

## Original Article

# Predictive clinical features and efficacy of preoperative anti-VEGF treatment on visual acuity in patients with proliferative diabetic retinopathy

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**Abstract:** Objective: To study the efficacy of anti-VEGF therapy for proliferative diabetic retinopathy and preoperatively identify patient characteristics and factors that may predict visual outcomes. Methods: Retrospective review of the electronic medical records of 216 consecutive vitrectomies in 154 patients with a minimum follow-up period of 6 months. Results: The mean change in vision was  $0.68 \pm 0.82$  LogMAR for all eyes. The mean improvement in vision was greater in the anti-VEGF group (0.77) than in the pars plana vitrectomy (PPV) group (0.48) ( $t = 2.443$   $p = 0.015$ ). The results show that 141 eyes (65.3%) improved by at least 0.2 LogMAR, 46 (21.3%) changed by <0.2 LogMAR, and 29 (13.4%) worsened by at least 0.2 LogMAR. Univariate logistic regression showed that preoperative anti-VEGF therapy (OR = 2.148  $p = 0.018$ ), preoperative vision in the operated eye (OR = 2.367  $p < 0.001$ ), tractional retinal detachment (OR = 0.480  $p = 0.025$ ), and the use of silicone oil tamponade (OR = 0.478  $p = 0.020$ ) were independent predictors of greater improvement in best corrected visual acuity (BCVA). Multivariate analysis showed that preoperative vision in the operated eye (OR = 2.852  $p < 0.001$ ) and the use of silicone oil tamponade (OR = 0.331  $p = 0.002$ ) were independent predictors of improved BCVA. Preoperative anti-VEGF therapy (OR = 2.984  $p = 0.002$ ) and tractional retinal detachment (OR = 0.437  $p = 0.020$ ) were independent predictors of improved BCVA by 0.2 LogMAR. Conclusions: Most diabetic patients showed improved visual acuity after vitrectomy within six months. Preoperative anti-VEGF therapy is highly likely to improve BCVA by 0.2 LogMAR, and preoperative LogMAR BCVA is the strongest predictor of postoperatively improved BCVA.

**Keywords:** Proliferative diabetic retinopathy, pars plana vitrectomy, anti-VEGF, visual acuity, prognosis

## Introduction

The vascular endothelial growth factor (VEGF) system represents the key medium for the angiogenesis of tumor initiation and is the first target of anti-vascular endothelial growth factor (anti-VEGF) introduced in clinical practice [1]. When neovascularization arises from the choroid or retina, it can lead to age-related macular degeneration and proliferative diabetic retinopathy (PDR). This fact led to the development of therapeutic strategies to anti-VEGF in the treatment of ocular neovascular disease [2]. Currently, three anti-VEGF drugs are commercially available in China: bevacizumab (Avastin; Genentech and Roche, Basel, Switzerland),

ranibizumab (Lucentis; Genentech, Inc., South San Francisco, CA) and conbercept (KH902; Chengdu Kanghong Biotech Co., Ltd., Sichuan, China) [3].

PDR is a major sight-threatening complication of diabetic retinopathy characterized by neovascularization. While relatively recent studies have revealed that treating PDR with anti-vascular endothelial growth factor (anti-VEGF) agents may lead to reduced need for vitrectomy [4, 5], pars plana vitrectomy (PPV) is still an effective treatment for severe PDR. Anti-VEGF agents used as adjuncts before PPV for PDR were first described in 2006 [6], and several studies showed that they could reduce intraop-

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**Table 1.** Clinical and laboratory characteristics of patients

