

Vitreotomy for branch retinal vein occlusion with vitreous hemorrhage: proposal for a new grading system

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Abstract

Purpose

To investigate the long-term surgical outcomes after treatment with pars plana vitrectomy (PPV) combined with photocoagulation in different severities of branch retinal vein occlusion (BRVO) with vitreous hemorrhage (VH) in order to propose a new grading system.

Methods

We retrospectively reviewed the medical records of 117 eyes of 117 patients who underwent PPV for VH associated with BRVO and who were followed up for at least 12 months. Preoperative best-corrected visual acuity (BCVA), surgical intervention, final BCVA, and central foveal thickness (CFT) were evaluated using optical coherence tomography. We proposed a system to grade BRVO with VH from Grade I to Grade III with increasing severity: Grade I, pure persistent VH; Grade II, VH with epiretinal membrane (EM) (Grade IIa, VH with EM without macular involvement; Grade IIb, VH with EM with macular involvement); and Grade III, VH with tractive retinal detachment. Different surgical methods were applied according to the different retinal conditions.

Results

BCVA significantly improved at final follow-up in all groups. There was no significant difference among the four groups in terms of preoperative BCVA, final BCVA, CFT, or the number of patients whose macular edema recurred after surgery ($p > 0.05$), but there was a significant difference in vision improvement ($p < 0.05$). Vision improvement in the Grade IIb group was significantly worse than in the Grade I group ($p = 0.006$) and in the Grade IIa group ($p = 0.046$). The percentage of patients in the Grade I, Grade IIa, Grade IIb, and Grade III groups needing further laser treatment after surgery was 0%, 8.3%, 16.3%, and 23.5%, respectively ($p < 0.05$).

Conclusion

We proposed a new grading system for BRVO treated with PPV. Vitrectomy is a safe and effective treatment for BRVO with VH. Visual acuity improvement was significantly worse when the EM had macular involvement (Grade IIb).

Introduction

Retinal vein occlusion (RVO) is one of the most common causes of vision loss among older adults worldwide [1]. Among patients with RVO, branch retinal vein occlusion (BRVO) is the most prevalent, accounting for up to 80% of all RVO cases [2–4]. Vision may be affected by the complications of BRVO, including retinal macular edema (ME) [5], retinal detachment (RD) [6], the development of an epiretinal membrane (ERM) [7], and vitreous hemorrhage (VH) [8, 9]. Of such complications, ME is the most

common. Secondary to chronic ME, VH was a common ocular complication in the past that caused impaired vision [3, 10]. However, there has not been as much research on VH as on ME.

Currently, management is focused on secondary complications of RVO that affect vision. The treatment of BRVO is comprised of three main stages—the identification and treatment of modifiable risk factors, specific treatment of the vascular occlusion, and treatment of BRVO complications [11]. Anti-vascular endothelial growth factor (anti-VEGF) is a first-line therapy for ME due to RVO [12]. Other treatments for RVO include retinal laser photocoagulation [13], corticosteroids [14], medical treatment [15], isovolemic hemodilution [16], and surgery, such as vitrectomy (VT) and radial optic neurotomy [15, 17]. For unresolved VH, pars plana vitrectomy (PPV) performed concurrently with retinal laser photocoagulation is the management strategy [18, 19]. Liu and Wang reported that visual acuity (VA) improved after vitrectomy (VT) in 80% of the eyes in their study and that recurrent VH can be effectively prevented by endophotocoagulation during surgery [20]. Amirikia et al. [21] showed that improved VA was achieved in the majority of their study patients with VH associated with BRVO after VT. Unfortunately, the few published studies that report the outcomes of PPV for BRVO complications consist only of case reports and small case series. There is a significant lack of post-operative evaluations of different severities of BRVO, and there has not been a standard treatment for BRVO with VH until now. An extended study of the effects of VT for different severities of RVO is greatly needed. The purpose of this retrospective study is to investigate the long-term surgical outcomes after treatment with PPV combined with photocoagulation in different severities of BRVO with VH in order to propose a new grading system.

