ORIGINAL RESEARCH

Demographic, Socioeconomic, and Clinical Factors Associated with Severe Vision Loss in Patients with Neovascular Glaucoma

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Purpose: To investigate the association between demographic, socioeconomic, and clinical factors and severe vision loss in patients with neovascular glaucoma (NVG).

Patients and Methods: A retrospective chart review of patients referred to the University of Virginia (UVA), diagnosed with NVG, and treated for NVG between January 2010 and December 2020 was performed. Patients were grouped according to vision outcomes after 1 year of treatment: mild – moderate vision loss (best corrected visual acuity [BCVA] > light perception [LP]) and severe vision loss (BCVA ≤ LP). The associations between patient characteristics and BCVA were also examined.

Results: Of the 89 patients (99 eyes), those with progression to severe vision loss presented with higher intraocular pressure (IOP) (p < 0.001) and lower visual acuity (p = 0.003) on average. However, there was no difference in IOP between the vision loss groups after one year of treatment. Univariate analysis showed a moderate association between a history of type 2 diabetes mellitus (T2DM) and severe vision loss (p = 0.033). Increasing age was associated with an increased likelihood of progression to severe vision loss (odds ratio [OR] 1.074, p = 0.008). Females were more likely to exhibit severe vision loss (OR 3.281, p = 0.036). Patients with Medicare (OR 0.098, p = 0.005) or private insurance (OR 0.110, p = 0.006) were less likely to progress to severe vision loss than those without insurance.

Conclusion: Progression of vision loss in patients with NVG may be influenced by the stage of disease at diagnosis, age, sex, T2DM, and insurance status.

Keywords: glaucoma, vision loss, risk factors, disease progression

Introduction

Neovascular glaucoma (NVG) is a severe type of secondary glaucoma, characterized by neovascularization in the anterior chamber of the eye. Neovascularization leads to trabecular meshwork dysfunction and elevated intraocular pressure (IOP). Early recognition and treatment are crucial to prevent or delay the development of sight-threatening complications and thus necessary to provide the best possible outcomes in patients with NVG.[1] Unfortunately, many patients with NVG present with refractory disease that is challenging to manage. NVG treatment aims to reduce IOP and the ischemic drive that causes new vessel formation. Often, a combination of medical, procedural, and surgical interventions is used in treatment, but there is a lack of randomized control trials and high-quality evidence demonstrating which interventions are most efficacious in managing NVG.[2–5] Even with a combination of multiple interventions, the outcomes of NVG are often poor and result in significant, irreversible vision loss.[6,7]

Understanding the risks for developing NVG is important for the prevention and treatment of disease. Although there is extensive research describing the risk factors for developing NVG[8,9] such as central retinal vein occlusion, proliferative diabetic retinopathy (PDR), and ocular ischemic syndrome, there are significantly fewer data investigating the predictive factors of disease progression. The limited studies available have primarily focused on predictors of

surgical outcomes, and even less data exist that analyze the associations of socioeconomic status and NVG.[10–16] Of these studies, none investigate socioeconomic and demographic factors in relation to overall disease progression independent of specific surgical outcomes.[17,18] In comparison, there has been extensive research in other medical specialties examining the impact of socioeconomic characteristics on healthy aging and health outcomes.[19–25] These studies have led to a better understanding of disease risk factors, disease management, and improved healthcare practices.

Given that literature on the relationship between demographic, socioeconomic, and clinical characteristics with disease progression in patients with NVG is limited, this study investigated the association between these variables and disease progression to provide better insights for individualizing treatment and optimizing visual outcomes.

Materials and Methods

Study Design

This single-center retrospective chart review was approved by the Institutional Review Board of the University of Virginia (UVA) and adhered to the Declaration of Helsinki. As this study analyzed de-identified data, the review board exempted it from requiring patient consent. The medical records of all patients referred to the UVA Health System Ophthalmology Department who were newly diagnosed with NVG and received treatment between January 2010 and December 2020 were reviewed.

