Early vitrectomy in eyes with non-diabetic vitreous hemorrhage

Edward Foo*, Piergiacomo Grassi* (iD) and Kurt Spiteri-Cornish

Abstract

Background: Optimal management of non-diabetic vitreous hemorrhage (NDVH) is controversial, and reliability of B-scan ultrasonography in detecting retinal tears (RTs) has been reported to be highly variable by previous literature.

Objectives: To report outcomes of conservative versus surgical management of NDVH and reliability of B-scan ultrasonography in detecting RTs and rhegmatogenous retinal detachment (RRD).

Design: Retrospective observational single-center cohort study.

Methods: Ninety-six consecutive NDVH from 96 eyes (96 patients) with minimum follow-up duration of 12 months were included.

Results: Seventy-two eyes (75%) underwent early pars plana vitrectomy (PPV), 19 (20%) were managed conservatively and 5 (5%) underwent late PPV. Initial mean best corrected visual acuities (BCVAs) were 1.95 ± 1.19, 1.19 ± 1.38, and 1.14 ± 1.04 logMAR respectively, the difference was statistically significant ($p = 0.039$). Mean final BCVAs were 0.92 ± 1.19, 0.59 ± 0.87, and 1.25 ± 1.89 logMAR, respectively, the difference was not significant ($p = 0.447$). When comparing initial and final BCVAs, the difference was significant only in the early PPV group ($p = 0.00001$) and was not significant in the conservative group ($p = 0.066$) and in the late PPV group ($p = 0.46$). Complications included RRD ($n = 2$) and re-bleed in vitrectomized cavity ($n = 1$) in the early surgical group, need for additional laser or cryoretinopexy to RTs ($n = 2$), retinal detachment ($n = 1$), neovascular glaucoma ($n = 1$), persistent vitreous hemorrhage ($n = 2$) in the conservative group. B-scan ultrasound showed preoperative 11.53% sensitivity and a 60.0% positive predictive value for diagnosing retinal tears (RTs) in NDVH.

Conclusion: The benefit of early PPV in NDVH seems to outweigh the risks of surgery, especially in the context of low sensitivity of B-scan in identifying RTs, and significant improvement in final BCVA following surgery may occur. NDVH should be promptly referred to vitreoretinal services, as surgery may be a safer and more advisable option.

Keywords: conservative management, early vitrectomy, posterior vitreous detachment, vitrectomy, vitreous hemorrhage, ultrasonography

Correspondence to:
Kurt Spiteri-Cornish
Consultant Ophthalmic and Vitreoretinal Surgeon, Department of Ophthalmology, Royal Hallamshire Hospital, Sheffield University Hospitals NHS Foundation Trust, Glossop Road, Sheffield S10 2JF, UK.
kurt.spiteri-cornish@ nhs.net

Edward Foo
Department of Ophthalmology, Royal Hallamshire Hospital, Sheffield University Hospitals NHS Foundation Trust, Sheffield, UK

Piergiacomo Grassi
School of Medical Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Department of Vitreoretinal Surgery, Moorfields Eye Hospital NHS Foundation Trust, London, UK

Department of Ophthalmology, Royal Hallamshire Hospital, Sheffield University Hospitals NHS Foundation Trust, Sheffield, UK

*Both authors contributed equally to this paper and are both first authors.

Introduction

Posterior vitreous detachment (PVD) may be associated with retinal tears (RTs) and detachment, more so if associated with dense vitreous hemorrhage (VH).[1] It is a common presentation in the emergency setting, and the incidence is thought to be approximately 7 cases per 100,000 population.[2] VH has a high risk of proliferative vitreoretinopathy (PVR) and poor visual outcomes.[3]

Vitreoretinal surgery has become safer with lower complication subsequently early surgical intervention for VH has become more popular.[4] Early pars plana vitrectomy (PPV) can also help in reducing PVR rates.[3] Patients without RTs need to be identified, as false diagnoses can lead to unnecessary surgery. This is particularly relevant in non-progressive VH, where it gradually clears at a rate of 1%.[2] B-scan is an useful adjunct to diagnose RTs

and rhegmatogenous retinal detachment (RRD), however it has shown only a 44-62% positive predictive value for diagnosing RTs and is therefore not considered accurate.[5,6] Some literature suggested early vitrectomy regardless of B-scan findings when the fundus view is obscured and the patient is presumed to have a RT or RRD.[7,8]

