomic factors at play. Furthermore, to our knowledge, the clinical risk factors for recurrent VH after 25-gauge PPV have not previously been investigated in a US-based population. The University of Illinois Hospital also mostly performs 25-gauge PPVs based on surgeon preference.

Our study examined the history, examination findings, and intraoperative decisions that are associated with recurrent VH after 25-gauge PPV to better understand this vision-threatening surgical complication.

Methods

This retrospective observational study comprised patients with PDR who had 25-gauge PPV between February 2015 and May 2022 at the University of Illinois Hospital. Patients who were 21 years or older and had diagnostic codes for PDR, billing codes for PPV, and a minimum postoperative follow-up of 3 months were included. Specifically, patients with International Classification of Diseases (ICD) codes for stable PDR, PDR with macular edema (ME), and PDR without ME were included. In addition, patients with Current Procedural Terminology (CPT) codes for PPV with PRP and complex repair of RD, including diabetic TRDs, were included. All surgeries were performed using a pars plana approach with the Constellation 25-gauge surgical vitrectomy system (Alcon Laboratories Inc). Approval for this study was obtained from the University of Illinois at Chicago Institutional Review Board. The study was in compliance with the US Health Insurance Portability and Accountability Act of 1996 and institutional review board requirements.

After the patient's chart and operative report were reviewed, the following data regarding patient demographic and medical history were collected: name, date of birth, sex, race, date of surgery, type of diabetes and duration, hypertensive status, anticoagulant use, PRP status, and laboratory values (last glycosylated hemoglobin [HbA_{1c}] within 3 months before surgery, serum creatinine, and urea). Incomplete PRP was defined as less than 1 quadrant of PRP because of the obscuration of the retina from a VH.

The preoperative characteristics collected were most recent Snellen best-corrected visual acuity (BCVA), intraocular pressure (IOP), phakic status, glaucoma, intravitreal (IVT) antivascular endothelial growth factor (anti-VEGF) injection, beta-blocker use, fasting blood glucose, and if/when anticoagulant medication was stopped before surgery. The intraoperative characteristics were blood pressure on the day of surgery, anesthesia type, cataract surgery performed, corticosteroid use, membrane peeling, segmentation and delamination performed, presence of retinal breaks, air–fluid exchange, tamponade use, sclerotomies sutured, and IVT bevacizumab use. The postoperative characteristics collected were the BCVA, IOP, positioning recommended, ME, IVT bevacizumab use, date of postoperative recurrent VH, and severity of recurrent VH.

After the data for patients who met the inclusion criteria were collected, patients were excluded if they were missing data. Specifically, patients who were missing 3 or more datapoints or variables of interest from their chart were excluded from the patient sample and analysis. Approximately 35 patients were excluded based on these criteria.

Recurrent VH was defined as new blood in the vitreous cavity occurring up to 3 months postoperatively. BCVAs were converted into logMAR notation for analysis. The primary outcome was the incidence of recurrent VH after 25-gauge PPV. Secondary outcomes measured included risk factors for recurrent VH, including preoperative, intraoperative, and postoperative characteristics. Log transformations were applied to the continuous variables to create a linear scale.

Logistic regression was used to compare patients with recurrent VH and those without recurrent VH. Demographic and clinical characteristics of patients that differed with respect to recurrent VH status were first determined. The Fisher exact test was used for categorical variables with any cell count less than 5; otherwise a χ^2 test was used. This allowed calculation of the exact P values to more reliably assess associations between categorical variables. For continuous variables, the Levene homogeneity of variance test was performed. If the $P < .01$, an unequal variance t test was conducted. If $P > .01$, an equal variance t test was used.

Univariate and multivariate analyses were completed to identify risk factors for recurrent VH (Figure 1). Factors that were significantly associated with the main outcome of recurrent VH and other clinically important variables were considered for further logistic regression analyses. Specifically, these factors were