Patients who received treatment for NVG prior to their referral appointment, presented with no light perception in the affected eye(s), did not receive treatment for NVG at UVA after diagnosis, or were lost to follow-up within the 1-year period after initial treatment were excluded from analysis. For patients with bilateral NVG (10 patients, 20 eyes), both eyes were included and analyzed separately.

The remaining patients were divided into two categories to assess disease progression: patients with mild - moderate vision loss 1 year after initiating treatment for NVG and patients with severe vision loss 1 year after initiating NVG treatment. Severe vision loss was defined as patients whose best corrected visual acuity (BCVA) declined to light perception only (LP) or no light perception (NLP). Mild - moderate vision loss was defined as BCVA that remained better than LP/NLP one year after the initial treatment for NVG.

Study Cohort

We collected information on the patients' demographic characteristics, including age at the date of diagnosis, sex, and race. Medical history and patient characteristics included medical risk factors (type 2 diabetes mellitus (T2DM), hypertension (HTN), or hyperlipidemia (HLD)), prior diagnosis of glaucoma, number of prescribed glaucoma medications at initial presentation, and treatment modalities (medical, procedural, and surgical). Lastly, the socioeconomic data gathered from these patients included primary insurance coverage, national Area Deprivation Index (ADI), Median Household Income (MHI), travel distance from home to the UVA ophthalmology clinic, and the number of missed follow-up appointments in the 1-year period after initiating treatment for NVG. The national ADI and MHI were obtained using patients' home zip codes. National ADI data were obtained from the Neighborhood Atlas of the University of Wisconsin–Madison School of Medicine and Public Health.[26] MHI data were obtained from the United States Census Bureau.[27] The distance between patients' homes and the UVA ophthalmology clinic was calculated using the CDXGeoData Excel add-on. BCVA and intraocular pressure (IOP) were recorded at the initial visit, 6-month follow-up, and 1-year follow-up appointments after initial NVG treatment.

Statistical Analysis

Data analysis was performed using SPSS Statistics v.29.0 (IBM Analytics, Chicago, IL, USA). Two-sided Student's t-tests and chi-square test (Fisher's exact test) were used to compare continuous and categorical variables between each group in univariate analysis. Binary logistic regression was performed for variants with a P value < 0.10 shown in univariate analysis. Statistical significance was set at $P < 0.05$.

A sensitivity analysis was performed by including only one eye per patient. If a patient had bilateral NVG, the first eye diagnosed was included in the analysis. If a patient presented with bilateral NVG at the first appointment, both eyes were removed from the analysis to avoid confounding variables.

Results

A total of 254 patients (261 eyes) were referred to UVA Ophthalmology and were diagnosed with NVG between January 2021 and December 2020. After applying the exclusion criteria, 89 patients (99 eyes) were included in this analysis. Univariate analysis of the baseline characteristics of the groups is shown in Table 1. The average age at