The purpose of this study is to assess the outcomes of conservative management, early and late surgery in non-diabetic vitreous hemorrhage (NDVH) and related complications, and to assess the reliability of B-scan ultrasonography in detecting RTs and RRD to determine its usefulness in the outpatient clinical setting.

Methods

A retrospective observational single-center chart review study of 101 consecutive patients diagnosed with NDVH between 30 June 2017 and 26 July 2018, inclusive was carried out in agreement with the tenets of the Declaration of Helsinki. The Institutional Review Boards ruled that approval was not required for this study, given its retrospective nature. Patients were adult, in a vitreoretinal emergency setting verbal informed consent for research and written informed consent for treatment were obtained from all patients in adherence to the tenets of the Declaration of Helsinki and were recorded using the institutional ophthalmology electronic patient database (Medisoft Ltd, Leeds, UK). Patients were referred to the vitreoretinal service at the Royal Hallamshire Hospital, Sheffield, and had a minimum of 12 months follow-up. Electronic records of all patients diagnosed with NDVH at the participating center between 30 June 2017 and 26 July 2018 were retrospectively analyzed. Cases were identified using the institutional ophthalmology electronic patient database (Medisoft Ltd, Leeds, UK). Eyes with VH from penetrating eye injury and who had undergone previous vitrectomy were excluded from the analysis. Baseline characteristics recorded included referral source, presenting best corrected visual acuity (BCVA), clinical diagnosis and presenting B-scan findings, intraoperative diagnosis, intra- and post-operative complications and final BCVAs at last follow-up examination. BCVA was recorded at each visit and reported in Snellen Fraction, which was converted into logarithm of the minimal angle of resolution (logMAR) values for statistical analysis.

Descriptive statistics were calculated for all variables of interest. Mean and standard deviation values were calculated for continuous variables, while percentage was calculated for categorical variables. One-tailed student t-test and analysis of variance test were used to compare the statistically significant difference in continuous variables among all subgroups. Outcome measures included time to surgery, pre- and intraoperative diagnosis of VH cause, complications and visual outcome. B-scan ultrasonography findings were analyzed.

Results

One hundred and one eyes of 101 patients were diagnosed with NDVH between 30 June 2017 and 26 July 2018. Five patients were excluded as had undergone previous surgery ($n = 3$) or VH was secondary to open globe injury ($n = 2$). Ninety-six eyes of 96 patients were included, of whom 72 (75%) underwent early PPV, 19 (20%) were managed conservatively and 5 (5%) were initially managed conservatively and then underwent late PPV. Table 1 shows the range of diagnoses. Sources of referral were Emergency Eye Clinic (45 patients - 47%), Subspecialist clinics within the Trust (7 patients - 7%), District General Hospitals (20 patients - 21%) and unknown for 24 patients (25%). Mean BCVA at presentation was 1.75 ± 1.27 (20/1124 Snellen equivalent), and in the subgroup analysis was 1.95 ± 1.19 (20/1782) in the early PPV group, 1.19 ± 1.38 (20/309) in the conservative management group and 1.14 ± 1.04 (20/276) in the late PPV group, respectively. The difference among the three subgroups was statistically significant ($p = 0.039$, analysis of variance test). When comparing initial BCVAs between the group surgically managed with early PPV and the groups managed conservatively or with late PPV, the difference was statistically significant ($p = 0.005$, one-tailed Student t-test). The number of days between initial assessment and surgery ranged between 0 and 143 (mean 19.81 ± 34.97) in the early PPV group and between 89 and 181 (mean 126 ± 112.61) in the late PPV group. The difference was statistically significant ($p = 0.00001$, one-tailed Student t-test).

