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Systemic antiplatelet agents and anticoagulants in eyes with branch retinal vein occlusion

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Abstract

Purpose: The purpose of this study was to investigate the effect of systemic antiplatelet agents and anticoagulants on the structural and functional outcomes of eyes with branch retinal vein occlusion (BRVO).

Methods: A retrospective longitudinal cohort study was performed on BRVO patients evaluated at a single tertiary care referral center between 2009 and 2017. Medical records were reviewed for antiplatelet agent and anticoagulant use including aspirin, clopidogrel, warfarin, rivaroxaban, apixaban, or dabigatran prior to BRVO onset. In addition, optical coherence tomography (OCT) parameters, clinical outcomes, and treatment patterns were also recorded.

Results: A total of 354 BRVO eyes were identified with a mean follow-up time of 36 months. Antiplatelet or anticoagulant use was associated with presence of cystoid macular edema (CME) at presentation after controlling for potential confounding variables in a multivariate logistic regression. Multivariate regression also revealed an association between foveal hemorrhage at presentation and use of antiplatelet or anticoagulant medications. There were no significant differences in visual acuity or prevalence of CME at the final visit in those with antiplatelet/anticoagulant use compared to those not on these agents.

Conclusion: Although the use of systemic antiplatelet or anticoagulant agents was associated with increased prevalence of CME and foveal hemorrhage at presentation of BRVO, the use of these medications was not associated with different visual or structural outcomes at the final visit.

Keywords: anticoagulation, antiplatelet agents, branch retinal vein occlusion, optical coherence tomography

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Introduction

Branch retinal vein occlusion (BRVO) is a common retinal vascular disease, with a reported prevalence rate between 0.3% and 1.1%, which can lead to significant visual impairment.[1–4] The major risk factors include age, hypertension, arteriosclerosis, hyperlipidemia, diabetes mellitus, and smoking.[2–4] Although visual acuity (VA) improves in a subset of BRVO eyes without intervention, improvement beyond 20/40 is less common during the natural history of disease.[2] Intervention with intravitreal anti-vascular endothelial growth factor (VEGF) injections and laser photocoagulation is currently recommended for cystoid macular edema (CME) and neovascularization in eyes with BRVO.[5,6] Intravitreal steroid injections are also used for treatment of CME, particularly in pseudophakic or treatment refractory eyes.[7]

There have been many studies assessing the role of systemic anticoagulation and antiplatelet agents in retinal vein occlusion, but the results have been conflicting. Some of these studies

specifically focus on the role of these agents in central retinal vein occlusion (CRVO), as the pathogenesis is thought to be similar to that of systemic thrombogenesis.[8] In contrast, the pathogenesis of BRVO has been frequently attributed to local factors such as arteriosclerosis of the branch retinal artery leading to compression of the distensible adjacent branch retinal vein, which may indicate that systemic anticoagulation and antiplatelet agents may have a different effect in BRVO eyes compared to CRVO eyes.[4] Though the use of systemic agents commonly prescribed for the prevention or treatment of systemic thrombogenesis has not been uniformly recommended for those with retinal vein occlusion.[8,9]

Several case series and small randomized controlled trials have suggested some visual benefit with medications such as ticlopidine, troxerutin, aspirin, and low-molecular-weight heparin in retinal vein occlusions.[4] However, these studies have sample size limitations and often include both BRVO and CRVO in a combined analysis.[4] Despite the prevalence of BRVO being more widespread than CRVO,[3] there are few studies on the use of systemic antiplatelet or anticoagulant agents in the prevention or treatment of BRVO specifically. Because BRVO is a common retinal vascular disease with a lack of consensus on the role of systemic antiplatelet and anticoagulant agents, we evaluated the association of these medications with the clinical presentation and outcomes in eyes with BRVO.

Methods

Study population

Duke University Institutional Review Board (Pro00075701) approval was obtained, and the informed consent requirement was waived for this retrospective study. In addition, research adhered to the tenets of the Declaration of Helsinki. The Duke Enterprise Data Unified Content Explorer (DEDUCE) was used to identify all patients diagnosed with a BRVO between January 1, 2009 and July 1, 2017 at the Duke Eye Center. Exclusion criteria included unclear documentation of antiplatelet or anticoagulant use and inadequate chart information regarding demographics, baseline visit, or follow-up visit information. Patients who received treatment such as grid-pattern laser, sectoral scatter laser, intravitreal steroid injection, or intravitreal anti-VEGF injection within 3 months prior to presentation were also excluded.