**Table 1** Univariate Analysis Identifying Potential Predictors of Vision Loss

		Mild-Mod Vision Loss (n = 74)	Severe Vision Loss (n = 25)	Total (n = 99)	P value
Demographic					
Age at diagnosis, mean (SD), years		62 (12.3)	71 (13.9)	64 (13.3)	0.005*
Sex: females, No. (%)		22 (29.7)	17 (68.0)	39 (39.4)	<0.001*
Race, No. (%)	White	42 (56.8)	13 (52.0)	55 (55.5)	0.887
	Black	18 (24.3)	8 (32.0)	26 (26.3)	
	Hispanic	8 (10.8)	2 (8.0)	10 (10.1)	
	Other	6 (8.1)	2 (8.0)	8 (8.1)	
Clinical History					
Risk Factors, No. (%)	T2DM	60 (81.1)	15 (60.0)	75 (75.7)	0.033*
	HTN	43 (58.1)	16 (64.0)	59 (59.6)	0.604
	HLD	32 (43.2)	7 (28.0)	39 (39.4)	0.177
Prior Dx of Glaucoma, No. (%)		11 (14.8)	7 (28.0)	18 (18.2)	0.141
Number of Glaucoma Medications, mean (SD)		2.15 (1.5)	2.32 (1.5)	2.39 (1)	0.317
Socioeconomic					
Insurance, No. (%)	None	6 (8.1)	9 (36.0)	15 (15.1)	0.002*
	Private	19 (25.7)	2 (8.0)	21 (21.2)	
	Medicare	43 (58.1)	14 (56.0)	57 (57.6)	
	Medicaid	6 (8.1)	0 (0.0)	6 (6.1)	
Area Deprivation Index, mean (SD)		53 (23.8)	57 (21.3)	54 (23.2)	0.584
Mean Household Income, mean (SD), thousands		68 (21.4)	60 (16.7)	66 (20.5)	0.055
Distance from UVA, mean (SD), miles		53 (50.4)	43 (26.7)	50 (45.7)	0.461
Missed follow-up appointments, mean (SD)		2 (2.0)	2 (2.2)	2 (2.1)	0.839
Intervention					
Treatment: Anti-VEGF Injections, No. (%)		44 (59.4)	18 (72.0)	62 (62.6)	0.336
Treatment: Surgical, No. (%)	None	24 (32.4)	10 (40.0)	34 (34.3)	0.714
	AGV	41 (55.4)	13 (52.0)	54 (54.5)	
	Baerveldt	6 (8.1)	2 (8.0)	8 (8.1)	
	Trabeculectomy	3 (4.1)	0 (0.0)	3 (3.0)	
Treatment: Procedural, No. (%)	None	32 (43.2)	16 (64.0)	48 (48.4)	0.201
	PRP	29 (39.2)	8 (32.0)	37 (37.4)	
	Anterior Chamber Tap	7 (9.5)	1 (4.0)	8 (8.1)	
	Cyclophotocoag-ulation	6 (8.1)	0 (0.0)	6 (6.1)	

Note: *Statistically significant P<0.05.