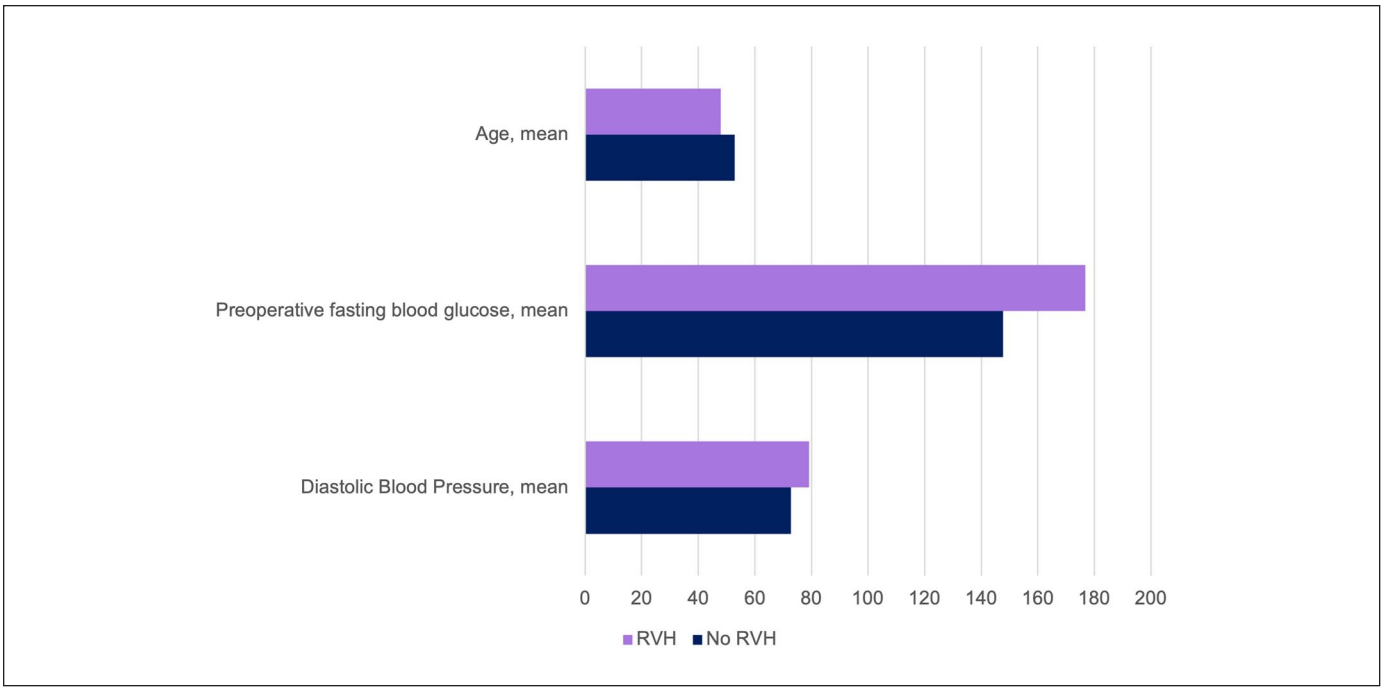

Figure 1. The risk factors and mean values of patients who developed recurrent vitreous hemorrhage (RVH). $P < .05$.

included in the multivariate logistic regression model to control for potential confounders. For instance, if age was selected to be the independent variable to be analyzed, all other variables included in the multivariate model were controlled as potential confounders.

Statistical significance was set at $P < .05$. Mean values are ± SD. All analyses were performed using R software (R Core Team 2023).

Results

The study included 220 eyes of 185 patients. Of the patients, 82 (44.3%) patients identified as Hispanic and 62 (33.5%) as Black. Seventy-six eyes (34.5%) had recurrent VH after 25-gauge PPV. Table 1 shows the clinical characteristics of the patients.

The incidence of recurrent VH was 34.5% (76 eyes). The VH was categorized as early (0 to 2 weeks postoperatively) in 46 eyes (60.5%), delayed (2 to 4 weeks postoperatively) in 8 eyes (10.5%), and late (4+ weeks postoperatively) in 22 eyes (28.9%). Mild/moderate recurrent VH (optic disc, macula, and retinal vessels visible) was seen in 68 eyes (89.5%) and severe recurrent VH (retina details not visible) in 8 eyes (10.5%). One hundred eyes (45.5%) had a diagnosis of VH, 56 (25.5%) eyes had TRD, and 64 (29.1%) eyes had combined rhegmatogenous RD and TRD (Table 1).

