Original article

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Neovascular glaucoma as a chronic neuroischemic optic neuropathy: the impact of cumulative burden on vision-related quality of life in a 36-month prospective study

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Purpose. To evaluate the impact of treatment burden as a functional marker of chronic neuroischemic optic neuropathy progression on vision-related quality of life in patients with neovascular glaucoma.

Methods. This prospective cohort study included 351 patients (351 eyes) with secondary neovascular glaucoma associated with proliferative diabetic retinopathy or retinal vein occlusion. Patients were followed for 36 months. Vision-related quality of life was assessed using the validated NEI VFQ-25 questionnaire at baseline, 12 months, and 36 months. Cumulative Burden Index (CBI) was defined as a composite cumulative measure incorporating both treatment intensity (number of transscleral cyclophotocoagulation (TSCPC) procedures) and disease-related burden (severity of complications present at baseline and during follow-up). Statistical analysis included descriptive statistics, linear and logistic regression, ROC analysis, and multilayer perceptron (MLP) neural network modeling.

Results. Patients with successful treatment outcomes (n = 282; 80.3%) demonstrated improvement in vision-related quality of life (ΔQoL = +10.26 ± 6.18), whereas patients with resistant disease (n = 69; 19.7%) showed significant deterioration (ΔQoL = −7.43 ± 6.97; $p < 0.001$). Higher CBI values were independently associated with lower NEI VFQ-25 scores (β = −1.78; 95% CI −2.57 to −0.99; $p < 0.001$). The between-group difference corresponded to a very large clinical effect size (Cohen's d = 2.77). In the logistic regression model, CBI remained an independent predictor of unfavorable treatment outcome (OR = 0.48; 95% CI 0.34–0.68; $p < 0.001$). The neural network model demonstrated good discriminative performance for outcome prediction (AUC = 0.83; 95% CI 0.78–0.88).

Conclusions. The CBI was independently associated with vision-related quality of life in patients with neovascular glaucoma and may serve as an integrated marker of chronic neurovascular disease burden. Increased CBI values were associated with significant functional impairment and a poorer clinical prognosis. Integration of composite clinical indices with machine learning approaches may improve risk stratification, personalized treatment planning, and digital clinical decision support in patients with neovascular glaucoma.

Keywords: *neovascular glaucoma; neuroischemic optic neuropathy; proliferative diabetic retinopathy; retinal vein occlusion; transscleral cyclophotocoagulation; Cumulative Burden Index; NEI VFQ-25; neural network analysis*

Introduction

Neovascular glaucoma (NVG) is one of the most severe forms of secondary glaucoma, characterized by an aggressive clinical course, treatment resistance, and a high risk of vision loss [1, 2]. It may be considered not only an ocular hypertensive disorder but also a form of chronic neuroischemic optic neuropathy, in which mechanical injury, ischemia, systemic inflammation, and progressive neurodegeneration of the visual pathway converge [3, 4].

Chronic retinal ischemia is associated with an energy deficit in retinal ganglion cells, activation of oxidative stress, impaired axonal transport, and glutamate accumulation, thereby triggering a cascade of excitotoxicity [5, 6]. Excessive activation of N-methyl-D-aspartate (NMDA) receptors leads to intracellular calcium overload, mitochondrial dysfunction, and subsequent activation of apoptotic pathways [7].

Neuroinflammation plays an important role in the progression of glaucomatous optic neuropathy. Microglial activation, endothelial dysfunction, and increased expression of intercellular adhesion molecules contribute to persistent neuronal injury even after partial stabilization of intraocular pressure (IOP) [5].

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Oxidative stress and vascular dysregulation establish a self-perpetuating cycle of ischemic and inflammatory injury to retinal ganglion cells. Apoptosis represents a final common mechanism of retinal ganglion cell death, involving activation of both intrinsic (mitochondrial) and extrinsic (death receptor-mediated) pathways [6, 7].

In addition to local retinal and optic nerve head injury, transsynaptic degeneration has been described in glaucoma, extending to the lateral geniculate nucleus and visual cortex [4, 8]. These findings support the concept that glaucoma is a systemic neurodegenerative process involving central components of the visual system.

Current approaches to the treatment of secondary NVG include pharmacological, laser, and surgical interventions. Transscleral cyclophotocoagulation (TSCPC) is widely used in refractory forms of the disease [9–12]. The management of such patients is often multistage and associated with a substantial treatment burden due to repeated interventions and the development of complications.

In patients whose affected eye is the only seeing eye, as well as in those with relatively preserved visual acuity at treatment initiation, even moderate deterioration in visual function or treatment-related complications may result in a substantial reduction in daily activities and quality of life [13, 14]. Overall, glaucoma imposes a considerable functional, social, and economic burden on patients [15,16], while quality of life is determined not only by the degree of visual dysfunction but also by the complexity and intensity of treatment [17, 18]. Therefore, vision-related quality of life may be regarded as an integrated functional indicator reflecting the cumulative neurodegenerative burden of the disease. Reduced scores on the validated National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25) in patients with a high treatment burden may indicate the accumulation of chronic neurovascular injury and progressive loss of retinal ganglion cells [5].