Characteristic	Value
Age (years)	54.5 ± 10.4
Sex (male/female)	77/77
Study eye (left/right)	109/107
Duration of diabetes (years)	12.2 ± 7.6
Hypertension	79 (51.3%)
HbA1c%	7.66 ± 2.15
PT (sec)	11.1 ± 0.7
INR	0.97 ± 0.06
APTT (sec)	27.2 ± 3.3
BUN (mmol/L)	6.90 ± 2.93
Scr (μmol/L)	97.39 ± 137.07
Pre-op LogMAR BCVA, operated eye	1.56 ± 0.72
Pre-op LogMAR BCVA, fellow eye	1.10 ± 0.86
Pre-op IOP, operated eye	14.21 ± 3.75
Pre-op IOP, fellow eye	14.37 ± 4.58
AL (mm), operated eye	22.97 ± 0.99
AL (mm), fellow eye	23.07 ± 1.10
Pseudophakia	16 (7.4%)
Nonclearing vitreous hemorrhage	49 (22.7%)
Diffuse fibrovascular proliferation	50 (23.1%)
Tractional retinal detachment	117 (54.2%)
Pre-op anti-VEGF therapy	146 (67.6%)
Combined cataract and vitrectomy	128 (59.3%)
Iatrogenic break	58 (26.9%)
PFCL use	25 (11.6%)
Silicone oil tamponade	85 (39.4%)
C3F8 tamponade	27 (12.5%)

Values in parentheses are percentages. HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>; PT = prothrombin time; INR = international normalized ratio; APTT = activated partial thromboplastin time; BUN = blood urea nitrogen; Scr = serum creatinine; LogMAR = logarithm of minimal angle of resolution; BCVA = best-corrected visual acuity; IOP = intraocular pressure; AL = axial length; VEGF = vascular endothelial growth factor; PFCL = perfluorocarbon liquid; C3F8 = perfluoropropane.

erative bleeding, iatrogenic retinal breaks, duration of surgery, early postoperative vitreous hemorrhage (VH), and neovascular glaucoma (NVG) [7–11]. Before the advent of anti-VEGF treatment, Yorston and co-workers reported that visual outcomes for PDR after vitrectomy were unpredictable [12]. It remains uncertain whether patients receiving preoperative anti-VEGF have a better best corrected visual acuity (BCVA) prognosis and better BCVA improvement six months after surgery compared to those not undergoing pre-PPV anti-VEGF therapy.

The purposes of this study were to determine whether pre-PPV anti-VEGF was related to improved BCVA six months postoperatively and identify any preoperative characteristics or operative factors that may predict visual outcomes.

### Methods

Consecutive patients aged ≥18 years with diabetes mellitus (DM) who underwent primary vitrectomy for complications secondary to PDR were included in the study. The operations and examinations were performed at the Eye Hospital of Wenzhou Medical University between July 2012 and December 2015. We reviewed all the electronic medical records (EMRs) of these patients and included their eyes if PPV was performed for nonabsorbent VH, fibrovascular proliferation adherent to the macula or at least two quadrants, or tractional retinal detachment (TRD) involving or threatening the macula. The exclusion criteria were a previous history of vitrectomy, PPV for other reasons, and follow-up time of less than six months. After being informed of the cost, benefits, and risks of anti-VEGF therapy, each patient decided whether to undergo pre-PPV anti-VEGF therapy and selected the specific anti-VEGF agent. If the time interval between anti-VEGF injection and vitrectomy was >15 days, the patient was placed in the PPV-only group. The study followed the principles of the Declaration of Helsinki and was approved by the Institutional Review Board and Ethics Committee of Wenzhou Medical University.

Visual acuity was measured using a standard logarithmic vision chart and was analyzed on a LogMAR scale, where counting fingers (CF), hand motion (HM), light perception (LP), and no light perception (NLP) were assigned values of 2.1, 2.4, 2.7, and 3.0, respectively [13]. The following data were collected: patient age, gender, and follow-up time; systemic factors such as duration of diabetes and systemic hypertension; laboratory results including hemoglobin A1c (HbA1c) at time of surgery, prothrombin time (PT), prothrombin international normalized ratio (INR), activated partial thromboplastin time (APTT), blood urea nitrogen (BUN), and serum creatinine; and ophthalmic factors such as preoperative BCVA, preoperative intraocular pressure (IOP), axial length (AL), PDR stage,