From the medical records of all eligible patients, we collected data retrospectively in compliance with the Health Insurance Portability and Accountability Act. Informed consent was not obtained as this is a retrospective study with minimal risk to subjects. The use of antiplatelet and anticoagulant medications at presentation was recorded and patients were grouped by baseline use of a single antiplatelet agent (aspirin 81 mg or 325 mg, clopidogrel), use of a single anticoagulant agent (warfarin, rivaroxaban, apixaban, or dabigatran), use of a combination of more than one of these medications, or use of none of these medications. We also recorded demographic data including age, sex, and race. The presence of other systemic and ocular conditions at the time of BRVO diagnosis (e.g. systemic hypertension, hyperlipidemia, diabetes mellitus, tobacco use, and glaucoma) were collected. We reviewed clinical data including corrected Early Treatment Diabetic Retinopathy Study (ETDRS) VA, intraocular pressure (IOP), and spectral-domain optical coherence tomography (OCT) findings at the baseline and final visits as well as presence of neovascularization. Any interventions, including the number of grid-pattern and sectoral scatter laser photocoagulation sessions and number of intravitreal injections of either anti-VEGF agents or steroids, were also noted. Baseline was defined as the first visit for the evaluation of BRVO at our institution, and the final visit was the last available examination of the BRVO eye during the study period.

Statistical analysis

VA measured with an ETDRS chart was converted to the logarithm of minimum angle of resolution (logMAR) equivalent for the purpose of statistical analysis. Presentation characteristics and outcomes from each of the medication exposure groups (single antiplatelet agent, single anticoagulant, multiple antiplatelet agents, and/or anticoagulation) were compared to the control group consisting of patients not on any antiplatelet or anticoagulation agents. Continuous variables were statistically compared with one-way ANOVA with post hoc Bonferroni correction. Categorical variables were compared with the Pearson Chi-square test for dichotomous outcomes. Significance was defined as a p-value less than 0.05. Multivariate logistic regression analyses of presentation characteristics and outcomes

Table 1. Patient demographics and risk factors.

	All BRVO eyes ($n = 354$)	No antiplatelet/ anticoagulant ($n = 137$)	One antiplatelet ($n = 132$)	One anticoagulant ($n = 14$)	> 1 antiplatelet/ anticoagulant ($n = 71$)	*p*-value
Age (mean ± SD)	69.1 ± 13.3	66.0 ± 13.0	70.8 ± 10.5	74.0 ± 10.3	72.48 ± 10.6	0.0001*
Males (%)	42.4	35.0	43.1	50.0	53.5	0.0718
Race (%)						
White	70.6	64.4	74.0	71.4	61.1	0.4199
Black	20.8	17.8	16.8	21.4	29.2	
Asian	3.9	3.7	2.3	0	5.6	
Native American	0.3	0.7	0	0	0	
Multiracial	2.1	3.7	1.5	0	0	
Other	2.4	4.4	1.5	0	0	
Not reported	5.0	5.2	3.8	7.1	4.2	
Hypertension (%)	80.2	69.3	84.1	64.3	97.2	< 0.0001*
Diabetes mellitus (%)	30.2	25.4	29.2	28.6	42.0	0.1055
Current tobacco use (%)	21.5	17.4	18.2	14.3	12.7	0.1692
Glaucoma (%)	29.1	26.5	32.6	21.4	29.6	0.6521

BRVO, branch retinal vein occlusion; SD, standard deviation; Statistically significant results are denoted by asterisk (*) when $p < 0.05$ (as determined by one-way ANOVA with post hoc Bonferroni correction for continuous variables and Chi-square test for categorical variables).

were used to account for confounding factors, including patient sex, age, race, and the presence of other systemic and ophthalmic conditions, such as hypertension, hyperlipidemia, smoking status, diabetes mellitus, and glaucoma. Confounding factors were included in the multivariate regression if the univariate analysis had a p-value < 0.25. Additional factors including use of anticoagulant or antiplatelet agents and treatment-naïve status at the time of presentation were also accounted for in the regression analysis.

Results

Baseline demographics and risk factors

A total of 354 BRVO eyes of 354 patients were identified with patient demographic data summarized in Table 1. The mean age of all patients at BRVO onset was 69.1 ± 13.3 years with males comprising 42.4% ($n = 150$) and Whites comprising 70.6% (n = 250) of the total cohort. At BRVO presentation, 284 (80.2%) had systemic hypertension, 107 (30.2%) had diabetes mellitus, 103 (29.1%) had glaucoma, and 76 (21.5%) were current tobacco users. Of all identified BRVO patients, 95 (26.8%) had both diabetes and hypertension. Mean time between presentation and final visit was 36 months.