The final visual outcomes and the proportion of eyes managed conservatively or with non-surgical treatments and with surgery in each diagnostic group with the related complications are summarized in Tables 1 and 2, respectively. Thirty-seven patients (38.5% of our cohort) had a haemorrhagic PVD (hPVD) associated with an RT.

Table 1. Causes of vitreous hemorrhage (N = 96) in patients grouped as early vitrectomy, late vitrectomy, and conservative non-surgical group.

Cause	Surgical	%	Final BCVA (mean ± SD)	Non-surgical	%	Final BCVA (mean ± SD)	Late vitrectomy	%	Final BCVA (mean ± SD)	p
Haemorrhagic posterior vitreous detachment with retinal tear	28	29.2%	0.38 ± 0.61 [20/48 Snellen equivalent]	9	9.4%	0.21 ± 0.42, [20/32 Snellen equivalent]	1[a]	1.0%	0.78	p = 0.23
Haemorrhagic posterior vitreous detachment with avulsed vessels	2	2.1%	0.09 ± 0.09 [20/25 Snellen equivalent]							
Haemorrhagic posterior vitreous detachment without retinal tear	10	10.4%	0.88 ± 1.07, [20/152 Snellen equivalent]	1	1.0%	0.18 logMAR [20/30 Snellen equivalent]				
Retinal detachment	10	10.4%	1.08 ± 1.49, [20/240 Snellen equivalent]				1[a]	1.0%	0.78	
Retinal vein occlusion	4	4.2%	Mean 1.31 ± 1.05 [20/408 Snellen equivalent]	8	8.3%	2.07 ± 1.55 [20/2350 Snellen equivalent]	2	2.1%	1.74 ± 1.26 [20/1099 Snellen equivalent]	p = 0.742
Neovascular age-related macular degeneration	10	10.4%	2.07 ± 1.55 [20/2350 Snellen equivalent]	4	4.2%	0.69 ± 0.81 [20/98 Snellen equivalent]				p = 0.072
Retinal artery macroaneurysm	7	7.3%	0.93 ± 0.70 [20/170 Snellen equivalent]							
Malignant melanoma	1	1.0%	0.18 logMAR [20/30 Snellen equivalent]							
Terson's			0.0 logMAR [20/20 Snellen equivalent]	1	1.0%		1	1.0%		
Uveitis-glaucoma-hyphema syndrome			0.0 logMAR [20/20 Snellen equivalent]	1	1.0%		1	1.0%		
Total	72			24		5				
Total	96									

BCVA, best corrected visual acuity.

Late vitrectomies are those patients in the non-surgical group who later underwent pars plana vitrectomy.

[a]Same patient. One patient with haemorrhagic posterior vitreous detachment with a retinal tear who was originally managed conservatively progressed to a retinal detachment and required vitrectomy.

Table 2. Proportion of eyes (*n* = 96) managed conservatively or with surgery with the related complications.

Cause (*n* of eyes, %)	Management	*n* (%)	Complications (%)
Haemorrhagic posterior vitreous detachment with retinal tear (37, 38.5%).	Clinical diagnosis followed by non-surgical management (laser retinoperxy/cryoretinopexy)	9 (24%)	• hegmatogenous retinal detachment needing late surgery. (1 eye - 11%) • Further laser retinopexy (1 eye - 11%). • Further cryoretinopexy (1 eye - 11%).
	Clinical diagnosis followed by surgery	9 (24%)	
	Surgery needed for diagnosis	19 (52%)	
Haemorrhagic posterior vitreous detachment without retinal tear (13, 13.5%)	Clinical diagnosis and conservative management	1 (8%)	
	Surgery needed for diagnosis	12 (92%)	
Retinal detachment (10, 10.5%)	Clinical diagnosis followed by surgery	5 (50%)	
	Surgery needed for diagnosis	5 (50%)	• Rhegmatogenous retinal redetachment requiring second vitrectomy (2 eyes – 40%)
Retinal vein occlusion (12, 12.5%)	Clinical diagnosis followed by non-surgical management (laser panretinal photocoagulation – 4 eyes, or anti-vascular endothelial growth factor injections – 4 eyes)	8 (66.5%)	• Persistent vitreous hemorrhage requiring late surgery (2 eyes – 25%). • Neovascular glaucoma (1 eye – 12.5%)
	Surgery needed for diagnosis	4 (33.5%)	
Neovascular age-related macular degeneration (14, 14.5%)	Clinical diagnosis followed by non-surgical management (anti-vascular endothelial growth factor injections – 3 eyes, or observation – 1 eye)	4 (28.5%)	
	Surgery needed for diagnosis	10 (71.5%)	• Rebleeding in vitrectomized cavity (1 eye – 10%)
Retinal artery macroaneurysm (7, 7.5%)	Clinical diagnosis		
	Surgery needed for diagnosis	7 (100%)	
Malignant choroidal melanoma (1, 1%)	Surgery needed for diagnosis	1 (100%)	
Uveitis-glaucoma-hyphema syndrome (1, 1%)	Surgery needed for diagnosis	1 (100%)	
Terson's syndrome (1, 1%)	Surgery needed for diagnosis	1 (100%)	

