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The Effect of Select Systemic Medications on Visual Outcomes in Diabetics With Branch Retinal Vein Occlusion

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Abstract

Purpose: The purpose of this article is to evaluate the effect of systemic medications and glycemic control on the visual outcome and treatment burden in patients with diabetes and branch retinal vein occlusion (BRVO). **Methods:** A retrospective review was performed for patients with diabetes diagnosed with a BRVO at an academic eye center from 2009 to 2017. The use of select antihypertensives, antiplatelet agents, anticoagulants, and hypoglycemics was reviewed. Data on visual acuity (VA), central subfield thickness (CST), treatment course, and hemoglobin (Hb)A1c were obtained throughout follow-up. **Results:** A total of 121 eyes met criteria with a median follow-up duration of 19.4 months. The mean baseline logarithm of the minimum angle of resolution (logMAR) VA was 0.56 (Snellen equivalent, 20/72) and mean final logMAR VA was 0.5 (20/63). At final follow-up, aspirin 325 mg was associated with 4.8 fewer injections ($n = 13$, $P = .04$), insulin was associated with 3.6 more injections ($n = 26$, $P = .04$), warfarin was associated with a 79 μm increase in CST ($P = .02$), and a 1% increase in HbA1c was associated with 0.86 more injections ($P < .01$). **Conclusions:** The VA outcome of BRVO in diabetics may be worse than that of BRVO in nondiabetics. Worse diabetic control was associated with a higher treatment burden. High-dose aspirin was associated with fewer injections.

Keywords

antiplatelet, branch retinal vein occlusion, cystoid macular edema, diabetes, metformin, warfarin

Introduction

Branch retinal vein occlusion (BRVO) is estimated to occur in up to 1.6% of the general population.[1-3] Its pathogenesis has been attributed to a combination of retinal arteriolar stiffness and retinal vein compression leading to impaired retinal venular wall integrity.[1,4] A common cause of reduced visual acuity (VA) in BRVO is cystoid macular edema (CME),[1,3] which is often treated with intravitreal antivascular endothelial growth factor (anti-VEGF) or steroid injections.[1,4]

The association of diabetes with BRVO remains controversial. Diabetes has been identified as a risk factor for BRVO in some studies, but not in others.[1,2,4] In the Eye Disease Case-Control Study of 270 patients with BRVO and 1142 controls, diabetes and higher serum glucose levels increased the risk of BRVO, but became nonsignificant when cardiovascular disease was included in the multiple logistic regression.[5] In a meta-analysis of 1518 people with BRVO, the risk factors of hypertension and hyperlipidemia were associated with a 3.0 and 2.3 odds ratio for BRVO development, respectively, whereas diabetes was not.[6] However, in a retrospective review of 907 277 individuals from the Taiwan National Health Insurance database, diabetics were at a 1.6-fold higher risk of developing a BRVO.[7] In that study, age, diabetic retinopathy, and hypertension were significant risk factors for BRVO.

Not only has diabetes been linked as a risk factor for BRVO, but diabetes may also affect the visual prognosis and treatment. Only a paucity of studies have evaluated BRVO outcomes in diabetics, and many studies evaluating BRVO outcomes have not specifically reported on diabetics.[8-13] In the most recent and comprehensive such study, to our knowledge, diabetics were on average 6 years younger at the time of BRVO onset and more commonly had cardiovascular disease when compared with case-matched controls.[14] In that study, diabetics also had worse

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VA at 1 and 2 years, required more argon laser spots and follow-up visits, had more severe macular edema, and had a greater area of retinal ischemia on fluorescein angiography than case-matched controls. However, this study was conducted before intravitreal anti-VEGF agents were commonly used.

Because glycemic control has a known impact on vessel wall integrity, it is also reasonable to explore the effect of glycemic control on BRVO outcomes.[15] In a study evaluating oral glucose tolerance tests in 17 nondiabetic patients with BRVO, 9 had an abnormal result compared with 0 of 11 age-matched nondiabetics without BRVO, proposing a relationship between glycemic levels and BRVO.[16] Overall, this suggests diabetics are a distinct population among patients with BRVO.

