Predictors of Neovascular Glaucoma in Central Retinal Vein Occlusion

ANDREW J. RONG, SWARUP S. SWAMINATHAN, ELIZABETH A. VANNER, AND RICHARD K. PARRISH, II

• PURPOSE: To determine the risk factors for development of neovascular glaucoma (NVG) in patients after an acute central retinal vein occlusion (CRVO).
• DESIGN: Retrospective cohort study.
• METHODS: Review of medical records of 646 patients with a diagnosis of CRVO between 2013 and 2017 at the Bascom Palmer Eye Institute. Inclusion criteria: (1) CRVO onset to presentation <90 days; (2) absence of anterior segment neovascularization on presentation; (3) no intravitreal anti–vascular endothelial growth factor (anti-VEGF) injection before presentation. Patients meeting inclusion criteria were screened for potential risk factors for development of NVG. Risk of developing NVG was assessed with Kaplan-Meier survival analysis and Cox proportional hazards models.
• RESULTS: Thirteen of 98 patients (13%) who met inclusion criteria developed NVG. The mean adjusted time to NVG diagnosis from onset of CRVO-related symptoms was 212 days. Patients presenting with a worse initial visual acuity ($P = .034$), a relative afferent pupillary defect (RAPD) ($P = .002$), or a history of systemic hypertension ($P = .026$) had an increased risk of NVG compared to those who did not. Age, body mass index, history of glaucoma, history of diabetes, and central retinal thickness were not significantly associated with development of NVG.
• CONCLUSIONS: Risk factors for NVG development included history of systemic hypertension, worse visual acuity on presentation, and RAPD on presentation. Patients presenting with these findings should be followed at closer intervals and informed of the greater risk for neovascularization. Intravitreal anti-VEGF therapy delayed but did not prevent NVG. (Am J Ophthalmol 2019;204:62–69. © 2019 Elsevier Inc. All rights reserved.)

DESPITE NUMEROUS NATURAL HISTORY STUDIES, the ability to predict which patients will develop neovascular glaucoma (NVG) after a central retinal vein occlusion (CRVO) remains limited.[1,2] CRVO has been classified into ischemic and nonischemic variants depending on the area of retinal ischemia.[1-3] The more common nonischemic variant occurs in 81% of cases and poses little risk for neovascular complications.[2,4-6] The criteria to separate ischemic from nonischemic CRVO has been a topic of debate.[1,2,7] In the Central Vein Occlusion Study (CVOS), an ischemic CRVO was classified as greater or equal to 10 disc diameter areas of nonperfusion observed on fluorescein angiography (FA). Neovascular glaucoma developed in 20% of patients with ischemic CRVO as defined by this criteria.[1]

Fundus findings have previously been reported to lack sensitivity in identifying ischemic CRVO, and FA is of limited utility in one third of patients who present with dense intraretinal hemorrhage.[2,3,8] Realizing the limitations of FA in patients with acute CRVO, Hayreh and associates studied multiple clinical factors such as relative afferent pupillary defect (RAPD), visual acuity (VA), visual fields, and electroretinograms (ERG) to classify ischemic CRVO.[2] This classification was recently used in the Rubeosis Anti-VEGF (RAVE) Trial to assess the ability of chronic vascular endothelial growth factor (VEGF) blockade in patients with ischemic CRVO for prevention of neovascular complications.[9] Although ERG and kinetic visual field testing are performed routinely in large academic centers, many practices lack this modality to assess acute CRVO patients. Without proper risk stratification, patients presenting with CRVO remain difficult to assess for the risk of NVG. The goal of this study is to analyze the characteristics of patients presenting with CRVO, identify risk factors for the subsequent development of neovascular glaucoma, and determine who might benefit from early intervention to prevent neovascular glaucoma in high-risk patients.

PATIENTS AND METHODS

WE IDENTIFIED PATIENTS PRESENTING TO THE BASCOM Palmer Eye Institute/Anne Bates Leach Eye Hospital (emergency department and outpatient visits) between January 2013 and December 2017 with an ICD-9 or ICD-10 diagnosis of CRVO. After screening, each patient's clinical records starting from the date of CRVO diagnosis to the most recent clinical visit were carefully reviewed. All charts were reviewed by 2 ophthalmologists (A.J.R.