Preoperative B-scan was highly suspicious of RT in three of these (8%), and this was confirmed intraoperatively. The difference in final BCVAs between surgical and conservative group was not statistically significant (*p* = 0.23, one-tailed Student *t*-test).

Thirteen patients (13.5%) had an hPVD not associated with RTs. An avulsed retinal vessel was the cause of NDVH in two of them. Final BCVA was 0.3 logMAR or better (20/40) for 6 out of the 12 operated patients, whereas the final BCVAs in the remaining six patients were limited

Table 3. Sensitivity (11.5%) and specificity (95.6%) of B-scan ultrasound in diagnosis of retinal tears.

	Gold standard positive	Gold standard negative	Total
Test positive	True positive [a], 3	False positive [c], 2	5
Test negative	False negative [b], 23	True negative [d], 43	66
Total	26	45	71

due to pre-existing ocular comorbidities (two eyes had previously had macula-off RRD, two had central retinal vein occlusion (CRVO), and two had age-related macular degeneration (AMD)).

Ten patients (10.4%) underwent surgery for NDVH associated with RRD. Five (50%) were correctly diagnosed clinically before surgery (four had adequate fundus view, one was diagnosed with macula-off RRD on B-scan), whereas the remaining five patients (50%) had no evidence of RRD on presenting B-scan but showed RD intra-operatively. The mean time between listing and surgery in these five patients ranged between 0 and 19 days (mean 3.2 ± 5.63 days). The difference between mean preoperative BCVA (2.27 ± 1.52, 20/3724) and mean final BCVA (1.08 ± 1.49, 20/240) was not statistically significant ($p = 0.075$, one-tailed Student t-test).

Twelve patients (12.5%) had ischaemic RVO. Four patients underwent early vitrectomy and pan-retinal photocoagulation (PRP), three having ischaemic branch retinal vein occlusion (iBRVO), and one having ischaemic CRVO (iCRVO), no postoperative complications were recorded. The remaining eight patients were managed conservatively (six with iCRVO, one with iBRVO, and one ischaemic hemi-retinal vein occlusion (iHRVO)). Of these eight patients, one patient had a re-bleed which cleared spontaneously with no further treatment required. One patient developed intractable neovascular glaucoma and had final BCVA 5 logMAR. The difference in the final BCVAs between early PPV, conservative and late PPV groups was not statistically significant ($p = 0.742$, analysis of variance test). The difference was not statistically significant also when comparing final BCVAs between the iRVO group which underwent early PPV with the iRVO group managed conservatively and with late PPV ($p = 0.230$, one-tailed Student t-test).

Fourteen patients (14.6%) were diagnosed with VH secondary to neovascular AMD (nAMD).