Table 2 shows a bivariate analysis of the characteristics of patients with recurrent VH and those without recurrent VH. The mean age of patients without recurrent VH was 52.8 years and of patients with recurrent VH was 47.9 years. The mean preoperative fasting blood glucose level was 147.7 ± 60.6 mg/dL in patients without recurrent VH and 176.7 ± 78.6 mg/dL in patients with recurrent VH. The mean diastolic blood pressure at time of surgery was 72.8 ± 17.4 mm Hg and 79.2 ± 14.5 mm Hg, respectively.

There was no significant association between anticoagulant use (warfarin, aspirin, or apixaban) and recurrent VH ($P = .1$). Recurrent VH developed in 21 eyes (27.6%) of patients taking anticoagulants; 56 eyes (38.9%) in patients who used anticoagulants did not develop recurrent VH.

There was no significant association between preoperative PRP and recurrent VH ($P = .06$). Eighty-one eyes that had complete PRP did not have recurrent VH, while 35 eyes that had complete PRP had recurrent VH (Table 2). Of eyes without complete PRP, 51 without PRP had no recurrent VH and 30 without PRP that had recurrent VH. Only 6 eyes had incomplete PRP, and the PRP status was unknown in 17 eyes as a result of severe preoperative VH and a lack of a specific description in the operative report.

Of the eyes that developed recurrent VH, 38.2% received no tamponade, 11.8% received air, 14.5% received SF_6, 25% received C_3F_8, and 10.5% received silicone oil (SO). Compared with eyes that did not develop recurrent VH, 43% received no tamponade, 9.7% received air, 12.5% received SF_6, 25.7% received C_3F_8, and 9% received SO (Table 2). The difference was not statistically significant ($P = .75$).

Age ($P = .027$), preoperative fasting blood glucose ($P = .020$), and diastolic blood pressure at time of surgery ($P = .005$) were found to be significant risk factors affecting recurrent VH (Table 3).

Using the previously identified significant factors, Kaplan-Meier curves were used to illustrate the differences in time to recurrent VH (Figure 2). To create these curves, a mean age

Table 1. Clinical Characteristics of 220 Eyes of 185 Study Participants.

Variable	Value
Age (y)	
Mean ± SD	51.12 ± 12.75
Range	21.03, 88.64
Sex, n (%)	
Male	125 (56.82)
Female	95 (43.18)
Duration of diabetes (y)	
Mean ± SD	14.26 ± 8.49
Range	1, 34
Type 1 DM, n (%)	30 (13.6)
Type 2 DM, n (%)	190 (86.4)
Last HbA_{1c} (%) [range]	
Mean ± SD	7.99 ± 2.28
Range	5.8, 14.4
Preoperative fasting blood glucose (mg/dL)	
Mean ± SD	157.89 ± 68.72
Range	34, 469
Mean serum creatinine (mg/dL) ± SD	5.95 (15.23)
Mean blood urea nitrogen, mean (mg/dL)	34.05 (29.11)
Diagnosis, n (%)	
Vitreous hemorrhage	100 (45.45)
TRD	56 (25.45)
Combined RRD and TRD	64 (29.09)
PRP, n (%)	
Complete PRP	116 (52.73)
Incomplete PRP	6 (2.73)
None	81 (36.82)
Unknown	17 (7.73)
Intraocular pressure (mm Hg)	
Preoperative	
Mean ± SD	15.74 ± 4.42
Range	8, 52
Postoperative day 1	
Mean ± SD	19.75 ± 7.92
Range	0, 58
Intraoperative IVT bevacizumab, n (%)	37 (16.82)

Abbreviations: DM, diabetes mellitus; HbA_{1c}, glycosylated hemoglobin; IVT, intravitreal; PRP, panretinal photocoagulation; RRD, rhegmatogenous retinal detachment; TRD, tractional retinal detachment.

(50 years), preoperative fasting blood glucose (158 mg/dL), and diastolic blood pressure (75 mm Hg) were used as cutoffs to determine the high-risk group and low-risk group. Patients with a higher value than the cutoff for each of these variables were placed in the high-risk group for that respective variable. Last, patients who were at high risk for all 3 variables were placed in the high-risk overall group.