Systemic medication use may also affect the relationship between diabetes and BRVO. Metformin use was associated with a lower incidence of BRVO in diabetics in 1 study.[17] Metformin has also been shown to affect the severity of diabetic retinopathy, although this has not been evaluated in BRVO.[18] If metformin has an impact on BRVO incidence and diabetic retinopathy severity, it raises the question as to whether it affects BRVO outcomes as well.

Other medications have been studied in retinal vein occlusion, although not specifically in the diabetic population. With regard to antiplatelet agents, the Beaver Dam and Beijing eye studies did not find a reduced risk of central retinal vein occlusion or BRVO among aspirin users of unspecified dosage.[2,3] In those trials, the presence or absence of diabetes was not studied. A recent retrospective review found aspirin and anticoagulants reduced the risk of BRVO in the nondiabetic population but did not have an effect in the diabetic population.[7]

Some medications have been shown to have an effect on retinal vascular anatomy but have not been evaluated in BRVO or in diabetics. The Blue Mountains Eye Study reported aspirin and antihypertensives were associated with wider retinal arteriolar and venular caliber, whereas the Beaver Dam Eye Study reported estrogen was associated with narrower diameters in a dose-dependent manner.[19,20] This raises the question as to whether multiple systemic medications may affect BRVO outcomes.

To our knowledge, the association of systemic medications, glycemic control, and clinical outcomes in diabetics with BRVO has not been evaluated. BRVO in diabetics is not clearly equivalent to BRVO in the general nondiabetic population, and therefore BRVO in diabetics warrants evaluation. The purpose of this study is to evaluate the effect of select antihypertensives, antiplatelet agents, anticoagulants, hypoglycemics, and the degree of glycemic control on the baseline characteristics, visual outcomes, and treatment burden in patients with diabetes and BRVO.

Methods

This research was approved by the Duke University Institutional Review Board in accordance with the Declaration of Helsinki. A retrospective review of medical records was performed for all patients newly diagnosed with a macula-involving BRVO by a retina specialist at the Duke Eye Center between January 2009 and June 2017. Of this group, those who also had diabetes mellitus of any type were further identified. Patients were considered to have diabetes if it was on their diagnosis list in the electronic medical record at the time of BRVO diagnosis. Patients were not excluded if their baseline hemoglobin A1c (HbA1c) was below 6.5, which is the recommended cutoff for diagnosing diabetes by the American Diabetes Association, as long as they were on at least 1 medication for glycemic control at the time of BRVO diagnosis. Eyes were excluded if there was a history of anti-VEGF therapy for diabetic macular edema (DME) in the year prior to the diagnosis of BRVO.

In addition to demographic information and eye examination details, the following data points were collected: BRVO duration, medical and ocular comorbidities, systemic medication use, ocular treatment course, and follow-up duration. The presence of nonproliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) was recorded from the diagnosis made by the attending retina specialist during the baseline examination. HbA1c levels were recorded if obtained within 1 year of the baseline visit and 1 year of the final visit. If there were multiple lab values, the one in closest proximity to the baseline and final visit dates was recorded.

Corrected VA that had been recorded using an Early Treatment Diabetic Retinopathy Study (ETDRS) chart was converted to the logarithm of the mean angle of resolution (logMAR) scale. Central subfield thickness (CST) was recorded from spectral-domain optical coherence tomography at the baseline and final visits. The use of the following medications at the time of BRVO diagnosis was reviewed: angiotensin-converting enzyme (ACE) inhibitors, apixaban, aspirin 81 mg, aspirin 325 mg, beta-blockers, clopidogrel, fish oil, hormone replacement, insulin, metformin, pioglitazones, rivaroxaban, statins, vitamin E, and warfarin.

Data were analyzed via R statistical software, version 3.5.1. To identify medications of interest, we fit a series of univariate linear models with a single independent variable (the selected medication) and single dependent variable (the outcome of interest) separately for each time point collected. Linear regressions were also used to evaluate any association between baseline glucose control and the above measured outcomes. A one-way analysis of variance (ANOVA) was performed to evaluate differences in follow-up durations between medication groups. Wilcoxon rank-sum tests were used to determine whether there were significant differences in follow-up duration between patients on a selected medication and patients not on that selected medication.