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From the Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, USA (A.J.R., E.A.V., R.K.P.); and Department of Ophthalmology, Duke Eye Center, Duke University, Durham, North Carolina, USA (S.S.S.).
Inquiries to Andrew J. Rong, Bascom Palmer Eye Institute, 900 NW 17th St, Miami, FL 33136, USA; e-mail: Ajr211@med.miami.edu

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TABLE 1. Clinical Characteristics of the 98 Patients Meeting Inclusion Criteria

Categorical Variables	Value	All Patients (N = 98)	Non-neovascular (N = 85, 86.7%)	Neovascular (N = 13, 13.3%)
Sex	Female	47 (48%)	40 (47%)	7 (53.8%)
	Male	51 (52%)	45 (53%)	6 (46.2%)
Age ≤50 years	No	78 (79.6%)	65 (76.4%)	13 (100%)
	Yes	20 (20.4%)	20 (23.6%)	0 (0%)
Afferent pupillary defect	No	84 (85.7%)	75 (88.3%)	9 (69.2%)
	Yes	14 (14.3%)	10 (11.7%)	4 (30.8%)
Anti-VEGF at first visit?	No	36 (36.7%)	30 (35.2%)	6 (46.2%)
	Yes	62 (63.3%)	55 (64.8%)	7 (53.8%)
History of primary open-angle glaucoma	No	74 (75.5%)	65 (76.4%)	9 (69.2%)
	Yes	24 (24.4%)	20 (23.5%)	4 (30.8%)
History of hypertension	No	32 (32.7%)	30 (35.2%)	2 (15.4%)
	Yes	66 (67.4%)	55 (64.8%)	11 (84.6%)
History of diabetes	No	65 (66.3%)	58 (68.2%)	7 (53.8%)
	Yes	33 (33.7%)	27 (31.8%)	6 (46.2%)
DR	No	21 (63.6%)	17 (63%)	4 (66.6%)
	Yes	12 (36.4%)	10 (37%)	2 (33.3%)
Degree of DR	Mild	4 (33.3%)	4 (40%)	0 (0%)
	Moderate	4 (33.3%)	2 (20%)	2 (100%)
	Severe	1 (8.3%)	1 (10%)	0 (0%)
	PDR	3 (25%)	3 (30%)	0 (0%)
Macular edema assessment	None	31 (31.6%)	27 (31.7%)	4 (30%)
	OCT	53 (54.1%)	45 (52.9%)	8 (61.5%)
	Clinical examination	14 (14.3%)	13 (15.4%)	1 (7.7%)

Continuous Variables	Mean	SD	Mean	SD	Mean	SD
BMI	28.5	(4.9)	28.7	(4.8)	27.0	(5.8)
Diastolic blood pressure (mm Hg)	79.1	(12.5)	79.1	(11.9)	79.3	(17.3)
Systolic blood pressure (mm Hg)	145.0	(24.9)	145.7	(24.9)	139.4	(24.9)
Age at first visit (years)	63.7	(15.3)	62.8	(15.7)	69.3	(11.1)
IOP at first visit (mm Hg)	16.9	(4.1)	16.7	(3.8)	18.3	(5.4)
LogMAR VA at first visit	0.93	(0.62)	0.90	(0.62)	1.14	(0.6)
OCT thickness at first visit (μm)	631.8	(238.1)	631.6	(221.4)	632.6	(334.5)

BMI = body mass index; DR = diabetic retinopathy; IOP = intraocular pressure; OCT = optical coherence tomography; PDR = proliferative diabetic retinopathy; VA = visual acuity; VEGF = vascular endothelial growth factor.

and S.S.S.) using a standardized protocol to ensure an accurate CRVO diagnosis that was consistent with the ICD coding. All reasonable means were used to ensure that the data were reliable and any patients with inadequate or unreliable information were excluded from the study. The Institutional Review Board at the University of Miami School of Medicine approved this protocol before beginning the study. This study followed the tenets of the Declaration of Helsinki.

• **INCLUSION AND EXCLUSION CRITERIA:** Only patients with clinical findings consistent with a diagnosis of CRVO (acute vision loss, diffuse intraretinal hemorrhage, venous tortuosity) were included in the study. We limited inclusion to patients presenting within the first 90 days of symptom onset as defined by day of subjective VA decrease.