Two out of the four patients managed conservatively responded to treatment with intravitreal anti-VEGF injections, whereas one had a pre-existing macular disciform scar and was not eligible for anti-VEGF injections. Preoperative B-scan had been inconclusive to identify the source of NDVH in the 10 operated patients, two of them had bleeding secondary to eccentric disciform and were discharged after surgery. The remaining eight patients were subsequently referred to the Medical Retina service for intravitreal anti-VEGF treatment. The difference in final BCVAs between surgical and conservative group was not statistically significant ($p = 0.072$, one-tailed Student t-test).

Retinal artery macroaneurysm (RAMA) was intraoperatively found to be the cause of NDVH in 7 patients (7.3% of our cohort of patients), preoperative clinical examination and B-scan had been inconclusive to identify the source of NDVH and early PPV + endolaser were carried out in all seven patients. The difference between mean preoperative BCVA (1.79 ± 1.10, 20/1233) and mean final BCVA (0.93 ± 0.70, 20/170) was not statistically significant ($p = 0.065$, one-tailed Student t-test).

One patient (1%) with dense NDVH and presenting BCVA of 3 logMAR was diagnosed with a choroidal lesion on B-scan, underwent early PPV and was subsequently diagnosed with choroidal melanoma and referred to the Ocular Oncology Service with postoperative BCVA of 0.18 logMAR (20/30).

One patient (1%) with Uveitis-Glaucoma-Hyphema syndrome and one with Terson's syndrome underwent late vitrectomy for persistent NDVH. Preoperative BCVAs were 1.47 logMAR (20/590) and 0.48 logMAR (20/60), respectively, final BCVAs were 0.0 logMAR (20/20) in both cases.

Mean final BCVA was 0.88 ± 1.19 (20/152), and in the subgroup analysis was 0.92 ± 1.19 (20/166)

Table 4. The role of early vitrectomy in diagnosis and treatment.

Cause of hemorrhage	Surgery essential in diagnosis (*n/N*, %)	Surgery essential in management (*n/N*, %)
Haemorrhagic posterior vitreous detachment with retinal tear	19/37 (51.4)	29/37 (78.4)
Haemorrhagic posterior vitreous detachment with avulsed vessel	2/2 (100)	2/2 (100)
Haemorrhagic posterior vitreous detachment with no tear	0/11[a] (0)	0/11 (0)
Retinal detachment	5/10 (50)	10/10 (100)
Retinal vein occlusion	4/12 (33.3)	6/12[b] (50.0)
Neovascular age-related macular degeneration	10/13 (69.2)	8/13 (53.8)
Retinal artery macroaneurysm	7/7 (100)	7/7[c]
Choroidal malignant melanoma	1/1 (100)	1/1 (100)
Uveitis glaucoma hyphaema syndrome	0/1 (0)	1/1 (100)
Terson's syndrome	0/1 (0)	1/1 (100)
Post-intravitreal injection	0/1 (0)	0/1 (0)
Total	48/96 (50.0)	58/96 (60.4)

[a]Surgery was not essential to diagnose haemorrhagic PVD without tear but was important in excluding any tear or avulsed vessel.
[b]One patient would have benefited from surgery, but neovascularization was untreated and ended up being end-stage rubeosis and glaucoma.
[c]All patients with RAMA underwent early vitrectomy. If observed, the patients whose hemorrhage cleared spontaneously may not have required surgery.

in the early PPV group, 0.59 ± 0.87 (20/78) in the conservative management group and 1.25 ± 1.89 (20/356) in the late PPV group, respectively. The difference was not statistically significant ($p = 0.447$, analysis of variance test), also when comparing final BCVAs between the group which underwent early PPV with the groups managed conservatively and with late PPV ($p = 0.252$, one-tailed Student *t*-test). When comparing initial and final BCVA at last follow-up examination, the difference was statistically significant only in the early PPV group ($p = 0.00001$, one-tailed Student *t*-test), whereas was not significant in the conservative group ($p = 0.066$, one-tailed Student *t*-test) and in the late PPV group ($p = 0.46$, one-tailed Student *t*-test).