Results

Demographics

A total of 121 individuals with diabetes mellitus and unilateral BRVO were identified. The mean age at BRVO onset was 68 years (range, 43-93 years). Of those, 55% were female and 45%

were male. The racial distribution included 59% Caucasian and 29% African American. Ninety-one percent had hypertension, 35% had hyperlipidemia, and 25% were current smokers. At the baseline visit, 33% had open-angle glaucoma, 35% had NPDR, 3% had PDR, 10% had an epiretinal membrane, 6% had dry age-related macular degeneration, and 3% had a previously repaired retinal detachment in the eye with the BRVO.

Visual Outcomes

Among all eyes, the mean baseline VA in the affected eye was logMAR 0.56 (Snellen equivalent, 20/72) and mean final VA was 0.5 (20/63). At 1 year, the mean VA was 0.57 (20/73). Mean baseline CST was 396 μm (range, 164-749 μm), and mean final CST was 323 μm (range, 84-626 μm). Seventy-five percent had a follow-up duration ≥6 months, with a median follow-up of 19.4 months (range, 0.1-17.7 years). There were no significant differences in follow-up times between medication groups ($P = .94$, F-statistic = 0.48, one-way ANOVA). Among 67 patients with >1 year of follow-up, the final logMAR VA was also 0.5 (20/63), and the mean final CST was 311 μm.

Systemic Medication Use

Univariate linear regressions were fitted with a selected medication used at baseline as the independent variable and 1 of the following as dependent variable: logMAR VA at 1 year, number of intravitreal anti-VEGF injections at 1 year, logMAR VA at final follow-up, number of anti-VEGF injections at final follow-up, CST at final follow-up, and follow-up duration (Table 1). Patients on metformin had statistically significant longer follow-up than patients not on metformin (median 25.2 months vs 14.9 months, $P = .04$ using Wilcoxon rank sum test). There were no other statistically significant differences in follow-up time between patients on a selected medication and not on that selected medication. Over the course of 1 year of follow-up, 2 statistically significant associations were found: Aspirin 325 mg use was associated with 2.2 fewer injections (n = 13, $P = .04$) and insulin use was associated with 2.4 more injections (n = 23, $P < .01$).

Among all eyes at the final follow-up, aspirin 325 mg use was significantly associated with 4.8 fewer injections (n = 13, $P = .04$), insulin use was significantly associated with 3.6 more injections (n = 26, $P = .04$), and beta-blocker use was significantly associated with 3.4 more injections (n = 51, $P = .04$). Also at the final follow-up, aspirin 81 mg use was significantly associated with 0.22 logMAR VA improvement ($P = .05$). The mean final logMAR VA of eyes with aspirin 81 mg was 0.4 (n = 53) compared with 0.62 (n = 43) among eyes without aspirin 81 mg. At final follow-up, warfarin use was significantly associated with a 79 μm increase in CST ($P = .02$). The mean CST of eyes with warfarin was 388 μm (n = 8) and without warfarin was 309 μm (n = 59).

Among a subset of 67 patients who had >1 year of follow-up, aspirin 325 mg was significantly associated with 4.9 fewer injections (n = 7, $P = .03$) and insulin was significantly associated with 3.6 more injections (n = 17, $P = .04$) by the final visit despite a similar mean length of follow-up between those taking and not taking these medications. However, beta-blocker use was no longer significantly associated with the number of injections among this subset (n = 36, $P = .45$). Also, at the final follow-up among this subset, aspirin 81 mg was significantly associated with 0.22 logMAR VA improvement (n = 39, $P = .047$), and warfarin was significantly associated with a 78.8 μm increase in CST (n = 8, $P = .02$).

For a subset of 33 patients who presented with a BRVO that had not been treated at a prior institution before presentation to the Duke Eye Center, and who had >1 year of follow-up, the use of any dose of aspirin was significantly associated with 3.1 fewer injections at 1 year (n = 22, $P = .04$) and 8.1 fewer injections by final follow-up (n = 17, $P < .01$), but was not associated with a difference in VA at any time point.