We excluded patients with a hemiretinal vein occlusion, branch retinal vein occlusion, or any retinopathy that mimicked a CRVO; patients who received any form of intravitreal anti-VEGF or corticosteroid treatment prior to presentations; patients who exhibited any form of neovascularization of the iris (NVI) or neovascularization of the angle (NVA) at time of presentation; patients younger than 18 years of age; patients lost to follow-up after their initial visit; and patients presenting with acute bilateral CRVOs.

• **DATA COLLECTION:** For the baseline visit, we recorded the date of presentation, probable estimated date of CRVO (as determined by subtracting the subjective symptom onset from the date of clinical presentation), age, sex, body mass index, history of glaucoma, history of systemic

TABLE 2. Categorical Variables for Risk of Neovascular Glaucoma

Categorical Variables	Value With Greater Hazard	Kaplan-Meier *P* Value	Cox Regression *P* Value	HR	HR 95% CI Low	HR 95% CI High
Sex	Female	.4842	.4868	0.68	0.22	2.04
Afferent pupillary defect	Yes	.0022[a]	.0068[a]	6.04	1.64	22.19
Anti-VEGF at first visit?	No	.4506	.4536	0.65	0.21	2.00
History of POAG	No	.9506	.9509	0.96	0.29	3.18
History of hypertension	Yes	.0255[b]	.0406[b]	5.05	1.07	23.78
History of diabetes	Yes	.3788	.3833	1.63	0.54	4.87
DR	No	.5682	.5717	0.61	0.11	3.45
Degree of DR	Moderate	.1231	–[c]			
Macular edema assessment		.5985				
Compare no macular edema to OCT	OCT		.3243	1.99	0.51	7.83
Compare no macular edema to clinical examination	Clinical examination		.7575	1.44	0.14	14.65

CI = confidence interval; DR = diabetic retinopathy; HR = hazard ratio; OCT = optical coherence tomography; POAG = primary open-angle glaucoma; VEGF = vascular endothelial growth factor.

[a] $P < .01$.

[b] $P < .05$.

[c] No Cox regression was possible owing to an absence of failures (eyes with a neovascular event) in 1 group.

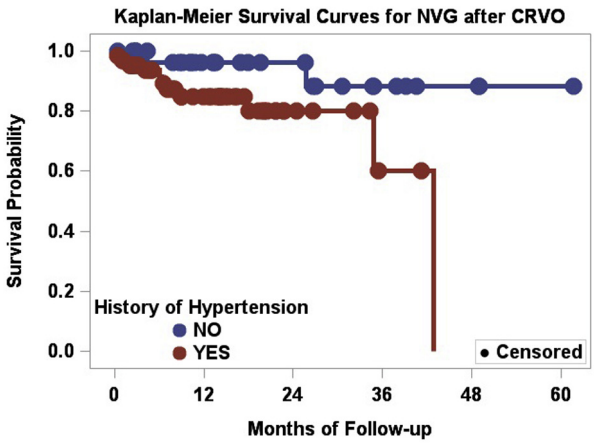

FIGURE 1. Kaplan-Meier survival curves for neovascular glaucoma after central retinal vein occlusion; systemic hypertension as a risk factor.

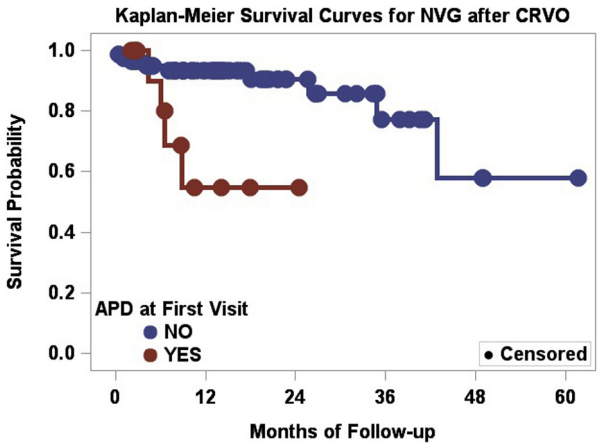

FIGURE 2. Kaplan-Meier survival curves for neovascular glaucoma after central retinal vein occlusion; relative afferent pupillary defect (APD) as a risk factor.

hypertension, history of diabetes, and degree of diabetic retinopathy, if present.