Use of antiplatelet and anticoagulation agents

At the baseline visit, 137 (38.7%) BRVO patients were not taking any antiplatelet or anticoagulant medications, 132 (37.3%) were on a single antiplatelet agent, 14 (4.0%) were on a single anticoagulant, and 71 (20.0%) of patients were on multiple agents (Table 1). Compared to patients not on anticoagulation or antiplatelet agents (mean age of 66.0 ± 13.0 years), patients who were on a single antiplatelet agent (mean age of 70.8 ± 10.5 years, $p = 0.004$) and patients who were on multiple agents (mean age of 72.5 ± 10.6 years, $p < 0.001$) were significantly different in age at BRVO onset. Patients on multiple agents were also more likely to be hypertensive compared to patients

Table 2. Baseline clinical characteristics.

	All BRVO eyes ($n = 354$)	No antiplatelet/ anticoagulant ($n = 137$)	One antiplatelet ($n = 132$)	One anticoagulant ($n = 14$)	> 1 antiplatelet/ anticoagulant ($n = 71$)	p-value
IOP (mmHg, mean ± SD)	15.0 ± 4.1	14.9 ± 3.7	15.2 ± 4.6	16.3 ± 2.6	14.3 ± 3.7	0.4460
Visual acuity (logMAR, mean)	0.466	0.447	0.472	0.346	0.513	0.7487
Cystoid macular edema (%)	63.9	61.2	65.8	54.5	67.2	0.7460
Subretinal fluid (%)	18.3	23.5	15.5	20.0	11.1	0.2730
Foveal hemorrhage (%)	17.4	14.4	19.6	33.3	16.3	0.4720
Neovascularization (%)	9.3	12.7	6.1	0	10.3	0.2357
Iris neovascularization	0.3	0	0	0	1.8	0.2435
Disk neovascularization	7.5	1.9	2.1	0	0	0.7507
Neovascularization elsewhere	1.6	11.0	4.3	0	7.0	0.2536
Vitreous hemorrhage	5.0	7.1	2.8	0	5.8	0.4211

BRVO, branch retinal vein occlusion; IOP, intraocular pressure; logMAR, logarithm of Minimum Angle of Resolution; SD, standard deviation; Statistically significant results are denoted by asterisk (*) when $p < 0.05$ (as determined by one-way ANOVA for continuous variables and Chi-square test for categorical variables).

on no antiplatelet agents or anticoagulants (97.2% vs 69.3%, $p < 0.001$). There were no significant differences in other baseline demographics and characteristics including sex, race, diabetes mellitus, smoking, or glaucoma among these groups – single antiplatelet agent, single anticoagulant, multiple antiplatelet agents and anticoagulants, and no antiplatelet agent or anticoagulant.

Baseline clinical characteristics

Baseline clinical features across groups are summarized in Table 2. There was no statistically significant difference in average IOP at baseline ($p = 0.446$) or VA ($p = 0.749$) among groups using a single antiplatelet agent, a single anticoagulant agent, multiple agents, or none of these agents. In addition, there was no significant difference in the proportion of individuals presenting with OCT structural parameters such as CME ($p = 0.746$), SRF ($p = 0.273$), or foveal hemorrhage ($p = 0.472$) among the four study groups. Baseline neovascular consequences were similar in prevalence across all study groups ($p = 0.236$).

Baseline CME

Univariate logistic regression analysis showed a significant association between the use of an antiplatelet agent or anticoagulant and the presence of CME at baseline (OR = 3.794, 95% CI (2.053 to 5.535), $p < 0.001$). To minimize possible effects from confounding variables, a multivariate analysis was performed and showed that the presence of CME at baseline was associated with the use of either an antiplatelet agent or an anticoagulant (OR = 2.678, 95% CI (1.585 to 4.529), $p < 0.001$). The multivariate model also included hypertension, which was found to be associated with the presence of CME at baseline, in addition to age, race, and any other treatments for BRVO – including intravitreal injections with either corticosteroid or anti-VEGF, sector scatter laser photocoagulation, and grid-pattern laser prior to presentation (Table 3). Hypertension was also found to be associated with CME in this multivariate model.