ACE inhibitors, statins, apixaban, clopidogrel, fish oil, metformin, pioglitazone, vitamin E, rivaroxaban, and hormone replacement therapy did not significantly affect VA, CST, or treatment course at any time point. Univariate linear regressions were fit with the following as independent variables: follow-up duration, diabetic retinopathy, epiretinal membrane, dry macular degeneration, and retinal detachment repair; there were no significant associations found with final VA, final CST, or treatment course as dependent variables.

Diabetes Control

The mean baseline HbA1c was 7.3 (range, 4.3-13.1) and mean final HbA1c was 7.1 (range, 4.3-9.7). The mean change in HbA1c from baseline to final visit was –0.24 (range, –3.9 to 1.5). A 1-point increase in baseline HbA1c was significantly associated with 0.86 more injections both at 1 year and at final follow-up ($P < .01$), but there was no association with VA or CST at either time point. We fit univariate linear regressions with baseline HbA1c or change in HbA1c from baseline to final visit as the independent variable, and the measured outcome as the dependent variable. There was no significant association with final HbA1c or change in HbA1c and final VA, final CST, or treatment burden. Individuals on insulin had a 1.24% increase in baseline HbA1c ($P < .01$) and a 1.14% increase in final HbA1c ($P < .01$).

There were no statistically significant differences in outcomes between 75 eyes without diabetic retinopathy at baseline compared with the 42 eyes with NPDR and 4 eyes with PDR present at baseline. Baseline visual acuity, vision at 1 year, final CMT, number of treatments at 1 year, and final treatment burden were all not statistically significant in a univariate linear regression with the presence or absence of diabetic retinopathy or PDR as the independent variable and the above outcomes as the dependent variable. There was also no statistically significant difference in follow-up duration between those with or without any diabetic retinopathy.

Table 1. Linear Model of Baseline Medication Use **W**ith Visual Acuity, Number of Injections, and Central Subfield Thickness at 1 Year and Final Follow-Up.[a]

	1-Year Outcomes					Final-Visit Outcomes							
		Visual Acuity (logMAR)		No. Injections			Central Subfield Thickness (μm)		Visual Acuity (logMAR)		Number of Injections		Follow-Up Duration (Months)	
Medication	No. Eyes	Coefficient	*P* Value	Coefficient	*P* Value	No. Eyes	Coefficient	*P* Value	Coefficient	*P* Value	Coefficient	*P* Value	Median	*P* Value[b]
ACE inhibitor	33	0.2	.18	–0.8	.28	37	–21.6	.35	0.02	.88	–1.2	.48	25.5	.29
Apixaban	7	–0.32	.34	0.5	.74	7	–13.2	.72	–0.16	.47	0	.99	16.5	.89
Aspirin 81 mg	41	–0.13	.38	–0.9	.24	53	–11.8	.6	**–0.22**	**.05**	–2.7	.08	23.1	.21
Aspirin 325 mg	13	–0.05	.79	**–2.2**	**.04**	15	0.57	.98	0.09	.57	**–4.8**	**.04**	12.4	.43
Beta-blocker	43	0.16	.29	1.2	.13	51	–41.2	.06	–0.07	.55	**3.4**	**.04**	21.9	.78
Clopidogrel	12	–0.33	.87	–1.9	.12	7	–25.5	.37	0.16	.29	–4.4	.08	30.3	.55
Fish oil	13	–0.26	.19	–0.7	.49	15	–31.8	.27	–0.1	.52	–2.3	.31	18.6	.76
Hormones	2	–0.18	.79	1.7	.6	2	–75.9	.42	–0.29	.46	–0.7	.91	10.7	.26
Insulin	23	0.16	.32	**2.4**	**<.01**	26	–4.7	.85	–0.7	.56	**3.6**	**.04**	17.3	.73
Metformin	41	–0.03	.85	–0.4	.59	51	–15.5	.5	0.67	.56	–1.2	.44	25.4	**.04**
Pioglitazone	9	0.38	.08	–1.7	.27	8	–32.4	.45	0.11	.56	–3.6	.21	14.9	.96
Rivaroxaban	4	–0.09	.8	–0.9	.71	4	86.9	.2	–0.14	.62	–0.7	.89	25.6	.41
Statin	45	0.03	.86	0.6	.42	50	–27.7	.2	–0.06	.59	1.8	.27	21.9	.22
Vitamin E	9	–0.18	.44	0	.99	10	–39.4	.31	0.08	.66	0.7	.82	23.1	.37
Warfarin	12	0.33	.11	1	.32	15	**79**	**.02**	–0.11	.49	1.3	.54	20.3	.47