For the baseline visit on presentation and for an additional 3 clinical visits, we assessed the following variables at each visit: VA, intraocular pressure (IOP), RAPD, macular edema, central retinal thickness by optical coherence tomography (OCT), and whether an intravitreal anti-VEGF injection was administered at that visit. Retinal thickness was measured with either Cirrus HD-OCT (Carl Zeiss Meditec, Inc, Oberkochen, Germany) or Spectralis HRA+OCT (Heidelberg Engineering, Inc, Heidelberg, Germany) instruments.

If a patient was noted to have NVI/NVA and an elevated IOP >22 mm Hg, it was recorded as an NVG event. We did not record posterior segment neovascularization as a neovascular event in this study.

• **STATISTICAL ANALYSIS:** Categorical variables are presented as frequencies and percentages, and continuous variables are presented as means and standard deviations. Time to the occurrence of neovascular glaucoma was assessed with Kaplan-Meier survival analysis and Cox proportional hazards regression. All analyses were done using SAS version 9.4 (SAS Institute, Cary, North Carolina, USA). A P value ≤ .05 was considered statistically significant.

TABLE 3. Continuous Variables for Risk of Neovascular Glaucoma

Continuous Variables	Values	HR Units	Cox Regression *P* Value	HR	HR 95% CI Low	HR 95% CI High
BMI	Lower	5 units	.3790	0.69	0.31	1.57
Weight	Lower	10 pounds	.3427	0.91	0.75	1.11
Height	Lower	3 inches	.7090	0.90	0.51	1.58
Diastolic blood pressure	Lower	5 mm Hg	.7934	0.97	0.74	1.26
Systolic blood pressure	Lower	5 mm Hg	.4680	0.95	0.82	1.10
Age at first visit	Higher	10 years	.1333	1.35	0.91	2.00
IOP at first visit	Higher	5 mm Hg	.0901	1.75	0.92	3.35
LogMAR VA at first visit	Higher (worse)	0.5 units	.0342[a]	1.70	1.04	2.77
OCT thickness at first visit	Lower	250 μm	.8365	1.09	0.50	2.37

BMI = body mass index; CI = confidence interval; HR = hazard ratio; IOP = intraocular pressure; OCT = optical coherence tomography; VA = visual acuity.
[a]$P < .05$.

RESULTS

WE EXAMINED THE MEDICAL RECORDS OF 646 PATIENTS over the 5-year period and 98 patients met the study inclusion criteria. Among the 646 patients, the majority of patients were excluded because of CRVO symptoms greater than 90 days (or without a clear date of initial symptomatic onset) or because of anti-VEGF injections by an outside provider prior to presentation. After review through the remaining charts, an additional 17 patients were excluded owing to lack of follow-up after their initial visit.

Of the remaining 98 patients, the mean follow-up time was 17 months (range 0.4–66.6 months). Of note, all patients who developed anterior segment neovascularization (NVI or NVA) in our data set had pressures above 22 mm Hg and met our criteria for NVG. Clinical characteristics are presented in Table 1.

• **DEVELOPMENT OF NEOVASCULAR GLAUCOMA:** The cumulative probability of developing NVG was 13% (n = 13). The mean time to development of NVG was 421 days (median = 198 days; range 21-1286 days). When accounting for the last intravitreal anti-VEGF injection given during the observation period (when the stimulus for neovascularization may be minimized and the day counter reset to day 0),[10] the mean time to development of NVG was 212 days after last anti-VEGF injection (median = 150 days; range 21-990 days).

At the onset of NVG, the mean VA was count fingers, with a mean IOP of 41.9 ± 10.3 mm Hg. Nine of 13 patients (69%) underwent subsequent panretinal photocoagulation (PRP). Eight of 13 patients (62%) underwent subsequent incisional surgery, with either valved or nonvalved glaucoma drainage devices (n = 4 for each respective group). One patient underwent cyclophotocoagulation. All but the one patient who underwent cyclophotocoagulation had an anti-VEGF injection at the time of NVG diagnosis. After medical and surgical intervention to control IOP, the mean VA remained count fingers with a mean IOP of 22.5 ± 11.9 mm Hg at an average follow-up of 25 ± 13 months. For the non-NVG cohort, the mean VA was 20/90 with a mean IOP of 16.4 ± 4.9 mm Hg at an average follow-up of 15 ± 12 months.