Conclusions

The incidence of recurrent VH in patients with PDR has decreased significantly, from 75% in the 1980s to 12% to 40% in the past decade.[6–8] In our study, 76 eyes (34.5%) had recurrent VH after 25-gauge PPV, which falls within the previously reported range. Although the etiology of recurrent VH is unknown, proposed causes include regressing residual neovascularization, fibrovascular growth at sclerotomy sites, and increased postoperative vascular permeability.[10,16] Late postoperative bleeding has been associated with persistent neovascularization.[16] Of the eyes with recurrent VH in our study, 46 (60.5%) had early recurrent VH (0-2 weeks postoperatively), 8 (10.5%) had delayed recurrent VH (2-4 weeks postoperatively), and 22 (28.9%) had late recurrent VH (4+ weeks postoperatively). Recurrent VH may also occur from iatrogenic injury of retinal blood vessels and significant residual blood clots in the vitreous cavity and retinal surface.[6,8] Postoperative contraction of residual vitreous may cause traction on fibrovascular membranes in patients with PDR, leading to bleeding.[7]

Our study found that age differed significantly between patients with and patients without recurrent VH ($P = .027$). Each additional year of a decrease in age was associated with a 3.5% increase in the odds of developing recurrent VH. Similar findings, including the association between younger age and recurrent VH, were previously reported.[7,8,17] The authors of these studies speculated that this may be because younger patients with PDR could have a more aggressive initial presentation. This may account for why these patients are developing VH at a younger age and are therefore predisposed to having recurrent VH. In addition, young patients have stronger vitreoretinal adhesion, raising the possibility of residual vitreoschisis at the time of hyaloid elevation. This residual vitreous may then exert traction on regressing neovascularization, leading to a higher rate of bleeding than in older patients.

A higher preoperative fasting blood glucose level was significantly associated with the development of recurrent VH ($P = .020$). The severity and uncontrolled nature of a patient's DM is associated with worse disease-related complications, including DR.[18,19] Although the duration of diabetes was longer for patients who developed recurrent VH, this result was not significant in our study ($P = .68$). We also found that a higher diastolic blood pressure was significantly associated with the development of recurrent VH after surgery ($P = .005$). One of the strongest predictors of the development of DR is the duration of diabetes and the blood pressure, which may lead to neovascularization as a result of the development of angiogenic factors such as VEGF.[10,19] Although our retrospective study was not able to evaluate causation, we hypothesize that improving a patient's glycemic control before PPV may help minimize recurrent VH in nonurgent cases, such as nonclearing VH with complete PRP.

Although a greater percentage of patients who received preoperative anti-VEGF treatments (bevacizumab, ranibizumab, or aflibercept) did not develop recurrent VH, this result was not statistically significant ($P = .38$). However, the number of anti-VEGF injections that patients received varied (mean, 1.13 injections). Patients who received more than 1 injection may have had a different outcome than those who received only 1 treatment before surgery. In addition, we included patients who

Table 2. Demographic and Preoperative, Intraoperative, and Postoperative Characteristics of Patients With and Patients Without Recurrent VH.