Abbreviations: ACE, angiotensin-converting enzyme; logMAR, logarithm of the minimum angle of resolution.
[a]Bolded values indicate $P < .05$.
[b]Wilcoxon rank sum test.

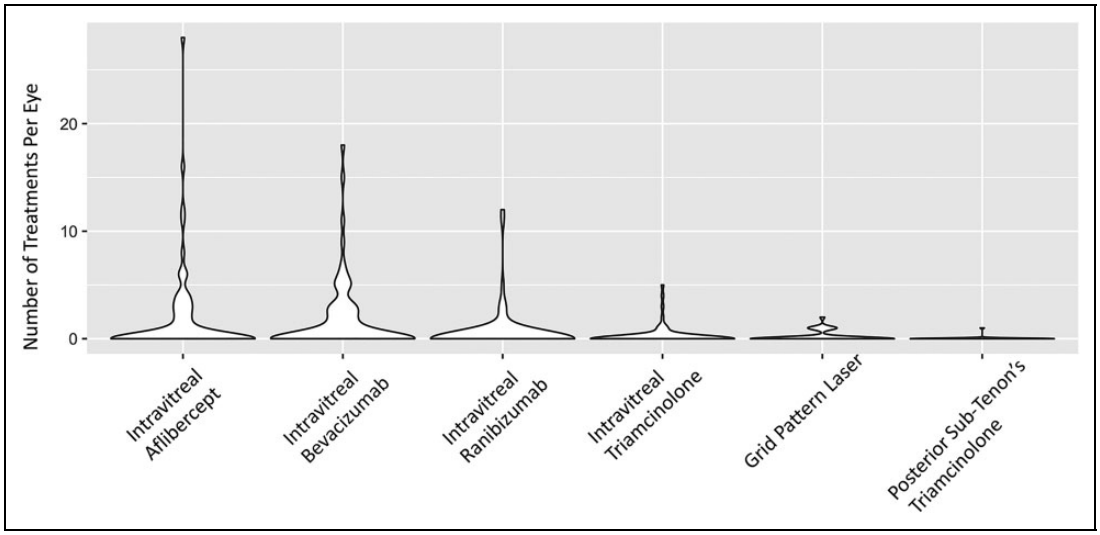

Figure 1. Violin-plot depicting the distributions of the number and type of treatments for eyes with branch retinal vein occlusion in individuals with diabetes through the final follow-up visit.

Treatment Course

The type and number of treatments are depicted in Figure 1. Sixty-two percent received intravitreal injections and 20% received grid-pattern laser photocoagulation. The mean number of injections at 1 year was 2.95. For those with >1 year of follow-up, the mean number of injections was 6.86 at the final visit. There was no association with baseline or final HbA1c and type of treatment.

Discussion

BRVO outcomes have not been studied comprehensively in diabetics. Our study has 3 key areas of interest among diabetics with a macula-involving BRVO: 1) VA and treatment frequency of diabetics compared with nondiabetics as is reported in the literature; 2) The relationship of glycemic control on VA and treatment burden; 3) The impact of systemic medications on VA and treatment burden.