• **CLINICAL FINDINGS:** Sex, body mass index, systolic or diastolic blood pressure at initial visit, history of diabetes, degree of diabetic retinopathy, and anti-VEGF injection at first visit were not significantly different in patients who did and did not develop NVG (Table 2). Of the patients who developed NVG, the average number of intravitreal anti-VEGF injections performed was 4 (range 0-18). Of the 27 patients with a history of glaucoma, 24 patients had a history of primary open-angle glaucoma (POAG), 2 patients had unspecified glaucoma (undefined per chart review), and 1 patient had a history of chronic angle closure glaucoma (CACG). The 1 patient with CACG had previous glaucoma shunt surgery before presenting with a CRVO; this patient did not develop NVI/NVA. Neither history of glaucoma (POAG, unspecified, CACG) nor history of POAG alone were significantly different among patients who did and did not develop NVG.

A history of systemic hypertension ($P = .026$) was associated with the development of NVG (Figure 1). Although age on presentation for the NVG group vs non-NVG group differed (69 ± 11 years and 63 ± 16 years, respectively), it was not found to be a significant risk factor ($P = .133$). None of the patients younger than 50 years of age developed NVG. When patients were arbitrarily divided into older (n = 78) vs younger (n = 20) than 50 years of age, this relationship was nonsignificant ($P = .053$).

• **EXAMINATION FINDINGS:** The mean baseline VA (Snellen equivalent) on presentation for the entire cohort was 20/170. For the non-NVG group, the mean initial VA

was 20/160, while those who developed NVG had a mean VA of 20/275. There was an increased risk of NVG for every 0.5 logMAR VA worse a patient presented with (hazard ratio [HR], 1.70; 95% confidence interval, 1.04–2.77; $P = .034$). Of the 25 eyes with an initial VA 20/50 or better, only 1 eye had NVG (representing 4% of eyes with initial VA of 20/50 or better and 7.7% of the 13 eyes with NVG), vs 24 eyes that did not (representing 96% of eyes with initial VA of 20/50 and 28.2% of the 85 eyes without NVG).

The mean IOP on presentation for the entire cohort was 17.0 ± 4.1 mm Hg. For those who did not develop NVG, the mean IOP was 16.7 ± 3.8 mm Hg, while the mean IOP on presentation for those who developed NVG was 18.4 ± 5.4 mm Hg. Patients presenting with elevated IOP were not found to be at increased risk of developing NVG ($P = .090$).

The risk of developing NVG was significantly greater in patients who had an initial RAPD ($P = .002$) (Figure 2). Patients presenting with an RAPD in the setting of an acute CRVO had an elevated HR of 6.04 and relative risk increase of 2.15 (Tables 2 and 3).

• **MACULAR EDEMA AND OPTICAL COHERENCE TOMOGRAPHY FINDINGS:** Sixty seven patients (68%) had macular edema on initial presentation either by clinical examination (n = 14) or by OCT imaging (n = 53). The presence of macular edema on presentation was not significantly associated with future development of NVG ($P = .5985$). Among patients who received an OCT on presentation (n = 54), the mean central retinal thickness was 632 ± 238 μm. When subdivided into NVG and non-NVG patients, mean central retinal thickness was 632 ± 221 μm and 632 ± 335 μm, respectively. Increased central retinal thickness on presentation was not found to be a significant risk factor ($P = .8365$).

DISCUSSION

COMPARISON OF THE INCIDENCE OF NEOVASCULAR GLAUcoma in our study vs other studies is difficult given the variability of methods and inclusion criteria among studies.[6,7,11,12] In studies where the population was limited to ischemic CRVOs, the incidence of NVG was 22%–50%,[6,7,9,12-14] and in studies where ischemic status was undefined, the incidence of NVG was 5%–21%.[3,6,15,16] We included all CRVO subtypes presenting within 3 months of symptom onset with an NVG incidence rate of 13%.