Materials And Methods

Eyes with a history of intravitreal injections of s The study adhered to the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of the Eye Hospital of Wenzhou Medical University. We retrospectively examined consecutive non-randomized patients who underwent PPV for BRVO with VH from January 2012 to December 2017 and who completed at least 12-months of follow-up. Steroids or anti-VEGF agents before surgery, rhegmatogenous RD, diabetic retinopathy, uveitis, VH without BRVO, central RVO, central retinal artery occlusion, trauma, ocular tumors, glaucoma (including neovascular glaucoma), or optic atrophy were excluded.

The data collected included patients' age, gender, previous ocular history, the presence of diabetes, the presence of hypertension, initial best-corrected visual acuity (BCVA), clinical manifestations, surgical intervention, final BCVA, central foveal thickness (CFT), and the frequency of requiring additional treatment after PPV. The BCVA was converted to a logarithm of the minimum angle of resolution (logMAR) for calculation. The visual acuities of counting fingers, hand motion, light perception, and no light perception were assigned values of 1/200, 1/400, 1/800, and 1/1600, respectively [22]. BCVA, fundus photography, and optical coherence tomography (OCT) (Heidelberg Engineering, Heidelberg, Germany) were routinely done after surgery. The severity of the baseline VH was scored on a 5-point scale: Grade 0 (no VH), Grade 1 (retinal vessels and optic disk were clearly visible), Grade 2 (most of the retinal vessels

and optic disk were visible), Grade 3 (retinal vessels or optic disk were barely visible), and Grade 4 (VH was too dense to allow visualization of the optic disk)[23].

All patients underwent VT and laser photocoagulation performed by two experienced retinal specialists. The presence of BRVO was identified and classified based on the intraoperative findings. We proposed a system of BRVO with VH from Grade I to Grade III with increasing severity: Grade I, pure persistent VH; Grade II, VH with EM (IIa, EM without macular involvement; IIb, EM with macular involvement); and Grade III, VH with tractive RD. For phakic eyes, phacoemulsification and intraocular lens implantation were performed, followed by PPV. Different surgical methods were applied according to different retinal conditions. Proliferative membrane peeling was performed for EBM eyes; internal limiting membrane (ILM) peeling was performed for macular EM eyes; and retinal reattachment was performed for eyes with RD (Table 1). Peripheral scatter laser photocoagulation was performed on the non-perfusion area observed by the surgeon to prevent neovascularization in all groups.

Table 1
Grading criteria and treatment

Grade	Signs	Treatment
I	pure persistent VH	PPV + photocoagulation
IIa	VH with ERM (without macular involvement)	PPV + photocoagulation + peeling proliferative membrane
IIb	VH with ERM (with macular involvement)	PPV + photocoagulation + peeling ILM
III	VH with RD	PPV + photocoagulation + retinal reattachment
Abbreviations: VH: vitreous hemorrhage; PPV: pars plana vitrectomy; ERM: epiretinal membrane; ILM: internal limiting membrane; RD: retinal detachment		

Postoperatively, ocular examinations were performed 1 week and 1, 3, 6, and 12 months after surgery. If OCT showed the ME did not improve or returned after 3 months, an intravitreal injection of ranibizumab (IVR) was administered. The eyes then underwent fluorescein angiography (FA), and laser photocoagulation was performed again if FA showed the fundus had a new capillary non-perfusion zone.

Statistical analyses were performed using SPSS version 25.0 (<http://www.spss.com>). All values are expressed as mean \pm SD or proportions, as appropriate. The normality of data distribution was assessed using the Kolmogorov–Smirnov test. Differences among groups were compared using the Kruskal–Wallis test. Continuous variables without a normal distribution were compared using the Mann–Whitney U test. A p-value of < 0.05 was considered to be statistically significant.