Baseline foveal hemorrhage

Evaluation for the presence of foveal hemorrhage was performed by image grading of color fundus photographs as previously described.[10] Univariate logistic regression analysis showed a significant association between the use of an antiplatelet or anticoagulant agent and baseline foveal hemorrhage (OR = 3.032, 95% CI (1.141 to 4.923), $p = 0.024$). Multivariate analysis to exclude possible confounding variables such as previous treatments, sex, tobacco history, and glaucoma revealed that the presence of foveal hemorrhage

Table 3. Multivariate logistic analysis examining contributing effects of various risk factors on the presence of cystoid macular edema at baseline.

Risk factor	Odds ratio	95% confidence interval	*p*-value
Age	1.020	0.9976 to 1.043	0.0849
Race (white reference category)			
Black	0.7782	0.4081 to 1.503	0.4490
Other	0.5173	0.2097 to 1.251	0.1446
Hypertension	1.902	1.021 to 3.543	0.0422*
Previous treatment (intravitreal injection, grid-pattern laser, sectoral scatter laser)	1.083	0.611 to 1.947	0.7861
Use of any antiplatelet/anticoagulant	2.678	1.585 to 4.529	0.0002*

Univariate logistic regression analysis of demographics and baseline characteristics were run and only variables with $p < 0.25$ were included in the multivariate regression. Statistically significant odds ratios from multivariate logistic regression are denoted by asterisk (*) when $p < 0.05$.

Table 4. Multivariate logistic analysis examining contributing effects of various risk factors on the presence of foveal hemorrhage at presentation.

Risk factor	Odds ratio	95% confidence interval	*p*-value
Sex (male reference category)	1.399	0.6147 to 3.323	0.4319
Smoking	0.3230	0.07303 to 1.007	0.0812
Glaucoma	1.760	0.7731 to 3.964	0.1721
Previous treatment (intravitreal injection, grid-pattern laser, sectoral scatter laser)	1.572	0.6599 to 4.069	0.3239
Use of any antiplatelet/anticoagulant	2.624	1.118 to 6.742	0.0333*

Univariate logistic regression analysis of demographics and baseline characteristics were run and only variables with $p < 0.25$ were included in the multivariate regression. Statistically significant odds ratios from multivariate logistic regression are denoted by asterisk (*) when $p < 0.05$.

at the baseline visit was associated with the use of an antiplatelet or anticoagulant agent alone (OR = 2.624, 95% CI (1.118 to 6.742), $p = 0.033$) as described in Table 4.

Treatment

Patients included in this study received treatments for BRVO sequelae such as CME and neovascularization. Frequency of receiving these treatments, including intravitreal corticosteroids ($p = 0.737$) or anti-VEGF ($p = 0.300$) injections, grid-pattern laser ($p = 0.410$), or sector scatter laser photocoagulation ($p = 0.633$) before presentation or during treatment at our institution, was not different across the four study groups–the single antiplatelet group, single anticoagulant group, multiple agent group, and those on none of these agents (Table 5). The average number of anti-VEGF injections at final visit was also no different between these four groups ($p = 0.479$). From the total cohort, 65% of BRVO eyes had CME and only 42% of eyes were treated with anti-VEGF agents by the final visit. Some patients were simply monitored as they had CME which did not extend to the foveal center and thus CME did not impact their vision while other patients had foveal atrophy from a chronic BRVO in which case anti-VEGF treatment would provide little benefit.

Table 5. Final clinical characteristics.

	All BRVO eyes ($n = 354$)	No antiplatelet/ anticoagulant ($n = 137$)	One antiplatelet ($n = 132$)	One anticoagulant ($n = 14$)	> 1 antiplatelet/ anticoagulant ($n = 71$)	*p*-value
Intravitreal corticosteroid (%)	4.8	4.4	6.0	0	4.2	0.7366
Grid-pattern laser (%)	20.9	23.4	22.0	7.1	16.9	0.4104
Sectoral scatter laser (%)	17.5	19.0	15.9	7.1	19.7	0.6325
Intravitreal anti-VEGF (%)	41.8	45.3	42.4	50.0	32.4	0.3003
Number of intravitreal anti-VEGF (mean)	5.1	5.5	5.3	4.5	3.6	0.4791
Visual acuity (logMAR, mean)	0.464	0.437	0.448	0.668	0.498	0.5360
Cystoid macular edema (%)	50.8	53.7	52.6	41.7	44.2	0.6287
Subretinal fluid (%)	5.7	4.8	2.7	8.3	12.2	0.1881
Baseline and follow-up neovascularization (%)	11.4	12.0	8.4	10.0	16.3	0.5592
Subsequent RVO in fellow eye (%)	5.1	5.3	6.4	0	3.2	0.6890

logMAR, logarithm of Minimum Angle of Resolution; VEGF, vascular endothelial growth factor; Statistically significant results are denoted by asterisk (*) when $p < 0.05$ (as determined by one-way ANOVA for continuous variables and Chi-square test for categorical variables).