BRVO Outcomes in Diabetics

We found diabetic eyes presented with an average logMAR VA of 0.56 (Snellen equivalent, 20/72). At 1 year, eyes had an average logMAR VA of 0.57 (20/73) and required an average of 2.95 injections. Diabetic eyes had a final average logMAR VA of 0.52 (20/65), with a median follow-up duration of 19.5 months. In our cohort, the presenting VA was similar to other studies on nondiabetic eyes, but our cohort's VA at 1 year was worse in comparison. The Branch Retinal Vein Occlusion: Evaluation of Efficacy and Safety (BRAVO) trial evaluated intravitreal ranibizumab in 265 eyes with macular edema from BRVO.[11] For eyes with a presenting VA of $\geq$55 ETDRS letters (approximately >20/80) in that study, eyes gained 13 letters on average at 6 months (approximately 20/40 to 20/50). Although the BRAVO trial did not evaluate the effect of diabetes, they excluded eyes with diabetic retinopathy. In the Standard Care vs COrticosteroid for REtinal Vein Occlusion (SCORE)-BRVO trial evaluating intravitreal triamcinolone vs grid photocoagulation, 52 of the 352 BRVO eyes enrolled (14%) were in patients with diabetes.[12] The mean baseline VA was 57.4 letters (approximately 20/70), which improved on average to 61.8. letters at 1 year (approximately 20/60) for the triamcinolone treatment arms. The outcomes for eyes with diabetes were not reported separately. It is difficult to compare our findings of mean VA of 20/65 at final follow-up with other studies, as study patients had variable time to presentation following BRVO onset and variable follow-up duration.

Our study suggests diabetic eyes with BRVO have a worse visual outcome at 1 year than nondiabetics. A possible explanation could be that diabetic eyes with BRVO may have more macular ischemia. Fluorescein angiograms were not routinely obtained on these patients, and we were unable to grade and monitor the degree of macular ischemia over time in this study, but it warrants further investigation. It is noteworthy that our findings of worse visual outcome have been corroborated in a small study reporting a mean VA of 20/63 in 28 diabetic eyes compared with 20/40 in 49 nondiabetic eyes at 1 and 2 years, although the primary treatment modality was grid-pattern laser.[14]

In our study, the number of injections that diabetic eyes required at 1 year is slightly higher than anti-VEGF treat-as-needed regimens for ranibizumab and bevacizumab. In a review of 21 eyes with BRVO on a treat-as-needed protocol with intravitreal ranibizumab, the average baseline VA was 20/72. The mean number of injections was 2.1, and mean VA was 20/40 at 1 year.[8] In a prospective trial evaluating intravitreal bevacizumab given on a treat-as-needed regimen in 25 BRVO eyes, the baseline VA was 20/63. The mean number of injections was also 2.1 and VA was 20/42 at 1 year.[9] Neither of these studies noted whether patients had diabetes mellitus, but eyes with diabetic retinopathy were excluded.

Glycemic Control

We found that worse glucose control and use of insulin were associated with a greater number of intravitreal injections both at 1 year and at final follow-up despite similar final CST and mean follow-up duration. It is unlikely that insulin itself led to persistent or recurrent CME, but rather that insulin use may be a marker of poorer diabetic control. We attempted to minimize any contribution of DME to our study by excluding eyes being treated for DME in the year prior to BRVO, but it is possible there was a component of DME in those with BRVO-related CME as well. One plausible explanation is that poorly controlled diabetes is associated with worse retinal vascular integrity, leading to recalcitrant vascular leakage after a sudden ischemic insult such as a BRVO. Thus, while poorly controlled diabetics may have responded well to anti-VEGF injections as evidenced by the similar CST and VA to those with better glycemic control, the effect of the anti-VEGF injections was shorter lived.

Aspirin

High-dose aspirin was associated with fewer injections at 1 year and fewer injections at final follow-up, although this trend was not significant for low-dose aspirin. To further evaluate these findings, our analysis was performed on a subset of patients who did not receive treatment prior to being evaluated at our institution and had greater than 1 year of follow-up. This subset also showed fewer injections with any aspirin use, but there were insufficient numbers to further divide aspirin into high-dose and low-dose in this analysis. It may be that high-dose aspirin assists in preventing platelet aggregation, thereby promoting faster reperfusion and resolution of macular edema, whereas low-dose aspirin does not confer such benefit or confers a weaker benefit that was not able to be detected at a statistically significant level in our study. In cardiovascular research, high-dose aspirin did not confer additional benefit over low-dose aspirin in the prevention of major cardiovascular events in patients undergoing percutaneous coronary intervention.[21] There have been no studies evaluating aspirin 325 mg in BRVO, but in a related prospective study of 42 patients with BRVO, ticlodipine decreased platelet aggregation in venous blood samples, whereas aspirin 100 mg did not.[22]