diagnosis of the severe vision loss group (71.04 ± 13.9, years) was significantly older than the mild - moderate vision loss group (61.76 ± 12.3, years) (p = 0.005). There was also a significant difference in the proportion of males to females between the vision loss groups (mild - moderate: 22 females (29.7%); severe: 17 females (68.0%); p = <0.001). Those who progressed to severe vision loss also presented, on average, with worse BCVA than those with mild - moderate vision loss (severe: LogMAR 2.22 ± 0.5; Median: HM (20/200 - LP) vs mild - moderate: LogMAR 1.43 ± 0.8; Median: 20/200 (20/25 - LP); p = 0.003) (Figure 1). Those who progressed to severe vision loss also presented with significantly higher IOP (severe: 47.70 ± 14.3 vs mild - moderate: 40.86 ± 13.3; p < 0.001) (Figure 2). Lastly, a significant association was found between the type of insurance and vision loss (p = 0.002) as well as a history of T2DM and vision loss (p = 0.033). There were no significant differences in race, ADI, MHI, travel distance to UVA, number of missed follow-up appointments, history of hypertension (HTN), hyperlipidemia (HLD), or previous glaucoma diagnosis, number of glaucoma medications, or treatment modalities between the two groups in univariate analysis (Table 1).
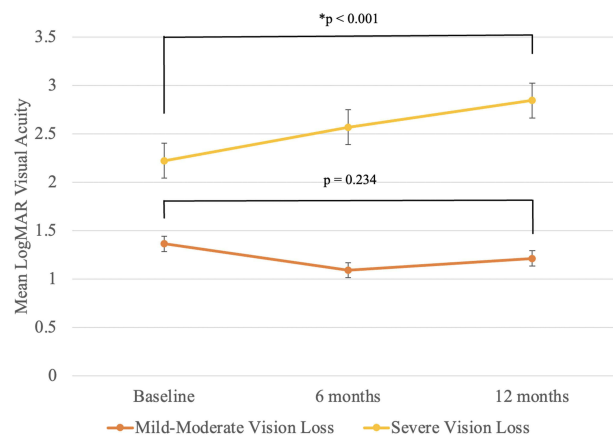
Figure 1 Comparison of Mean LogMAR BCVA of Patients with Mild - Moderate Vision Loss vs Severe Vision Loss. The average BCVA (LogMAR) of the mild - moderate vision loss group was 1.36 ± 0.8 at presentation, 1.09 ± 0.7 at 6 months after initiating treatment, and 1.21 ± 0.7 at 1 year. There was no significant difference between the average BCVA at 1 year versus the average BCVA at presentation (p=0.234). The average BCVA (LogMAR) of the severe vision loss group was 2.22 ± 0.5 at presentation, 2.57 ± 0.4 at 6 months after initiating treatment, and 2.84 ± 0.1 at 1 year. The average vision at 1 year was significantly worse than the average BCVA at presentation (p<0.001). The average BCVA of the severe vision loss group was significantly worse than the mild - moderate group at each timepoint (p<0.001, p<0.001, p<0.001). *statistically significant P<0.05.
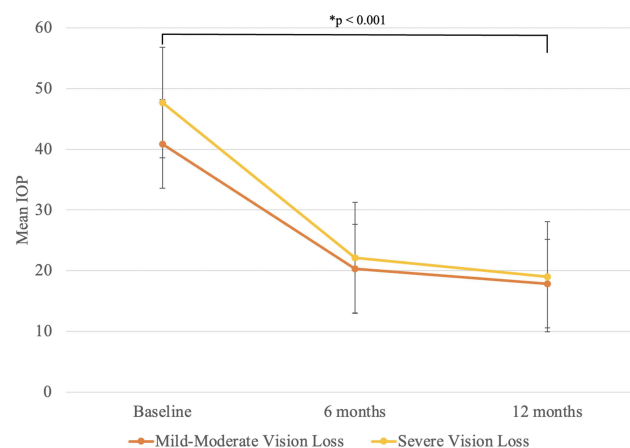
Figure 2 Comparison of Mean IOP of Patients with Mild - Moderate Vision Loss vs Severe Vision Loss. The average IOP of the mild - moderate vision loss group was 40.86 ± 13.3 at presentation, 20.30 ± 8.9 at 6 months after initiating treatment, and 17.85 ± 6.9 at 1 year. The average IOP at 1 year was significantly lower than the average IOP at presentation (p<0.001). The average IOP of the severe vision loss group was 47.70 ± 14.3 at presentation, 22.14 ± 15.9 at 6 months after initiating treatment, and 19.00 ± 15.5 at 1 year. The average IOP at 1 year was significantly lower than the average IOP at presentation (p<0.001). The average IOP of the severe vision loss group was significantly worse than the IOP of the mild - moderate vision loss at presentation (p = 0.032), but not significantly different at 6 months and 1 year (p = 0.618 and p = 0.613, respectively). *statistically significant P<0.05.

Table 2 Multivariate Analysis for Severe Vision Loss

	Odds Ratio	95% Confidence Interval	P value
Age at Diagnosis, years	1.074	1.019–1.132	0.008*
Sex: female	3.281	1.078–9.984	0.036*
T2DM	0.324	0.087–1.211	0.094
Primary Insurance Coverage			
Medicaid	0.000	0.000	0.999
Medicare	0.098	0.019–0.500	0.005*
Private	0.110	0.016–0.771	0.006*
Constant	0.011		0.026

Note: *Statistically significant P<0.05.