	Recurrent VH (N = 220)		
Demographic Variable	Yes (n = 76)	No (n = 144)	*P* Value
Age (y)			.01
Mean	47.9	52.8	
Range	21.0, 74.1	24.7, 88.6	
Sex, n (%)			1
Male	43 (56.6)	82 (56.9)	
Female	33 (43.4)	62 (43.1)	
Race, n (%)			.26
Black	23 (30.26)	53 (36.8)	
Hispanic	40 (52.6)	55 (38.2)	
White	4 (5.26)	13 (9.0)	
Other	9 (11.8)	23 (16.0)	
Diabetes, n (%)			1
Type 1	10 (13.2)	20 (13.9)	
Type 2	66 (86.8)	124 (86.1)	
Mean duration of diabetes (y) ± SD	15.2 ± 10.6	13.8 ± 7.5	.68
Anticoagulant use, n (%)	21 (27.6)	56 (38.9)	.1
PRP, n (%)			.06
Complete	35 (46.1)	81 (56.3)	
Incomplete	5 (6.6)	1 (0.7)	
None	30 (39.5)	51 (35.4)	
Mean HbA_{1c} (%) ± SD	8.0 ± 1.93	7.98 ± 2.53	.97
Mean serum creatinine (log) ± SD	5.3 ± 10.8	6.4 ± 17.7	.70
Mean urea (log) ± SD	32.1 ± 31.3	35.4 ± 27.6	.57
Preoperative visual acuity (logMAR)			.58
Mean	1.9 ± 1.0	1.81 ± 1.02	
Range	0.3, 5.0	0.1, 4.0	
Mean preoperative IOP (mm Hg) ± SD	15.3 ± 5.8	16.0 ± 3.4	.37
Phakia, n (%)	55 (72.4)	109 (75.7)	.51
Glaucoma, n (%)	16 (21.1)	24 (16.7)	.35
Glaucoma suspect, n (%)	1 (1.3)	7 (4.9)	
Preoperative anti-VEGF, n (%)	21 (27.6)	47 (32.6)	.38
Intraoperative IVT bevacizumab, n (%)	10 (13.2)	27 (18.8)	.35
Beta-blocker use, n (%)			.11
Timolol (drops)	19 (25.0)	19 (13.5)	
Carvedilol (oral)	23 (30.3)	51 (36.2)	
None	34 (44.8)	74 (50.4)	
Mean preoperative fasting blood glucose (mg/dL) ± SD	176.7 (78.6)	147.7 (60.6)	.01
Men blood pressure at time of surgery (mm Hg) ± SD			
Systolic	151.71 ± 21.52	148.38 ± 22.64	.29
Diastolic	79.21 ± 14.54	72.83 ± 17.35	.01
Anesthesia, n (%)			.8
MAC	69 (90.8)	133 (92.4)	
GA	7 (9.2)	11 (7.6)	
Cataract surgery performed, n (%)	28 (36.8)	61 (42.4)	.47
Corticosteroid use, n (%)	8 (10.5)	27 (18.8)	.17
Membrane peeling, segmentation, and delamination performed, n (%)	55 (72.4)	95 (66.0)	.36
Retinal breaks, n (%)	24 (31.6)	53 (36.8)	.46
Tamponade, n (%)			.75
None	29 (38.2)	62 (43)	
Air, SF_6, C_3F_8	39 (51.3)	69 (47.9)	
Silicone oil	8 (10.5)	13 (9)	
Sclerotomies sutured, n (%)	36 (47.4)	89 (61.8)	.11
Postoperative day 1 VA (logMAR)			.41
Mean ± SD	2.19 ± 0.88	2.02 ± 1.48	
Range	0.4, 3.0	0.2, 12.0	
Mean postoperative day 1 IOP (mm Hg) ± SD	19.39 ± 7.5	19.9 ± 7.48	.65
Postoperative month 1DME, n (%)	23 (30.3)	53 (36.8)	.30

Abbreviations: anti-VEGF, antivascular endothelial growth factor; C_3F_8, perfluoropropane; DME, diabetic macular edema; GA, general anesthesia; IOP, intraocular pressure; IVT, intravitreal; MAC, monitored anesthesia care; PRP, panretinal photocoagulation; SF_6, sulfur hexafluoride; VA, visual acuity; VH, vitreous hemorrhage.

Table 3. Binomial Logistic Regression Analysis for Risk Factors of Recurrent VH After 25-Gauge Pars Plana Vitrectomy.

	Univariate		Multivariate	
Risk Factor	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
Age	0.969 (0.947, 0.991)	.007	0.966 (0.937, 0.996)	.027
Type 1 DM	1.06 (0.48, 2.49)	.88	2.466 (0.827, 7.354)	.105
Complete PRP	1.130 (0.877, 1.455)	.343	1.444 (0.758, 2.748)	.263
Anticoagulant used	0.837 (0.383, 1.828)	.654	0.764 (0.370, 1.578)	.467
Anti-VEGF used	0.610 (0.255, 1.35)	.242	0.865 (0.420, 1.781)	.693
Beta blocker (timolol drops)	2.09 (0.98, 4.47)	.05	3.399 (1.368, 8.446)	.008
Preoperative fasting blood glucose	1.006 (1.002, 1.011)	.004	1.006 (1.001, 1.011)	.020
Air tamponade	1.17 (0.76, 1.81)	.48	0.900 (0.390, 2.076)	.804
Retinal breaks	0.792 (0.435, 1.421)	.440	0.717 (0.323, 1.592)	.413
Diastolic blood pressure	1.032 (1.010, 1.059)	.010	1.036 (1.011, 1.061)	.005
Sclerotomies sutured	0.721 (0.526, 0.983)	.040	0.513 (0.251, 1.049)	.067
Intraoperative IVT bevacizumab	0.66 (0.29, 1.40)	.29	0.584 (0.236, 1.445)	.245

Abbreviations: Anti-VEGF, antivascular endothelial growth factor; DM, diabetes mellitus; GA, general anesthesia; IVT, intravitreal; PRP, panretinal photocoagulation; VH, vitreous hemorrhage.