Results

Demographics and clinical data are presented in Table 2. This study recruited 117 eyes of 117 patients (62 men and 55 women). The patients had been diagnosed with BRVO after clearing the VH. The age (mean standard deviation) of the patients was 62.9 ± 9.27 years. Approximately 72.6% (85 patients) of affected eyes were complicated with hypertension, 10.3% (12 patients) suffered from diabetes; 95 eyes (81.2%) were phakic, and other 22 eyes (18.8%) were pseudophakic. Of the 117 patients, 49 (41.9%) had a history of smoking. The mean follow-up time was 15.8 ± 3.1 months.

Table 2
Demography and baseline characteristics

Variable	Values
No.	117
Male/ Female	62/55
Age(years)	62.9 ± 9.27
Hypertension, No. (%)	85 (72.6%)
Diabetes mellitus, No. (%)	12 (10.3%)
Lens status	
Phakic, No. (%)	95 (81.2%)
Pseudophakic, No. (%)	22 (18.8%)
Follow-up (months)	15.8 ± 3.1
Smoking history	49 (41.9%)
Severity of the baseline VH	3.12 ± 0.96
Note: Values are presented as the mean \pm standard deviation.	
Abbreviations: VH: vitreous hemorrhage.	

Of the 117 eyes, 33 had pure persistent VH (Grade I), 24 eyes had VH with EM without macular involvement (Grade IIa), 43 eyes had VH with EM with macular involvement (Grade IIb), and 17 eyes had VH with tractive RD (Grade III). There were no significant differences between the groups in terms of age, gender, diabetes, hypertension, lens status, smoking history, follow-up time, and severity of the baseline VH. Preoperative BCVA values (logMAR) were 2.57 ± 0.23 , 2.23 ± 0.91 , 2.13 ± 0.23 , and 2.06 ± 0.25 for the Grade I, Grade IIa, Grade IIb, and Grade III groups, respectively ($p > 0.05$). Vision was significantly improved to 0.73 ± 0.59 in the Grade I group, to 0.62 ± 0.43 in the Grade IIa group, to 0.86 ± 0.64 in the Grade IIb group, and to 0.64 ± 0.74 in the Grade III group after surgery. We found no significant difference in BCVA among the groups ($p > 0.05$), but there was a significant difference in the degree of vision improvement ($p < 0.05$). In comparing the groups, we found a significant difference in the degree of vision improvement between the Grade I group and the Grade IIb group ($p = 0.006$) and between the Grade IIa

group and the Grade IIb group ($p = 0.046$). The degree of vision improvement in the Grade IIb group was significantly less than that in the Grade I group and the Grade IIa group. During VT, 22 eyes were not found to have macular lesions; the number of eyes in the Grade I, Grade IIa, Grade IIb, and Grade III groups was 10, 8, 0, and 4, respectively ($p = 0.001$). At the last follow-up after surgery, the CFT was $227.91 \pm 87.01 \mu\text{m}$, $224.96 \pm 80.35 \mu\text{m}$, $242.47 \pm 95.35 \mu\text{m}$, and $222.47 \pm 72.14 \mu\text{m}$ in the Grade I, Grade IIa, Grade IIb, and Grade III groups, respectively. There was no significant difference in CFT among the groups ($p > 0.05$).

In total, transient elevation of intraocular pressure occurred in 13 eyes (11.1%) ($31.2 \pm 5.4 \text{ mmHg}$, ranging from 25.9–44.6 mmHg). All eyes recuperated after short-term treatment with topical glaucoma drugs (0.25% timolol alone or combined with 1% brinzolamide). No serious postoperative complications, such as RD or endophthalmitis, were found. Postoperatively, the number of patients in the Grade I, Grade IIa, Grade IIb, and Grade III groups whose ME recurred after 3 months was 0, 3, 6, and 1 ($p > 0.05$), respectively, and an IVR was administered. No eyes underwent repeated IVR. The percentage of patients in the Grade I, Grade IIa, Grade IIb, and Grade III groups needing further laser treatment after surgery was 0%, 8.3%, 16.3%, and 23.5%, respectively. There was no significant difference in the proportion of resolution among the groups ($p < 0.05$) (Table 3).