Structural and functional outcomes

Among the four study groups, a single antiplatelet agent, a single anticoagulant agent, multiple agents, and no antiplatelet/anticoagulant use, there was no significant difference in the proportion of individuals with CME ($p = 0.629$) or with SRF ($p = 0.188$) at the final visit (Table 5). Univariate logistic regression did not show a relationship between the use of an anticoagulant or antiplatelet agent and the prevalence of CME or SRF at the final visit. There was also no statistically significant difference in final VA ($p = 0.536$) whether patients were on an antiplatelet agent, anticoagulant, multiple, or none of these medications. There was also no difference in the incidence of neovascularization at baseline or final visits among these groups (Table 5). A subsequent new retinal vein occlusion occurred in 4.9% of fellow eyes in patients on an antiplatelet agent or anticoagulant. There was no difference in the frequency of a new retinal vein occlusion across treatment groups using a single antiplatelet agent, a single anticoagulant agent, multiple agents, or none of these agents ($p = 0.689$).

Discussion

In this study, we retrospectively investigated whether the use of systemic antiplatelet agents or anticoagulants is associated with differences in baseline clinical and imaging characteristics as well as structural and visual outcomes. We found that the use of antiplatelet or anticoagulant agents was associated with the presence of CME and foveal hemorrhage at presentation; however, use of either of these medications was not associated with a significant difference in VA, treatment burden, or CME at final follow-up. Furthermore, 4.9% of patients with BRVO who were taking an antiplatelet agent and/or anticoagulation at presentation developed a subsequent retinal vein occlusion in the fellow eye.

Pharmacologically, antiplatelet agents and anticoagulants are considered to be separate classes of medications as they have distinct mechanisms of action affecting either platelet aggregation or the coagulation cascade, respectively. Because these systemic agents may have different effects on the retinal vasculature, use of a single antiplatelet agent, single anticoagulant, or multiple agents were grouped separately for analysis, although outcomes from BRVO were not found to be different across these groups.

Given that long-term antiplatelet and anticoagulant use has been associated with bleeding in various organ systems due to impaired thrombogenesis,

the potential association between intraretinal hemorrhage and the use of these agents has been heavily debated in retinal conditions such as retinal vein occlusion.[8,11,12] In CRVO eyes, a previous study with a large sample size found that aspirin use was associated with a significant increase in retinal hemorrhage with accompanying visual loss and without any perceived benefits.[8] In contrast, a systematic review suggested that antiplatelet agents may be associated with partial VA improvement in retinal vein occlusion; however, meta-analysis of VA improvement was not done across the studies included in the review.[13]

Using multivariate regression models, we found that taking any combination of either single or multiple antiplatelet and anticoagulant agents was associated with an increased prevalence of foveal hemorrhage at presentation in this cohort of BRVO patients. This analysis included a newer P2Y12 inhibitor, clopidogrel, as well as factor Xa inhibitors, apixaban and rivaroxaban, which were not investigated in prior studies as mentioned above. There was no associated difference in functional or structural outcomes despite the increased prevalence of foveal hemorrhage and CME on presentation. Future studies with a larger sample size may be used to investigate whether any of these newer agents are individually associated with increased retinal hemorrhage and worse macular edema in eyes with retinal vein occlusion.

Our study also found that CME prevalence at baseline is more common in BRVO patients on any combination of single or multiple antiplatelet and anticoagulant agents after accounting for possible confounding factors through multivariate analysis. In the setting of BRVO, CME is hypothesized to occur by injury to the tight junctions between endothelial cells during the acute phase of obstruction, thereby disrupting the blood retinal barrier and allowing egress of fluid from the affected retinal vessels.[14] Anticoagulation with warfarin has been shown to disrupt the blood brain barrier, thereby increasing vascular permeability.[15] This could compound the likelihood of developing CME in the setting of a BRVO with antiplatelet and anticoagulant medications broadly having a similar effect on the blood-retinal barrier. Our group previously found that warfarin use at BRVO onset in a diabetic cohort was associated with increased final central subfield thickness which is also consistent with this hypothesis.[16]

Interestingly, newer direct oral anticoagulants including dabigatran, rivaroxaban, and apixaban have been associated with limited disruption of the blood brain barrier as compared to warfarin.[15,17] However, use of these direct oral agents was less common than warfarin in our cohort precluding our ability to perform subgroup analyses and evaluate these agents separately. Further studies with a larger sample size of patients taking these newer oral agents would be needed to investigate whether these agents are associated with a lower prevalence of CME on presentation compared to warfarin in eyes with BRVO.