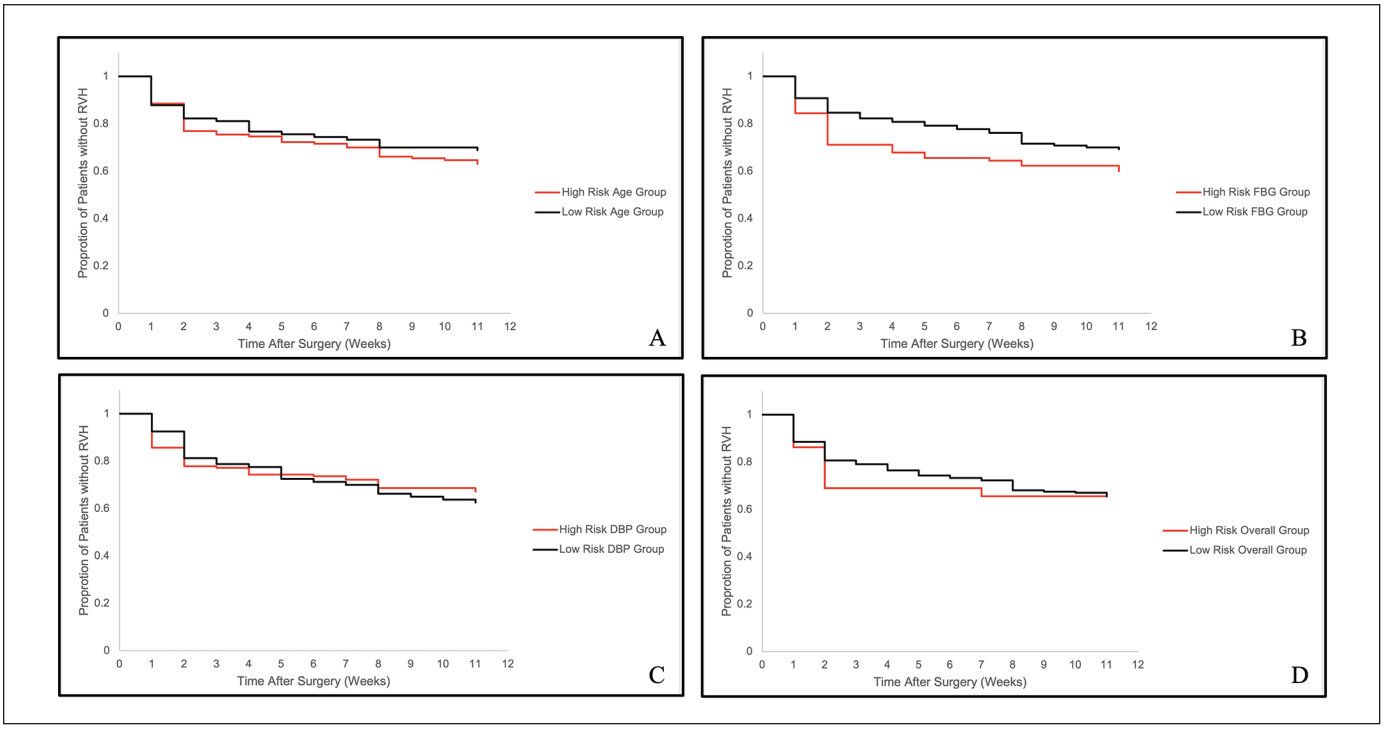

Figure 2. Kaplan-Meier survival curves for time to recurrent vitreous hemorrhage (RVH) between high-risk and low-risk groups for (A) age, (B) fasting blood glucose (FBG), (C) diastolic blood pressure (DBP), and (D) overall.

received anti-VEGF injections at any time before PPV, with the mean interval before surgery being 107 days. Based on a meta-analysis by Wang et al,[16] anti-VEGF treatment given 6 to 14 days preoperatively was shown to be most efficacious in reducing the incidence of recurrent VH. The large variability in the anti-VEGF timing in our patients likely explains the lack of significance in anti-VEGF treatments being protective against recurrent VH.