Table 3
Characteristics of Study Eyes in different grades (n = 117)

	I	IIa	IIb	III	p
No.	33	24	43	17	
Pre-BCVA (logMAR)	2.573 ± 0.226	2.225 ± 0.907	2.126 ± 0.234	2.059 ± 0.247	0.265*
End BCVA (logMAR)	0.727 ± 0.596	0.621 ± 0.431	0.856 ± 0.637	0.647 ± 0.737	0.381*
VA Improvement (logMAR)	1.876 ± 0.828	1.738 ± 0.737	1.270 ± 0.950	1.412 ± 1.169	0.039*
No macular involvement	10	8	0	4	0.01*
CFT	227.91 ± 87.009	224.96 ± 80.353	242.47 ± 95.353	222.47 ± 72.143	0.883*
re-LP	0	2 (8.3%)	7 (16.3%)	4 (23.5%)	0.045*
Anti-VEGF	0	3 (12.5%)	6 (14.0%)	1 (5.9%)	0.152*
Abbreviations: BCVA: best-corrected visual acuity; VA, visual acuity; logMAR: logarithm of the minimal angle of resolution; CFT: central foveal thickness; re-LP: re-requiring laser photocoagulation after surgery.					
Data are shown as means \pm SD.					
* Kruskal–Wallis test.					

Discussion

To our knowledge, this report is the first to propose a new grading system for BRVO with VH. With this new grading system, we can guide surgery according to the different grades. We discussed the postoperative effect of VT combined with laser photocoagulation for different severities of BRVO with VH. Vision acuity was improved in all groups, which is in agreement with the results obtained by Hidetaka Noma et al, who described cases of branch retinal vein occlusion[24]. This indicates that the majority of the eyes treated with VT combined with laser photocoagulation could maintain resolution of VH and improved VA without additional treatments for an extended period of time.

However, the quality of vision depends on the macula status. It is recognized that earlier intervention probably is favourable to later to prevent macular scarring from longstanding edema.[25] Researchers have different views on the effect of PPV with ILM peeling for ME associated with BRVO. Kang reported that only 48.5% of patients with ERM associated with BRVO experience visual improvement after surgery, and visual decrease was observed in 9.1%[26]. Mandelcorn [27] and Liang [28] reported that patients with ME secondary to RVO improved after PPV with ILM peeling. However, Radetzky et al. [29] reported no visual improvement in four patients after PPV and ILM peeling. In the present study, improved VA and reduced ME after VT were observed in the Grade I and Grade IIa groups. After VT, ME reappeared in three eyes, and CFT was reduced after IVR was performed once. We believe that the removal of the ILM is not necessary when there is no macular involvement.

Vision improvement was also observed in the Grade IIb group. ILM peeling may contribute to the complete removal of traction in the macular area[30]. ILM peeling also improves the oxygen supply to the retina, and VT may ameliorate retinal ischemia by allowing oxygenated fluid to circulate in the vitreous cavity [31]. Nevertheless, the degree of vision improvement in the eyes without macular membranes (the Grade I and Grade IIa groups) was much better than in the eyes with macular membranes (the Grade IIb group) in our study. Poor results may be due to the stretching effect of fibroblasts that deforms the macular structure, the underlying ischemic condition, or subtle trauma during removal of the ERM. Some study suggest that the percentage of eyes with secondary ERMs disrupted photoreceptor inner segment/outer segment (IS/OS) integrity (39.4%) and external limiting membrane (ELM) integrity (30.3%) were higher than those of idiopathic ERMs (15–28%)[32, 33]. In our study, vision improvement and ME reduction in the Grade IIb group suggest that ILM peeling is necessary for ERMs with macular involvement. Ota et al.[34] reported that substantial damage to the foveal photoreceptor layer was associated with poor VA prognosis. But Andreev et al. [35] think a high degree of photoreceptors resistance to long-term distraction by ERM, the retina in fovea was spontaneously restored after several years of relieving tractional deformation. Therefore, we believe ERM with macular involvement affects the results of surgical treatment, but we need more time to observe the development of vision.