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**Table 2.** Pre- and postoperative visual acuities with best correction or pinhole

LogMAR visual acuity	Preoperative visual acuities				Postoperative visual acuities			
	VH (n = 49)	FVP (n = 50)	TRD (n = 117)	All eyes (n = 216)	VH (n = 49)	FVP (n = 50)	TRD (n = 117)	All eyes (n = 216)
0.0-0.2	0 (0)	0 (0)	1 (0.9)	1 (0.5)	6 (12.2)	2 (4)	3 (2.6)	11 (5.1)
>0.2-0.4	4 (8.2)	2 (4)	2 (1.7)	8 (3.7)	15 (30.6)	21 (42)	25 (21.4)	61 (28.2)
>0.4-0.6	3 (6.1)	6 (12)	5 (4.3)	14 (6.5)	9 (18.4)	7 (14)	15 (12.8)	31 (14.4)
>0.6-0.8	3 (6.1)	12 (24)	15 (12.8)	30 (13.9)	7 (14.3)	9 (18)	21 (17.9)	37 (17.1)
>0.8-1.0	6 (12.2)	3 (6)	15 (12.8)	24 (11.1)	3 (6.1)	3 (6)	8 (6.8)	14 (6.5)
>1.0-1.3	4 (8.2)	5 (10)	10 (8.5)	19 (8.8)	6 (12.2)	4 (8)	16 (13.7)	26 (12.0)
>1.3-1.99	3 (6.1)	3 (6)	15 (12.8)	21 (9.7)	1 (2.0)	0 (0)	6 (5.1)	7 (3.2)
CF	15 (30.6)	8 (16)	28 (23.9)	51 (23.6)	1 (2.0)	2 (4)	9 (7.7)	12 (5.6)
HM	11 (22.4)	10 (20)	24 (20.5)	45 (20.8)	1 (2.0)	1 (2)	10 (8.5)	12 (5.6)
PL	0 (0)	1 (2)	2 (1.7)	3 (1.4)	0 (0)	1 (2)	4 (3.4)	5 (2.3)

Values in parentheses are percentages. VH = vitreous hemorrhage; FVP = fibrovascular proliferation; TRD = tractional retinal detachment; CF = counting fingers; HM = hand motions; PL = perception of light; NPL = no perception of light.

and intraoperative and postoperative complications.

One week before surgery, all eyes in the anti-VEGF group received a sterile syringe injection of either 1.25 mg of intravitreal bevacizumab (IVB) (Avastin; Genentech, South San Francisco, CA), 0.5 mg of intravitreal ranibizumab (IVR) (Lucentis; Genentech, Inc and Novartis International AG, Basel, Switzerland), or intravitreal conbercept (IVC) (Conbercept; Chengdu Kanghong Biotech, Inc., Chengdu, Sichuan, China) in dosages of 0.5 mg in the superior temporal quadrant and 4 mm behind the limbus. Each patient underwent a standard 23-gauge 3-port PPV under local or general anesthesia, according to their general condition. All surgeries were performed by the same experienced surgeon (Zongming Song). In phakic patients aged  $\geq 50$  years, phacoemulsification and intracapsular acrylic foldable intraocular lens implantation were performed if necessary. Otherwise, phacoemulsification was accomplished during silicone oil removal after 3-6 months. Any operative factors (such as phacoemulsification, iatrogenic break, perfluorocarbon liquid (PFCL) use, and silicone oil/perfluoropropane tamponade) were recorded.

Statistical analysis was performed with SPSS software version 19.0 (SPSS, Inc., Chicago, IL, USA). Quantitative data were presented as the mean  $\pm$  standard deviation, whereas qualitative variables were expressed using percentages. An independent *t*-test and one-way analysis of variance were used to analyze quantitative

data, and chi-square tests were used to analyze qualitative data respectively. Univariate logistic regression was run on the following outcome variables six months after surgery: (1) improvement from baseline BCVA, (2) improvement from baseline BCVA by  $\geq 0.2$  LogMAR, (3) final BCVA of 1.0 LogMAR or better, and (4) final BCVA of 0.52 LogMAR or better. Predictors with a *p*-value of  $< 0.2$  in the univariate analysis were included in a multivariate logistic regression by applying a forward conditional procedure; *p*  $< 0.05$  was considered significant.