In evaluating the change in IOP and BCVA over time, both groups had a significant decrease in IOP 1 year after initiating treatment compared to their average IOP at diagnosis (1 year: mild - moderate: 17.85 ± 6.9, p < 0.001; severe: 19.00 ± 15.5, p < 0.001) (Figure 2). The differences in IOP between the two groups were not statistically significant at 6 months (p = 0.618) or 1 year (p = 0.613) after treatment initiation (Figure 2). The average BCVA of the severe vision loss group significantly declined 1 year after treatment initiation (1 year: logMAR 2.84 vs initial: 2.22; p < 0.001). In comparison, the average BCVA of the mild - moderate vision loss group was not significantly worse 1 year after initiating treatment compared to the average BCVA at diagnosis (1 year: logMAR 1.21 vs initial: 1.36; p = 0.234) (Figure 1).

In binary logistic regression analysis (Table 2), increasing age at diagnosis was associated with an increased likelihood of severe vision loss over time (odds ratio [OR] 1.074, p = 0.008). Female patients were also more likely to exhibit severe vision loss (OR 3.281, p = 0.036). Patients with Medicare (OR 0.098, p = 0.005) or private insurance (OR 0.110, p = 0.006) were less likely to progress to severe vision loss than those without insurance. There was no significant association between BCVA outcomes and patients with T2DM (p = 0.094) or Medicaid insurance (p = 0.999) in binary logistic regression analysis.

Sensitivity analysis was performed (n = 79) as shown in Supplemental Table 1. All significant relationships remained significant (p < 0.05), with some change in the strength of the significance, except for the relationship between a medical history of T2DM and vision outcomes (p = 0.116).

Discussion

The main objective of this study was to better understand the demographic, socioeconomic, and clinical characteristics that may increase the risk of significant progression of vision loss in patients with NVG. Overall, we found that older age at diagnosis, female sex, and a history of T2DM were associated with progression to severe vision loss (LP or NLP). Additionally, patients with Medicare or private insurance were less likely to progress to severe vision loss than those without medical insurance.

When analyzing the BCVA and IOP between the patient groups, the severe vision loss group presented on average with significantly lower visual acuity and significantly higher IOP than the mild - moderate vision loss group (Figures 1 and 2). The severe vision loss group also lost significantly more vision during the 1 year after initiating treatment than the mild - moderate group. The mild - moderate vision loss group did not show a significant difference between the average BCVA at diagnosis versus 1 year after initiating treatment. Together, these data suggest that those with severe vision loss presented at their initial visit with more severe, advanced disease that was more refractory to treatment. The significantly older average age in the severe vision loss group also supports the conclusion that these patients presented later in their disease course (Table 1). Interestingly, patients in the severe vision loss group experienced significant disease progression despite treatment, with a substantial response in IOP reduction. Similarly, the average IOP in the mild - moderate vision loss group also decreased significantly after a year of treatment, suggesting successful management of elevated IOP in both groups. Additionally, there was no significant difference between the average IOP of the two vision groups at both 6 months and 1 year after initial treatment. The continued decline in vision in the severe vision loss group despite improved IOP suggests that individuals who present at later stages of disease with worse BCVA may require more aggressive initial

treatment or treatment escalation to save their remaining sight. This conclusion has been similarly suggested in previous studies on patients with primary open angle glaucoma[28,29] and one case of NVG.[30] Diniz-Filho et al's study on IOP control in patients with primary open-angle glaucoma suggested that even 1 mmHg increase in IOP can impact the risk of progression.[31] Although this concept has not been specifically investigated in patients with NVG, lower IOP goals in patients with advanced stages of disease may be useful in preserving sight.