Retinal neovascularization may lead to RD. One retrospective study reported an incidence of 3% retinal breaks in 230 eyes of 214 BRVO patients[36]. VT and laser photocoagulation combined with retinal reattachment does improve vision for VH with RD. Ikuno et al. [37] performed VT on 22 eyes with RD after

BRVO; 19 eyes (86%) attained total retinal reattachment and 13 eyes (59%) achieved VA better than 0.1 at the final examination. In our study, all eyes in the Grade III group attained total retinal reattachment, and 12 eyes (71%) experienced vision improvement. No statistical difference was found between the Grade III group and the other groups, which could be because the surgery has a high success rate and not all the eyes in the Grade III group had macular involvement.

In normal circumstances, retinal laser photocoagulation is the first-line therapy for neovascular complications of RVO [38]. In treating ME due to RVO, grid laser photocoagulation is generally considered to be the second-line therapy after anti-VEGF). Although VA results lag behind those for anti-VEGF therapy, laser photocoagulation remains a safe and effective therapy [39, 40]. The Branch Vein Occlusion Study (BVOS) is the largest multicenter, randomized, controlled clinical trial to evaluate the efficacy of grid-pattern laser photocoagulation to treat ME due to BRVO [13, 41, 42]. In the research, 65% of treated eyes gained improvement of two or more lines from baseline. Until recently, this study served as the gold standard treatment for ME associated with BRVO. In the past, laser photocoagulation was performed to prevent macular damage, and it was useful to reduce ME and intraretinal fluid collection. However, VH hinders examination and treatment with laser photocoagulation. In our study, all groups were treated with laser photocoagulation therapy in combination with VT. Only 10 eyes suffered from ME again after surgery.

The retinal non-perfusion ischemic area, which accelerates the increase in intraocular VEGF, is an important underlying cause of recurrent ME in BRVO [43]. FA cannot be performed before or during surgery, so an accurate assessment of the non-perfusion ischemic area is difficult. During the 12-month follow-up, 13 eyes were observed to have a non-perfusion ischemic area and needed further laser treatment; the percentage of patients in the Grade I, Grade IIa, Grade IIb, and Grade III groups was 0%, 8.3%, 16.3%, and 23.5%, respectively. This indicates that the eyes in the Grade I group could maintain improvement without additional treatments for an extended period of time. VH with ERM and RD has higher rates of re-requiring laser treatment; this may be due to hypoxia caused by ERM and RD and suggests that RD can lead to more serious hypoxia. Photoreceptor cells receive oxygen and nutritional support from the underlying retinal pigment epithelium. RD results in photoreceptor cell hypoxia and time-dependent death [44].

This study suggests that VT combined with laser photocoagulation is effective for BRVO with VH. Savastano et al. [45] reported that RD developed in 1.77% of the eyes that underwent 25-G high-speed PPV. A recent large-scale study reported that the incidence of postoperative endophthalmitis was low for PPV [46]. Except for the transient elevation of intraocular pressure that occurred in 13 eyes, no serious complications—such as RD or endophthalmitis—were found in this study.

There were some limitations to this study, such as the small sample size (especially eyes with RD), the retrospective study design, and the fact that we cannot eliminate the possibility that there may have been a bias in the choice of patients. In addition, the follow-up time was short. We need a longer time to observe the development of vision and the recovery of the macular structure. Moreover, although macular

status is better evaluated using OCT, we could not conduct this examination before surgery. Therefore, further validation of our classification scheme is warranted.

In conclusion, we proposed a new grading system for BRVO treated with PPV. BRVO with VH hindered timely and thorough evaluation and treatment. VT combined with laser photocoagulation for different severities of BRVO with VH has proven to be effective and safe. However, the VA improvement was significantly worse when EM had macular involvement(Grade IIb).

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets during and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

GMT and QTP contributed to research design, data collection and analysis, generating the figures, data interpretation as well as preparation of the manuscript. QTP contributed to data analysis and data interpretation and provided major revisions to the manuscript. XTH,CLZ,ZQG,XHC and LNG contributed to the data collection as well as the analysis of data. GMT contributed to the study design, study analysis, writing of the discussion and revision of the manuscript. All authors read and approved the final version of the manuscript.

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