### Results

A total of 216 eyes from 154 patients with severe PDR were included in this study. Seventy-seven (50%) patients were male. The average age at surgery was  $54.5 \pm 10.4$  years; 11 patients were under age 40, and 8 patients were aged 70 or older. Of the patients in the study, 5 had type 1 diabetes, and 149 had type 2. The mean duration of diabetes on admission was  $12.2 \pm 7.6$  years, and the mean HbA1c was  $7.66 \pm 2.15$ . The most common associated systemic condition was hypertension, which was present in 79 (51.3%) patients. The mean BUN was  $6.90 \pm 2.93$  mmol/L, the mean serum creatinine was  $97.39 \pm 137.07$   $\mu$ mol/L, and six patients were diagnosed with renal failure. The clinical and laboratory characteristics of the patients are summarized in **Table 1**.

A total of 146 (67.6%) eyes underwent anti-VEGF injections before surgery (82 in the IVB group, 29 in the IVR group, and 35 in the IVC

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**Table 3.** Univariate logistic regression analysis of factors related to visual outcome

Postoperative visual acuity	Factor	Odd ratio (95% CI)	p-value
BCVA improved	Pre-op anti-VEGF therapy	2.148 (1.141 to 4.044)	0.018
	Pre-op LogMAR BCVA, operated eye	2.367 (1.509 to 3.715)	<0.001
	Stages of PDR	0.658 (0.438 to 0.988)	0.044
	Tractional retinal detachment	0.480 (0.253 to 0.913)	0.025
	Silicone oil tamponade	0.478 (0.257 to 0.890)	0.020
BCVA improved by 0.2 LogMAR	Pre-op anti-VEGF therapy	3.426 (1.877 to 6.252)	<0.001
	Pre-op LogMAR BCVA, operated eye	4.576 (2.846 to 7.357)	<0.001
	Pre-op LogMAR BCVA, fellow eye	0.691 (0.499 to 0.958)	0.026
BCVA>1.0 LogMAR	HbA1c %	0.823 (0.707 to 0.958)	0.012
	Pre-op LogMAR BCVA, operated eye	0.418 (0.270 to 0.648)	<0.001
	Stages of PDR	0.577 (0.394 to 0.844)	0.005
	Tractional retinal detachment	0.383 (0.210 to 0.697)	0.002
	Combined cataract and vitrectomy	2.291 (1.286 to 4.083)	0.005
	Iatrogenic break	0.457 (0.246 to 0.851)	0.014
	PFCL use	0.233 (0.097 to 0.559)	0.001
	Silicone oil tamponade	0.253 (0.140 to 0.460)	<0.001
	Long-acting tamponade (C3F8 or oil)	0.223 (0.115 to 0.429)	<0.001
	BCVA>0.52 LogMAR	Scr	0.987 (0.977 to 0.997)
Pre-op LogMAR BCVA, operated eye		0.504 (0.336 to 0.758)	0.001
Pre-op LogMAR BCVA, fellow eye		0.636 (0.446 to 0.906)	0.012
Stages of PDR		0.619 (0.439 to 0.873)	0.006
Tractional retinal detachment		0.393 (0.220 to 0.703)	0.002
Combined cataract and vitrectomy		2.326 (1.263 to 4.285)	0.007
PFCL use		0.241 (0.070 to 0.835)	0.025
Silicone oil tamponade		0.248 (0.127 to 0.484)	<0.001
Long-acting tamponade (C3F8 or oil)	0.300 (0.166 to 0.541)	<0.001	