Monthly anti-VEGF injections alone are a viable treatment for PDR and lead to regression of neovascularization.[20] Ding et al[7] investigated anti-VEGF use but because of the small sample were unable to determine a correlation to recurrent VH. Baget-Bernaldiz et al[10] found a similar rate of recurrent VH between eyes that received 3 monthly ranibizumab injections preoperatively and those that did not. A meta-analysis of 26 randomized controlled trials found that anti-VEGF injections given 6 to 14 days before PPV significantly improved postoperative BCVA and reduced the incidence of recurrent VH.[16] Arevalo et al[21] found that recurrent VH occurred in 28.4% of eyes that received IVT bevacizumab 3 to 5 days preoperatively

compared with 42.8% of eyes that did not ($P = .028$). In our study, 13.2% of eyes that received IVT bevacizumab developed recurrent VH compared with 18.8% of eyes that did not ($P = .35$). The efficacy of administering anti-VEGF medications perioperatively to reduce the likelihood of recurrent VH is unclear, and prospective randomized controlled trials may be beneficial.[22]

A higher percentage of eyes that did not develop recurrent VH had complete PRP (56.3%) before surgery than eyes that did develop recurrent VH (46.1%); however, the difference was not statistically significant ($P = .06$). For many patients with PDR, a VH prevents complete PRP from being performed before a vitrectomy. The benefits of PRP before PPV for PDR have been previously documented.[23] Patel et al[24] found that eyes that had PRP within 6 months of a PPV had a significantly lower rate of recurrent VH (5.3%) than eyes that received PRP more than 6 months before a PPV (27.3%) ($P = .04$). Although not statistically significant, the trend in our study is similar to that in many other studies that found fewer recurrent VH events in patients who had PRP before surgery.[6,8,10]

A higher percentage of patients who did not develop recurrent VH were taking anticoagulants (38.9%) compared with those who did develop recurrent VH (27.6%); however, this result was not significant ($P = .1$). Of the 77 patients who were taking anticoagulants, 74 were on aspirin 81 mg, 2 were on aspirin 325 mg, and 1 was taking apixaban. Khuthaila et al[6] similarly found that 63% of patients who did not develop recurrent VH were taking anticoagulants compared with only 50% of patients who developed recurrent VH ($P = .13$). The Early Treatment Diabetic Retinopathy Study found no effect of aspirin 650 mg in altering the disease course, including those with early PDR, compared with placebo.[25] However, these findings contradict those of Fabinyi et al,[26] who found an increased risk for recurrent VH in patients on anticoagulants/antiplatelet therapy at the time of surgery. They found that preoperative cessation of treatment appeared to reduce the risk for recurrent VH. In a univariate model, Mahalingam et al[8] found that the perioperative use of anticoagulants (discontinued 5 days before surgery) was significantly associated with recurrent VH ($P < .0001$). In a meta-analysis of 22 studies, researchers found that anticoagulants do not increase the risk for hemorrhagic complications after PPV.[27] Further prospective investigation would help answer the question of whether to stop anticoagulant treatment before surgery.

Our study did not find a significant association between the type of tamponade used and recurrent VH. A previous study by Yang et al[28] found C_3F_8 gas to be effective in decreasing recurrent VH. They propose that this efficacy may attributed to the exertion of mechanical force on the retinal vessels by the surface tension of the gas. They also propose that a decrease in liquid volume of the vitreous cavity leads to a high concentration of coagulation factors near bleeding sites.[28] However, Khuthaila et al[6] did not find a significant association between the type of gas used and recurrent VH.

There was a significant association between sclerotomies that were sutured and recurrent VH in our univariate analysis ($P = .040$); however, this was not maintained in our multivariate analysis after controlling for other factors ($P = .067$). Similarly, Patel et al[24] found no significant association between sclerotomy suturing and postoperative complications.

This study identified higher fasting blood glucose levels and higher diastolic blood pressures as potential risk factors for recurrent VH. We hypothesize these factors may be particularly important in this patient population because they may reflect the unique social determinants of health that these patients face. For instance, 39% of patients at University of Illinois Hospital had an income less than $50,000. Patients with lower incomes are less likely to dedicate as many resources to postoperative care, such as at-home assistance. This is consistent with lower income individuals having worse postoperative outcomes after other kinds of surgery, such as joint, spine, or heart surgery.[29,30]

Moreover, 35% of the patients at University of Illinois Hospital had an education level of high school or less. A lower education level may also result in a lower functional health literacy, leading to poorer health outcomes.[31] Similarly, populations that have a limited English proficiency may also have lower functional health literacy, leading to poorer health management. This is consistent with Smith et al's[32] findings that Spanish-speaking patients had lower functional health literacy and a lack of understanding with regard to emergency department discharge instructions.