B-scan ultrasound was performed in 71 out of 96 patients (74%) with NDVH. Sensitivity and specificity of B-scan ultrasonography in the diagnosis of RTs is summarized in Table 3. RTs were missed at preoperative B-scan in 23 patients and were diagnosed intraoperatively. B-scan had a preoperative

11.53% (2.45%–30.15%, 95% confidence interval) sensitivity and a 60.0% (21.13%–89.36%, 95% confidence interval) positive-predictive value for diagnosing RTs in NDVH. RRDs were not detected at preoperative B-scan in five out of six cases, preoperative sensitivity of B-scan in detecting RRD measuring 17%. The role of early PPV in the diagnosis (50.0%) and management (60.4%) of cases of NDVH is summarized in Table 4.

Discussion
The management of NDVH can be controversial. Traditionally, these patients are observed in an outpatient setting with serial ultrasound scans.[9] Treatment is then undertaken once the view becomes clear enough to make a diagnosis (such as in the case of RVO or RT). PPV is an established treatment for eyes with RRD (including challenging cases complicated by PVR), with vitreoretinal interface syndrome and with aqueous misdirection,[10–12] but less so for NDVHs.[13–15] Surgical intervention is reserved for patients

where RT or RRD is diagnosed on B-scan ultrasonography. To our knowledge, our study is one of the largest observational case series of NDVH to date, the aim of which was to assess outcome of conservative, early and late surgery in this group of patients.

There are no randomized controlled trials to date comparing surgical against non-surgical intervention in NDVH. However, previous literature suggested that early PPV will reduce the overall RRD rate in this group of patients.[9]

In this series, the choice between surgical and non-surgical management depended on diagnosis and on the assessment of the vitreoretinal surgeons involved, and NDVH was caused by PVD in almost two-thirds of the patients (62.5%, $n = 60$). Surgical intervention was required in 75.7% ($n = 28$) of patients who had hPVD associated with RT. B-scan ultrasound detected RTs in only three cases (8%) and was found to be sensitive in only 11.5% of cases (Table 3). These results seem to support the role of early PPV in fundus-obscuring NDVH when the cause is uncertain. Furthermore, a clinical diagnosis of one or more RTs does not exclude the possibility of multiple RTs. In our nine patients with hPVD and RTs managed conservatively, additional treatment was required in three of them (33.3%).

In absence of any obvious cause, fundus-obscuring NDVH caused by an hPVD should be suspected, and a high index of suspicion of RTs should be adopted. If patients were managed conservatively, a follow-up on at least a two-weekly basis was required to repeat indirect fundoscopy with scleral indentation. This should be considered for every patient in which conservative management is chosen.

In our series, five patients had no initial evidence of RD on B-scan, underwent late surgery (average 8 days after first assessment, range 1–19) which showed evidence of RD. Four out of them may have progressed from an undetected RT to RRD. This highlights the importance of expedited surgery in dense fundus-obscuring NDVH, where rates of up to 67% for RTs and 39% for RRDs have been previously reported.[16]

Thirteen patients in our study had hPVD but no RT. The natural history is likely that of spontaneous resolution with no need for surgical intervention, if observation had been chosen. However,

surgery provided rapid visual rehabilitation and effective exclusion of retinal pathologies in the operated patients, thus avoiding repeated outpatient B-scan assessment and scleral indentation. Furthermore, if observed, a proportion of these patients may have required later surgery for persistent VH (especially in the subset with avulsed retinal vessel) or symptomatic floaters from chronic haemorrhagic debris.[17–19]

In our study, VH in 36 patients (37.5%) was not caused by PVD, the main causes of bleeding being nAMD ($n = 14$), iRVO ($n = 12$), and RAMA ($n = 7$). Early PPV is important to diagnose patients with iRVO. Left untreated, this can lead to VH (as in our study) and potentially tractional RD or rubeosis and neovascular glaucoma.[20]

The diagnosis of nAMD may be challenging if the macula is not visible on examination. Only two patients in our series had a preoperative diagnosis of nAMD and anti-VEGF treatment started without the need for vitrectomy, whereas one patient had a previously documented macular disciform scar thus surgery and anti-VEGF treatment were not required. Preoperative B-scan ultrasound was suggestive of submacular hemorrhage which was confirmed intraoperatively, and early PPV with subretinal injection of tissue plasminogen activator and gas displacement were performed. The remaining patients were intraoperatively diagnosed with nAMD, and early anti-VEGF treatment was arranged postoperatively. If observation had been chosen, a delayed diagnosis of nAMD would have been likely with potential permanent central visual impairment.[21]