group). There were 62 (40.3%) patients who accepted vitrectomy in both eyes, and 33 (21.4%) patients were severely visually impaired (LogMAR >1.0) in both eyes upon admission. A total of 200 eyes were phakic, 16 eyes were pseudophakic, and no eyes were aphakic. Of the phakic eyes, 128 (64.0%) had combined cataract surgery and vitrectomy, while 52 (26.0%) had combined cataract surgery and silicone oil removal. An iatrogenic break was identified in 58 (26.9%) eyes, and PFCL was necessary for 25 (11.6%) eyes. TRD was found during surgery in 117 (54.2%) eyes, and the use of a silicone oil tamponade was required in 85 (39.4%) eyes. Postoperative vitreous cavity hemorrhage was a common complication; seven eyes required a vitreous washout. Seven eyes developed retinal detachment and ten developed neovascular glaucoma within six months postoperatively.

Patient outcomes showed that 141 (65.3%) eyes improved by at least 0.2 LogMAR, 46 (21.3%) changed by <0.2 LogMAR, and 29 (13.4%) worsened by at least 0.2 LogMAR. The mean change in vision was  $0.68 \pm 0.82$  LogMAR for all eyes. The mean improvement was greater in the anti-VEGF group (0.77) than in the PPV group (0.48) ( $t = 2.443$ ,  $p = 0.015$ , independent  $t$ -test). There were no differences in visual improvement among the IVB, IVR, and IVC groups at six months ( $F = 0.442$ ,  $p = 0.644$ , variance test). After surgery, 16 (10.4%) patients still had a BCVA of <1.0 LogMAR in both eyes, compared to 33 (21.4%) patients before surgery. Preoperative and postoperative visual acuities are shown in **Table 2**.

In the preoperative anti-VEGF treatment groups, 110 (75.3%) eyes showed improved BCVA of 0.2 LogMAR, compared with 33 (47.1%) eyes in the PPV group ( $\chi^2 = 16.81$ ,  $p < 0.001$ , chi-square

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**Table 4.** Multiple logistic regression analysis of factors related to visual outcome

Postoperative visual acuity	Factor	Odd ratio (95% CI)	p-value
BCVA improved	Pre-op LogMAR BCVA, operated eye	2.852 (1.756 to 4.633)	<0.001
	Silicone oil tamponade	0.331 (0.166 to 0.658)	0.002
BCVA improved by 0.2 LogMAR	Pre-op anti-VEGF therapy	2.984 (1.503 to 5.924)	0.002
	Pre-op LogMAR BCVA, operated eye	4.713 (2.831 to 7.845)	<0.001
	Tractional retinal detachment	0.437 (0.217 to 0.879)	0.020
BCVA>1.0 LogMAR	HbA1c	0.838 (0.715 to 0.983)	0.030
	Pre-op LogMAR BCVA, operated eye	0.435 (0.269 to 0.704)	0.001
	PFCL use	0.361 (0.138 to 0.948)	0.039
	Long-acting tamponade (C3F8 or oil)	0.308 (0.151 to 0.626)	0.001
BCVA>0.52 LogMAR	Scr	0.986 (0.974 to 0.998)	0.023
	Pre-op LogMAR BCVA, operated eye	0.556 (0.351 to 0.881)	0.012
	Pre-op LogMAR BCVA, fellow eye	0.602 (0.406 to 0.892)	0.011
	Silicone oil tamponade	0.217 (0.105 to 0.450)	<0.001

test). In 77 eyes with vision of 1.0 LogMAR or better, 65 (84.4%) retained vision of 1.0 LogMAR or better, compared with 79 (56.8%) eyes with poor vision (worse than 1.0 LogMAR). There was no association between visual outcome and patient age, duration of diabetes, hypertension, PR, INR, APPT, intraocular pressure, axial length, or cataract surgery. The variables showing significant associations with visual outcomes are summarized in **Table 3**.