Furthermore, Andreae et al's study[33] found improved appointment adherence when patients were reminded of their appointments in their preferred language, indicating that a sufficient understanding in the patients' language of choice is important for management of their health.

As shown by the findings in the aforementioned studies, these social determinants of health may limit access to care, the understanding of care, and adherence to treatment plans. For a combination of these reasons, the patients in our sample may have had poorer control of their chronic diseases, such as hypertension or diabetes, leading to a higher incidence of recurrent VH at a younger age.

The sociodemographic characteristics of our patient sample may explain the differences in our study compared with other papers. After 25-gauge PPV, Mahalingam et al[8] and Ding et al[7] analyzed 190 eyes and 167 eyes of patients with DR and reported similar rates of recurrent VH (21.5% and 21.6%, respectively); this is in contrast to the 34.5% rate in our study. Similar to our methodology, both studies conducted a retrospective chart review in which similar preoperative, intraoperative, and postoperative characteristics of patients with DR who had a 25-gauge PPV were recorded.

We hypothesize that the higher recurrent VH incidence rate in our study may be the result of different patient populations. For instance, our patient population had higher mean fasting blood glucose levels (157.89 mg/dL), a longer mean duration of diabetes (14.26 years), and a higher mean blood pressure (150.05 mm Hg systolic) compared with the Ding et al[7] population (106 mg/dL, 12 years, and 136.13 mm Hg systolic, respectively). Furthermore, in a retrospective study by Khuthaila et al[6] of 173 eyes that had 23-gauge PPV in Philadelphia, the

reported incidence of recurrent VH was 32%, which is still lower than the 34.5% reported in our study. Our patient population had a younger mean age (51.12 years) and a higher average HbA_{1c} (7.99%) than patients in the Khuthalia et al[6] study (58.65 years and 7.75%, respectively). The higher reported recurrent VH rate in our study, in addition to the unique social determinants of health faced by our population, warrants further research into how postoperative outcomes may be affected.

Limitations of our study include its generalizability and retrospective nature. We evaluated outcomes at a single institution, which limits the generalizability of this study to other patient populations. Furthermore, these patients were cared for by multiple retina surgeons, who may have differing training backgrounds and years of experience. The variability introduced by these surgeons has the potential to bias the data and the consequent analysis, although this may also improve the generalizability of our results. In addition, patients who did not have at least 3 months of follow-up after surgery or were missing at least 3 datapoints were not included in our analysis, which may introduce another potential source of bias. Variability in the documentation in patient charts made identifying some datapoints difficult, such as postoperative positioning recommendations and when anticoagulants were stopped before surgery (if applicable). These datapoints were omitted from our analysis because information about them was available for only a few patients.

The retrospective nature of our study prevents causative analysis of the identified risk factors. As a result, our study identifies risk factors that serve as potential future research questions that can be tested more rigorously in randomized control trials.

Our study showed that recurrent VH is a common complication after 25-gauge PPV, consistent with the existing literature. Younger age, preoperative fasting blood glucose levels, and diastolic blood pressure were significantly associated with recurrent VH in patients with PDR. Unlike previous studies, we did not find phakia, a shorter duration of diabetes, higher serum creatinine levels, or incomplete PRP to be significantly associated with recurrent VH.[6–8] This may be a result of differences in our patient population, which may have less access to care and undergo fewer preventative measures before surgery. Based on our identified modifiable risk factors, our study supports the recommendation that tight glucose and blood pressure control at the time of surgery may minimize recurrent VH. Future prospective randomized control trials could help identify modifiable risk factors to improve patient outcomes after PPV for PDR.

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Authors' Note

Drs. Bitra and Sureshkumar contributed equally to this work and share co-first authorship.

Ethical Approval

Ethical approval for this study was obtained from the Institutional Review Board of the University of Illinois at Chicago (STUDY2021-1481). The collection and evaluation of all protected patient health information was performed in a US Health Insurance Portability and Accountability Act–compliant manner.

Statement of Informed Consent

Informed consent was not sought for the present study given its retrospective nature.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of the article.

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