We determined that systemic hypertension was associated with NVG; this has not been described in previous studies.[7,12,16] One possible explanation may be chronic changes in the retinal arteriolar vasculature from hypertensive retinopathy.[17] With these changes, the retinal vasculature would be less likely to adapt to acute ischemic events, such as a CRVO, thereby increasing the risk of neovascularization.[11,16] In our series, none of the patients younger than 50 years of age developed NVG. Those with younger age may have a more robust and healthy vasculature, protecting them from the effects of retinal ischemia. If this hypothesis of chronic damage to vasculature were true, however, then one would expect patients with diabetes and especially those with severe nonproliferative or proliferative diabetic retinopathy to be at equal if not higher risk for NVG. We did not observe this association, although the power to detect this was low, so this explanation does not fully account for the association between systemic hypertension and NVG.

Certain clinical signs, such as worse VA and RAPD on CRVO presentation, are associated with increased risk of NVG. Notably from our results, it is difficult to place an upper VA threshold on which to base NVG risk. A previous study reported that VA better than 20/400 was indicative of a nonischemic CRVO, with these eyes less likely to develop NVG.[2] However, approximately half of our patients (6/13) who developed NVG presented with VA better than 20/400. We found that of the 25 eyes with an initial VA of 20/50 or better, only 1 eye developed NVG. This suggests that patients with a VA 20/50 or better are at a lower risk for NVG. Additionally, we found that for every 0.5 logMAR VA worse on presentation, there was a corresponding 1.7 times increased risk of developing NVG (Table 3). Our findings are consistent with the results of the CVOS group, where a 3-line VA change translated to a 1.7 times increased risk of developing NVI/NVA.[12] Though not directly translatable to an absolute Snellen equivalent for clinical use, these results are still consistent with the previous findings that patients presenting with worse visual acuities have a higher risk of developing NVG.[12] An RAPD has also been strongly correlated with ischemic CRVO.[2,9,18] We identified RAPD to be the factor with the greatest HR (HR = 6.04) for progression to NVG. Additionally, the relative risk (= 2.15) increase for eyes with an RAPD highlights that this finding should at least double the concern that the eye will develop NVG. We propose that a simple pupil examination be performed at each visit and if an RAPD is present, that this be given appropriate clinical consideration when determining follow-up intervals.

We did not determine an association between macular edema and risk of developing NVG. As shown in previous studies, presence of macular edema has not been found to be associated with ischemic CRVO.[2,19] Although this finding was not a significant risk factor, we attempted to quantitatively compare central retinal thickness by OCT and its association with NVG. As central retinal thickness increased, we found no significant association with developing NVG, further supporting the observation that macular edema and NVG are independent,

unrelated sequelae of CRVOs. Notably, no significant difference has been reported when central retinal thickness was measured using 2 different OCT instruments (Cirrus HD-OCT and Spectralis HRA+OCT), as was done in this present study.[20]

The highest risk for neovascular glaucoma conversion, conventionally known as "100-day glaucoma,"[21-23] more accurately falls within the first 7 months of CRVO onset.[2] In our study, the mean time to NVG onset was 421 days, significantly outside this window. However, the original CRVO natural history studies occurred before the era of anti-VEGF therapy, which has since changed the treatment paradigm for CRVO macular edema. By taking into account a patient's last anti-VEGF injection, the mean adjusted time to NVG onset (from last anti-VEGF injection) was halved to 212 days, or around 7 months. The results of this "adjustment" highlight that anti-VEGF therapy may "reset the clock" to NVG onset, extending the risk beyond the 7 months. This extended timeline to NVG should be considered when following patients who receive serial injections. Mistakenly associating improved macular edema as a surrogate for decreased neovascular risk may lead to a false sense of security when extending follow-up visits. Instead, clinicians should realize that the highest risk for NVG conversion still persists into the 7 months following discontinuation of anti-VEGF therapy.