Multivariate analysis showed that preoperative anti-VEGF therapy, preoperative vision in the operated eye, TRD, and the use of silicone oil tamponade were independently associated with visual improvement. **Table 4** also shows that HbA1c, serum creatinine, preoperative vision in the operated eye, preoperative vision in the fellow eye, the use of PFCL, and the use of long-acting intraocular tamponade were associated with visual outcome.

### Discussion

PPV is widely accepted as an effective surgical treatment for PDR, and anti-VEGF agents have been popularly used as adjunctive pre-PPV therapy to minimize surgical complications [6, 8, 9, 14-17]. It is important to develop a method for predicting the prognosis of PPV for PDR since this will help in surgical decision-making and counseling PDR patients. This study reports six-month follow-up results after diabetic vitrectomy with or without preoperative anti-VEGF therapy. The anti-VEGF drugs used were bevacizumab, ranibizumab, and conbercept,

which can all be obtained on the Chinese market.

Predicting visual acuity after diabetic vitrectomy is complicated by the complexity of clinical factors that may affect visual outcome in diabetic patients. We found that those with better preoperative visual acuity had better visual outcomes and greater BCVA improvement. We believe that those patients were in earlier stages of PDR without macular detachment or ischemia, which will affect final vision. A series by Ostri and colleagues reported that low vision the first year after surgery was associated with preoperative visual acuity <0.1 in the operated eye [18]. However, patients with worse preoperative visual acuity achieved greater LogMAR improvement [19]. Patients with good baseline vision were more likely to have an excellent visual outcome but had smaller improvements in BCVA, likely because of a ceiling effect (patients with good BCVA at baseline had less vision to gain to return to normal vision, making very large improvements impossible) [20].

An important finding of the present study was that preoperative anti-VEGF therapy seemed to be associated with improved BCVA. We found that the ratio of BCVA improvement by 0.2 LogMAR was significantly higher in patients who underwent preoperative anti-VEGF therapy compared to those who had PPV only. Our data concur with previous reports in the literature. A high vitreous fluid VEGF level was a significant risk factor for, and a potential predictor of, postoperative PDR progression and diabetic vitrec-

tomy outcomes [21, 22]. Yang and colleagues reported that the IVC group showed significantly better postoperative BCVA within one month and improved BCVA throughout the follow-up period [10]. Modarres and collaborators found that the IVB group had significantly better mean visual acuity after six months [23]. However, Manabe and co-workers did not observe that postoperative BCVA and visual improvement were significantly different between the IVB group one day before vitrectomy and the control group [24]. It is apparent from the available literature and our study that preoperative anti-VEGF therapy plays an important role in achieving BCVA improvement. It is possible that the combined effects of anti-VEGF agents explain the functional result (such as short-term effects with reperfusion of abnormal vessels), shortening the time of diabetic vitrectomy and reducing complications during surgery and postoperative vitreous hemorrhage. The introduction of anti-VEGF therapy has enabled significant advances in the management of PDR. Preoperative anti-VEGF therapy does have, however, the potential disadvantages of fibrosis progression and membrane contraction [25].

Multiple factors may affect postoperative visual acuity in diabetic eyes, such as macular-off detachment, diabetic macular edema, cataracts, and ischemic damage, which can be a limiting factor for functional results after successful vitreoretinal surgery. However, the retrospective nature of the present study made it difficult to determine the exact macula-off detachment status in each patient, which may be an important factor affecting final BCVA. Rahimy and co-workers suggested that the lens status of the eye does not affect the ultimate anatomic and visual outcomes of primary diabetic vitrectomy [26]. Combined surgery enables better visualization for the surgeon and allows early postoperative visual rehabilitation for the diabetic patient. Visual loss produced by postoperative lens opacification is treatable; however, dramatic loss of visual function in the postoperative period is usually related to recurrent VH or retinal detachment.