BRVO has previously been correlated with specific platelet parameters, including increased mean platelet volume, platelet distribution width, and plateletcrit.[18,19] While these findings suggest that platelet production and activation play a role in BRVO onset and that antiplatelet medications may offer some benefit in BRVO, these studies had a relatively smaller sample size and focused on a subset of BRVO eyes without other RVO risk factors. Subjects were also excluded if they were taking any systemic medications or had risk factors such as smoking history, which may independently affect coagulability and endothelial function. In our study, however, these subjects were included in our BRVO cohort, and we found no significant difference in BRVO outcomes or subsequent new RVO in the fellow eye whether a subject was or was not taking an antiplatelet agent at BRVO onset. In contrast, our prior study investigating the effects of select systemic medications on BRVO outcomes in a diabetic cohort found that high-dose aspirin was associated with decreased treatment burden at 1 year.[16] Given that diabetes has been associated with platelet hyperactivity,[20,21] reduction of platelet aggregation by antiplatelet agents may contribute to quicker reperfusion and resolution of macular edema, resulting in a reduced number of intravitreal injections in a diabetic cohort taking aspirin at BRVO onset but not in a cohort with other contributing risk factors. Further work would be necessary to investigate if the subset of individuals with evidence of subclinical elevated platelet activation would benefit from antiplatelet therapies in BRVO.

Previous studies looking at the use of systemic anticoagulant or antiplatelet therapies did not separately analyze patients with BRVO versus CRVO. However, the pathogenesis of these two vascular occlusions is thought to be different.

BRVO is thought to be due to local arterial compression of the retinal vein at arteriovenous crossings. In contrast, the etiology of CRVO is postulated to share similarities with systemic thrombogenesis in which the broad contributing factors are described by Virchow's triad of endothelial injury, hypercoagulability, and stasis which can include adjacent vein compression.[4] This may explain our findings that the use of systemic anticoagulant and antiplatelet agents does not have a significant impact on BRVO outcomes which is in contrast to previous studies showing a significant effect of these agents on the visual outcome from CRVO or retinal vein occlusions broadly without distinction of central or branch vein occlusion. [4,7,8]

The strengths of this study include inclusion of newer antiplatelet and anticoagulation agents, such as the factor Xa inhibitors apixaban and rivaroxaban, which have not been extensively evaluated in retinal vein occlusion outcomes. In addition, all imaging was performed and evaluated in one center with a standardized imaging protocol. Moreover, this study specifically evaluated the use of these agents in a single cohort of BRVO eyes, without inclusion of any CRVO eyes.

Given that this study was retrospective, some limitations are inherent. Duration and dose of antiplatelet agent or anticoagulant use were not standardized across all patients in the study. Furthermore, some patients received various treatments for BRVO prior to presentation such as intravitreal corticosteroids or anti-VEGF injections, grid-pattern laser, and sector scatter laser photocoagulation, although for study inclusion such treatment needed to be at least 3 months prior to presentation. This potential limitation was further addressed through multivariate analysis by controlling for prior treatment. This single center study with its sample size precluded investigation of single medications or analysis of specific medication doses. Because chronic comorbidities were often managed outside of this single tertiary referral center, elements of the clinical history including length of diabetes, renal function, and so on were not always available. We thus chose to only include systemic parameters that could be confirmed by history or medication list.

In conclusion, we found that the use of a single or multiple antiplatelet agents and anticoagulants was associated with differences in presentation including increased prevalence of foveal hemorrhage and CME, after accounting for possible confounding variables. However, use of a single antiplatelet, single anticoagulant, or multiple such agents was not associated with differences in visual outcomes or prevalence of CME or SRF at the final visit. In addition, this study demonstrated that a proportion of patients on antiplatelet agents and/or anticoagulants may still develop a retinal vein occlusion in the fellow eye. This study suggests that these agents may not have a role in the prevention or treatment of BRVO.

Conflict of interest statement

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: DSB is a consultant for Genentech and Verana Health. AST is a consultant for Alimera, Avesis, Bauch & Lomb, Genentech, Zeiss. SF receives patent royalties from Alcon. The other authors have no disclosures to report.

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