Our series did not highlight significant differences in final BCVAs between the early PPV group and the conservative/late PPV groups and in any of the diagnostic subgroups, in agreement with previous literature.[22] Nevertheless, our results suggest that significant improvements in final BCVA may be expected in the group treated with early PPV ($p = 0.00001$).

Surgical complications are the main argument against early PPV. In our cohort, 4.1% in the early PPV group had complications directly related to surgery. However, in the non-surgical group, the need for subsequent intervention or complications occurred in 25% (6/24) of cases. There was no statistically significant improvement in final BCVA in the conservative ($p = 0.066$) and late PPV group ($p = 0.46$). This is explained by the underlying

cause of the hemorrhage rather than the presence or timing of surgery.

Our preoperative B-scan ultrasonography showed overall low sensitivity in detecting RTs in NDVH (11.5%). However, 26% of our cases did not receive a formal B-scan at presentation (in most cases due to obvious clinical diagnosis). These data suggest that although B-scan ultrasonography is an important ancillary test in fundus-obscuring NDVH, the lack of clinical signs such as RD or RT should not be relied on for clinical decision-making or delaying surgery.

The management of NDVH remains, to some extent, controversial. If surgery is discussed, all patients should be counseled about possible post-operative surgical complications. However, our results seem to suggest that the potential benefits of early surgery (significant improvement in BCVA, quicker visual rehabilitation, earlier treatment of underlying cause, and prevention of RD) may outweigh surgical risks.

This study has various limitations, including its retrospective design, which may have caused ascertainment bias, the limited number of cases in the conservative and late PPV group, the single-center setting, and the fact that cases were managed by different vitreoretinal surgeons who will have different clinical approach and surgical thresholds for non-surgical or surgical management. Moreover, this was an observational study with no randomization or control over interventions, and the conversion of BCVA from Snellen to logMAR could also result in inaccuracies as the relationships between the two measures are not directly proportional. We did not seek to risk stratify our patients as it is beyond the scope of our study and would require a higher number of patients to bear significance. Furthermore, the majority of patients in this series underwent surgery thus we could not confirm an increased predisposition to PVR in patients in the non-surgical group who developed RRD, which would require a randomized controlled trial with larger number of cases.

Conclusion
Our study suggests that the benefit of early referral and vitrectomy in patients with NDVH seem to outweigh the risks of surgery, especially in the context of low sensitivity of B-scan ultrasounds in identifying RTs, as well as significant improvement in final BCVA following surgery. We believe that the main advantages of early PPV over observation are the possibility to obtain an early correct diagnosis and management (which can be sometimes essential for patients' survival if intraocular tumors are suspected, as shown in the case with choroidal melanoma). In fact, PPV was essential for the correct diagnosis in over half of cases with hPVD with RT and with nAMD, in half of cases with RRD, and was required in the management of over half cases of hPVD with RT and with nAMD, in half of the cases with RVO and in all cases with RRD, RAMA, UGH, and Terson's Syndrome. Other advantages include lower proportion of patients requiring subsequent intervention (4.1% *vs* 25%), earlier treatment of underlying cause, prevention of RRD and the quicker visual rehabilitation compared to the conservative group. Also, the reduced need of multiple follow-up appointments could be particularly advantageous now during COVID-19 pandemic, when contact time between healthcare professionals and patients needs to be reduced and when significant changes to the vitreoretinal practice of a busy tertiary referral centers in response to COVID-19 restrictions are expected.[23,24] This study suggests that fundus-obscuring NDVH should be promptly referred to Vitreoretinal services, as surgery may be a safer and more advisable option in such conditions.

ORCID iD
Piergiacomo Grassi   (iD)   https://orcid.org/0000-0001-8741-5919

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