Postoperative recurrent VH severely impedes visual rehabilitation. Several studies have demonstrated that the rate of early VH after diabetic vitrectomy was reduced following administration of preoperative IVB [15, 17, 23]. Yang and

colleagues reported that the rate of prolonged blood reabsorption time was significantly lower in cases with bevacizumab pretreatment combined with intraoperative long-acting gas [27]. The effect of perioperative anti-VEGF injections on early postoperative VH is unclear, but there may be some temporary anti-VEGF effect in the early postoperative days, which may decrease the likelihood of prompt new vessel proliferation after surgery. However, Gupta and collaborators found no difference in the number of episodes of late post-vitrectomy VH with the use of bevacizumab [28]. Perioperative anti-VEGF therapy has been shown to be ineffective at reducing the incidence of late VH [15]. Almost all anti-VEGF medications injected preoperatively are removed during PPV.

In the present study, 58 eyes developed iatrogenic breaks, which were associated with an increased rate of postoperative retinal detachment. Jackson and co-workers reported that almost one in three operations were associated with complications, mainly related to retinal tears [13]. New skills such as bimanual surgery might be beneficial for reducing the rate of iatrogenic tears.

Although the present study showed an association between the use of silicone oil and a poor visual prognosis, this probably reflects the complexity of the surgical and the severity of the diabetic retinopathy [18]. Silicone oil was used in approximately 39% of the eyes in this study, compared to 23% reported by Ostri and colleagues [18]. However, other factors, such as different baseline systemic and ocular profiles, distinct surgical skills, and small sample size, should be taken into consideration. All our patients had severe PDR with persistent VH, TRD, or combined tractional/rhegmatogenous detachments. Silicone oil tamponade not only keeps the macula attached but also limits the flow of angiogenic factors reaching the anterior segment; it also significantly decreases the risk of recurrent postoperative hemorrhage [11]. Possible complications with extended silicone oil use, such as oil emulsification, glaucoma, band keratopathy, and corneal decompensation, were not observed in our study because of the timely removal of the silicone oil. Gupta and collaborators reported that silicone oil was only used in 9 of 185 eyes, which may be responsible for the better visual outcomes in their study [28].

Predicting the visual outcome of diabetic vitrectomy is clinically important but somewhat difficult. In this study, a univariate logistic regression analysis showed that several factors were associated with visual outcomes of PDR, including preoperative anti-VEGF therapy, preoperative LogMAR BCVA, HbA1c, serum creatinine, procedures such as combined cataract removal and vitrectomy, iatrogenic breaks, PFCL use, and long-acting tamponade. A multivariate logistic regression analysis also showed that preoperative anti-VEGF therapy and preoperative LogMAR BCVA were associated with improved BCVA and final BCVA in diabetic patients. These results suggest that preoperative anti-VEGF and BCVA may be useful for predicting visual outcomes of diabetic vitrectomy.

The authors are aware of the limitations caused by the retrospective nature of this study. Other limitations included a lack of evaluation of systemic risk factors six months postoperatively. It is likely that the surgeon elected to use anti-VEGF drugs in eyes with the most active neovascularization, so selection bias might make meaningful comparisons difficult. The preoperative features of patients who were not followed up after 6 months of surgery were similar to those of the study, but failure to follow up may cause bias.

Currently, the effectiveness of treating diabetic retinopathy is limited, and treatment is aimed at the later stages of the disease when the patient's vision has been seriously affected. A more effective prevention/intervention strategy in the early stages of diabetic retinopathy should lead to better vision outcomes. In fact, the pathogenesis of all patients is not the same as the drug reaction. In the near future, personalized treatment of diabetic retinopathy is needed.

In summary, this study found that preoperative anti-VEGF therapy is highly likely to result in improved BCVA. We also confirmed that preoperative LogMAR BCVA is the strongest predictor of postoperative BCVA improvement, even in patients treated with intravitreal anti-VEGF therapy. Further multicenter, large-sample studies may be required to evaluate the comparative effectiveness of different pre-vitrectomy anti-VEGF medications for the treatment of PDR.

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### Disclosure of conflict of interest

None.

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