Despite anti-VEGF therapy for CRVO-related macular edema, the value of this intervention in preventing neovascular glaucoma may be limited.[9,24] We hypothesized that during the acute phase of a CRVO, a robust VEGF release secondary to retinal ischemia could be counteracted by anti-VEGF therapy, allowing time for new collateral vessel formation.[25] However, we observed no difference in risk for patients who received an intravitreal anti-VEGF injection on presentation compared to those who did not. In light of these findings, as well as those of the RAVE trial, these results indicate that despite our improved ability to calculate risk of NVG in patients with CRVO, our ability to prevent this complication remains inadequate. Despite these findings, we still recommend intravitreal anti-VEGF injection to the affected CRVO eye on presentation. Given the inherent subjectivity of CRVO symptom onset, this injection would standardize the CRVO eye to a known day 0, especially in cases when the subjective onset of symptoms is unclear. We realize that there may be some delay in developing macular edema after the actual occlusive event, and thus the true CRVO event may predate the date of vision loss. However, with a "day 0" date established, a follow-up schedule may be planned that minimizes risk for NVG conversion between interval visits. Additionally, serial anti-VEGF injections during the acute phase may allow for intraretinal hemorrhage to resolve, allowing for more reliable characterization of retinal ischemia by FA.

The presence of decreased vision, RAPD, or systemic hypertension should alert the clinician of a higher NVG conversion risk and the need for timely subspecialty referral. If a patient's VA decreases or a new RAPD develops on a subsequent follow-up visit, conversion to an ischemic CRVO should be considered and a patient's NVG risk should be reevaluated with a series of closer follow-up intervals. Notably, although the presence of these factors portends a higher risk for conversion to NVG, the opposite does not necessarily hold true (ie, the lack of RAPD does not decrease the risk of NVG compared to all eyes with CRVO). There was no appreciable decrease in NVG risk for patients in the absence of these risk factors. It should be stressed that these eyes should still be regularly followed and screened for neovascularization. Upon establishing care with a subspecialist, ancillary retinal testing such as FA, ERG, or visual fields may be used to further stratify a patient's NVG risk. In patients with increased risk, therapies such as PRP may be considered, although this intervention is controversial and beyond the scope of this paper.[1,4,26]

Limitations to our study include the retrospective nature of the data set and the small sample size of NVG complications. The limited sample size, attributed to our stringent inclusion criteria, were carefully selected to limit any potential bias. We meticulously reviewed the complete medical records of 646 patients to generate our data set. We attempted to reduce the selection bias toward nonischemic CRVOs by limiting our study to patients presenting within the first 90 days of symptom onset, thus eliminating patients with chronic CRVOs outside the range of greatest conversion to NVG.[2] However, by eliminating chronic CRVOs, we eliminated from our sample set the 3%–33% of eyes that would typically convert from a nonischemic CRVO to ischemic CRVO.[12,27,28] Given our limited sample size, a multivariate analysis could not be performed. As gonioscopy was not uniformly performed by clinicians at each visit, patients with early NVG (NVA and normal IOP) could have been missed until they presented with an elevated IOP spike. This limitation would be expected to create a delayed time to NVG, but would not be expected to alter the underlying NVG risk factors. Another limitation is an assumption that patients not returning after 3 follow-up visits did not develop NVG. We attempted to limit this assumption by excluding any patient lost to follow-up after their initial visit. In addition, 80% of patients included in the data set resided in Miami-Dade County, Florida (where our institution is located). Given that our institute is the only tertiary care eye center in the region, we made an assumption that any patient who had already established care and had previously presented to our institute for acute CRVO would return to our 24-hour emergency department if pain or sudden-onset vision loss from neovascular glaucoma suddenly developed. This may not have been true of all patients.

Neovascular glaucoma is a complication of CRVO associated with poor visual outcomes. The use of OCT has become integral in the management of CRVO, but our results indicate that central retinal thickness measurement should not be used as a predictor for future risk of NVG. Clinical factors that are easily attainable on presentation, such as history of systemic hypertension, poor VA, and RAPD, can assist the clinician in rapidly stratifying a patient in terms of risk of NVG development. Such a classification would help identify those who require more frequent or earlier follow-up, and may benefit from further interventions such as PRP or anti-VEGF therapy. Anti-VEGF injections, though effective in improving macular edema, may functionally delay the onset of NVG and should not be seen as a curative therapy in patients presenting with CRVO.

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