Warfarin

The significance of warfarin's association with increased final CST is unclear. Anticoagulants have been associated with greater intraretinal hemorrhage and poorer VA in central and hemiretinal vein occlusions.[23] A similar study has not been conducted for BRVO but is currently being studied by our clinical research team. Warfarin may affect vascular properties; in mice, warfarin increased lung alveolar hemorrhage because of increased vascular permeability, but a similar study has not been published for the retina.[24]

Beta-Blockers

Despite our significant finding of beta-blocker use associated with greater number of injections at final follow-up, there may be no direct relationship of oral beta-blocker use to the treatment burden. Instead, this finding may possibly be related to the degree of hypertension in those patients who required beta-blockade in addition to the typical first-line medication, lisinopril. This relationship may be tenuous as it was not found at 1 year or among patients with >1 year follow-up in our study. The effect of beta-blockade on retinal vein occlusion has not been evaluated in the existing literature. Oral propranolol has been shown to decrease exercise-induced retinal arteriolar constriction, and topical betaxolol and timolol have been shown to increase retinal blood flow.[25,26] In neovascular age-related macular degeneration, beta-blockers have been inconsistently linked to reduced anti-VEGF treatment.[27,28] Further research is needed to clarify whether there is a relationship between beta-blocker use and BRVO both in diabetic and nondiabetic patient populations.

Metformin

Despite previously published findings supporting metformin's protective effect in preventing diabetic retinopathy and reducing the incidence of BRVO in the diabetic population, our study did not find a beneficial effect of metformin use on BRVO outcomes in diabetics. Note that our study did not evaluate the incidence of BRVO in diabetics. It may be that metformin reduces the risk of developing a BRVO in diabetics but does not have an effect on outcomes. Our study suggests the protective effects of metformin on the severity of diabetic retinopathy do not translate to BRVO. In several retrospective reviews of type 2 diabetics, metformin use was associated with a lower incidence and severity of diabetic retinopathy.[17,18] In mouse models of ischemic retinopathy and diabetic retinopathy, metformin reduced the extent of neovascularization, VEGF protein translation, and VEGF receptor expression, though it did not reduce the extent of avascular retina.[29,30] More studies are needed to duplicate a relationship or lack thereof between metformin use and BRVO.

Limitations

Our study has several limitations. As the data were collected retrospectively, there was no established treatment protocol and time to presentation was variable as was follow-up duration. Additionally, as this was a study of diabetic patients, it may be challenging in some eyes to differentiate the contribution of BRVO-related CME and DME to the macular thickening. We attempted to minimize this uncertainty by excluding patients being treated for DME in the year prior to the diagnosis of BRVO. A few patient subsets also had low numbers, increasing the risk of type II errors. Although we did record the presence of NPDR or PDR at baseline, we did not further classify the severity of the diabetic retinopathy at baseline or reevaluate

whether the retinopathy, when present, changed over the course of treatment; therefore, this limits our ability to analyze the effect of diabetic retinopathy on BRVO outcomes. Prospective trials would be helpful in further exploring the relationship of glycemic control and the role of systemic medications on BRVO outcomes in individuals with diabetes mellitus.

Conclusions

The VA outcome of BRVO in diabetics may be slightly worse than BRVO in nondiabetics. Poorly controlled diabetes and insulin use were associated with a greater burden of intravitreal anti-VEGF injections. High-dose aspirin was associated with fewer injections at 1 year and final follow-up. Warfarin was associated with greater CST at final follow-up. Metformin did not have a significant association with final VA or treatment burden.

Ethical Approval

Ethical approval for this study was obtained from the Duke University Institutional Review Board (approval number Pro00075701).

Statement of Informed Consent

Informed consent was not sought for the present study because it was a retrospective review of data already collected.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: SF is a consultant to Regeneron and receives patent royalties from Alcon. The other authors declare that there is no conflict of interest.

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