The question remains regarding which other characteristics are unique to patients in the severe vision loss group that may contribute to their later presentation and subsequent poorer outcomes. Males were less likely to progress to severe vision loss than females. Patients with Medicare or private health insurance were less likely to progress to severe vision loss than those without medical insurance (Table 2). However, no significant association was found between visual outcomes and patients with Medicaid. The impact of health insurance on patient healthcare utilization and health outcomes has been well-studied across medical specialties. Many studies have found that having health insurance is associated with better healthcare utilization and health outcomes among all ages.[32–39] Private insurance holders have consistently better outcomes than other insurance holders/uninsured patients in these studies, while patients with Medicaid have varying associations with outcomes comparatively.[40–42] In ophthalmology, Hwang et al showed that private health insurance was the main factor in ophthalmic resource utilization.[43] Additionally, Lee et al found that patients with Medicaid had more difficulty obtaining eye care appointments compared to patients with private insurance, indicating a barrier imposed by Medicaid and an inequality between different insurances.[44] Our findings associating Medicare and private primary payer status with better vision outcomes in patients with NVG parallel the results of many other studies among different specialties and overall patient health outcomes.

Surprisingly, there was no significant difference in the number of missed follow-ups, travel distance to UVA, mean household income, or area deprivation index between the two groups (Table 1). Previous ophthalmology studies have shown that lower income,[45,46] greater distance from ophthalmologic care,[45,47] and more missed doctor appointments in other specialties[48] are associated with increased loss to follow-up, lower odds of seeing an eye doctor, and poor medical adherence. In comparison, higher income and education have been associated with better visit adherence.[46] In patients with NVG specifically, Shalaby et al found lower-income may be associated with worse BCVA outcomes following NVG tube shunt surgery.[17] In contrast, we did not find any association between the aforementioned variables and vision outcome, although it is possible that some variable associations with stronger relationships with vision outcomes were limited by sample size.

Patients with a history of T2DM were slightly more likely to progress to severe vision loss (Table 1). However, there was no association between a history of T2DM and vision loss in binary logistic regression analysis (Table 2). The association between T2DM and NVG has been well studied and established, as NVG is an advanced manifestation of PDR.[8,49] This study suggests that patients with diabetes may have more significant disease progression than those without diabetes, although future studies with larger patient populations would better determine the strength of this relationship. Finally, no specific associations were found between other medical risk factors (HTN and HLD), the number of glaucoma medications the patient was prescribed and taking, or the types of treatment inventions and visual outcomes. The lack of association between treatment interventions and vision outcomes is particularly interesting, as many studies have focused on comparing vision outcomes between different types of surgeries or other interventions. However, the limited studies comparing interventions and outcomes have varying conclusions[3,15] and can be difficult to compare, as outcomes are often defined differently between studies.[2,12]

This study had some limitations. First, the study had limited and unbalanced subgroup sizes, although the total NVG sample size was considerable compared to other similar studies.[13,14,16] This study also used the United States Census Bureau data by zip code to report mean household income, as in previous studies, as opposed to using individual patient-reported income.[50–52] Finally, when evaluating treatment interventions, individual treatments were evaluated in relation to vision outcomes; however, specific combinations of multiple treatment interventions were not evaluated. The strengths of this study include a sensitivity analysis, which supported the study results. This minimized the uncertainty concerning confounding variables in including two eyes of the same patient.

Conclusion

In summary, we evaluated the association between NVG disease progression and patient demographic, socioeconomic, and clinical characteristics. On average, patients who progressed to LP or NLP 1 year after initiating treatment presented with a higher baseline IOP and worse BCVA at diagnosis than those with less severe vision loss. Our results suggest that older age at diagnosis and female sex are strongly associated with progression to severe vision loss, whereas a history of T2DM is moderately associated with severe vision loss. In contrast, patients with Medicare or private insurance were less likely to progress to severe vision loss than those without insurance. Additional studies across centers with larger sample sizes are warranted to further investigate and reinforce the relationship between socioeconomic and demographic variables and BCVA outcomes. Future prospective studies examining more aggressive treatments and lower IOP goals for patients who present with later stages of disease may help guide clinicians in providing individualized care for patients with NVG for more optimized visual outcomes.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

Disclosure

The authors report no conflicts of interest in this work.

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