Furthermore, treatment adherence and the effectiveness of physician–patient communication are important determinants of treatment outcomes. Poor adherence has been shown to be associated with reduced quality of life, whereas effective communication contributes to improved clinical and functional outcomes [19, 20]. In this context, treatment complexity, intervention frequency, and associated complications may not only influence the clinical course of the disease but also shape patients' subjective perception of treatment burden, thereby directly affecting quality-of-life measures. This provides a rationale for the use of composite indicators that integrate disease characteristics, treatment intensity, and their impact on patients' quality of life.

Objective: To evaluate the impact of treatment burden as a functional marker of chronic neuroischemic optic neuropathy progression on vision-related quality of life in patients with neovascular glaucoma.

Materials and methods

Study design and patient characteristics

A prospective cohort study was conducted involving 351 patients with secondary NVG associated with proliferative diabetic retinopathy (214 patients, 61.0%) or resulting from retinal vein occlusion (137 patients, 39.0%), who underwent diode TSCPC.

Patients were consecutively enrolled in the study at the Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine between 2019 and 2023. The follow-up period after the laser intervention was 36 months (***Fig. 1***).

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the local ethics committee. All patients provided written informed consent to participate in the study.

Inclusion criteria:

- established diagnosis of secondary NVG associated with proliferative diabetic retinopathy or resulting from retinal vein occlusion;
- presence of iris or anterior chamber angle neovascularization (NVI/NVA; Weiss) [21], confirmed by biomicroscopy and gonioscopy;
- indications for TSCPC (ocular pain or uncontrolled IOP despite maximal medical therapy);
- availability of clinical follow-up data for at least 36 months.

Exclusion criteria:

- previous cyclodestructive procedures;
- surgical interventions (antiglaucoma surgery or cataract surgery) within 6 months before study enrollment;
- severe ocular trauma;
- intraocular neoplasms;
- cognitive impairment preventing completion of the quality-of-life questionnaire (NEI VFQ-25);
- incomplete examination data, including missing follow-up data from scheduled visits;
- a follow-up period of less than 36 months for any reason.

Clinical ophthalmological examination

All patients underwent a standard ophthalmological examination before treatment and during scheduled follow-up visits.

The examination included:

- assessment of best-corrected visual acuity (BCVA);
- biomicroscopy of the anterior segment and ophthalmoscopy;
- Goldmann applanation tonometry;
- gonioscopy.

Laser treatment

TSCPC was performed using an 810-nm diode laser and a standard contact G-probe. The laser parameters were as follows: power, 1000–1500 mW; pulse duration, 2 s. Twenty to 24 laser applications were delivered 1.5 mm posterior to the limbus over approximately 270° of the scleral circumference, avoiding the 3- and 9-o'clock positions [22]. Repeat procedures were performed in cases of inadequate IOP control or the development of ocular pain during follow-up.

Assessment of quality of life

Vision-related quality of life was assessed using the validated NEI VFQ-25 questionnaire at three time points: before treatment ($QoL_{-baseline}$), at 12 months (QoL_12), and at 36 months (QoL_36).

The primary measure was the overall NEI VFQ-25 score, which ranges from 0 to 100 points, with higher scores indicating better quality of life.

The change in quality-of-life score was calculated as the difference between the score at 36 months and the baseline score:

$\Delta QoL = QoL_{36} - QoL_{baseline}$.

The primary endpoint of the study was ΔQoL.

Cumulative treatment and clinical burden index

To quantitatively assess the overall complexity of treatment, an integrated measure, the Cumulative Burden Index (CBI), was used. This index was developed as a composite measure to quantify the intensity of laser interventions and the severity of the disease course.

The CBI was calculated as the sum of two components:

1. Total number of TSCPC procedures performed throughout the follow-up period.

2. Disease severity, expressed as a complication severity score reflecting complications present before treatment initiation or developing during follow-up and representing the cumulative disease burden.

The complication severity score was assessed using a standardized scale throughout the 36-month follow-up period:

0 points — no complications;

1 point — transient complications (short-term anterior segment inflammation, pain requiring symptomatic treatment, or corneal edema);

2 points — moderate complications (persistent inflammation or transient hypotony requiring medical management);

3 points — severe complications requiring additional intervention or resulting in substantial deterioration of the functional status of the eye (neurotrophic keratopathy, bullous keratopathy, recurrent hyphema, or vitreous hemorrhage).

The CBI was calculated according to the following formula:

CBI = number of TSCPC procedures + complication severity score.

Thus, the CBI reflected both the intensity of laser treatment and the complexity of the disease course.

Statistical analysis

Statistical analyses were performed using the JASP statistical software and a machine-learning modeling package. Continuous variables are presented as the median (Me) and interquartile range (IQR), whereas categorical variables are presented as absolute values and percentages. Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and the χ^2 test for categorical variables.

The association between the CBI and quality-of-life measures was assessed using linear regression analysis. Multivariable analysis was performed after adjustment for the following clinical factors: age, HbA1c level, baseline IOP, and degree of iris neovascularization. Regression analysis results are presented as regression coefficients (β) with 95% confidence intervals (CIs).

To further assess the prognostic significance of clinical variables, a multilayer perceptron (MLP) artificial neural network model was applied. The dataset was divided into training (70%), validation (15%), and test (15%) sets. Model performance was assessed using receiver operating characteristic (ROC) analysis, with calculation of the area under the curve (AUC)

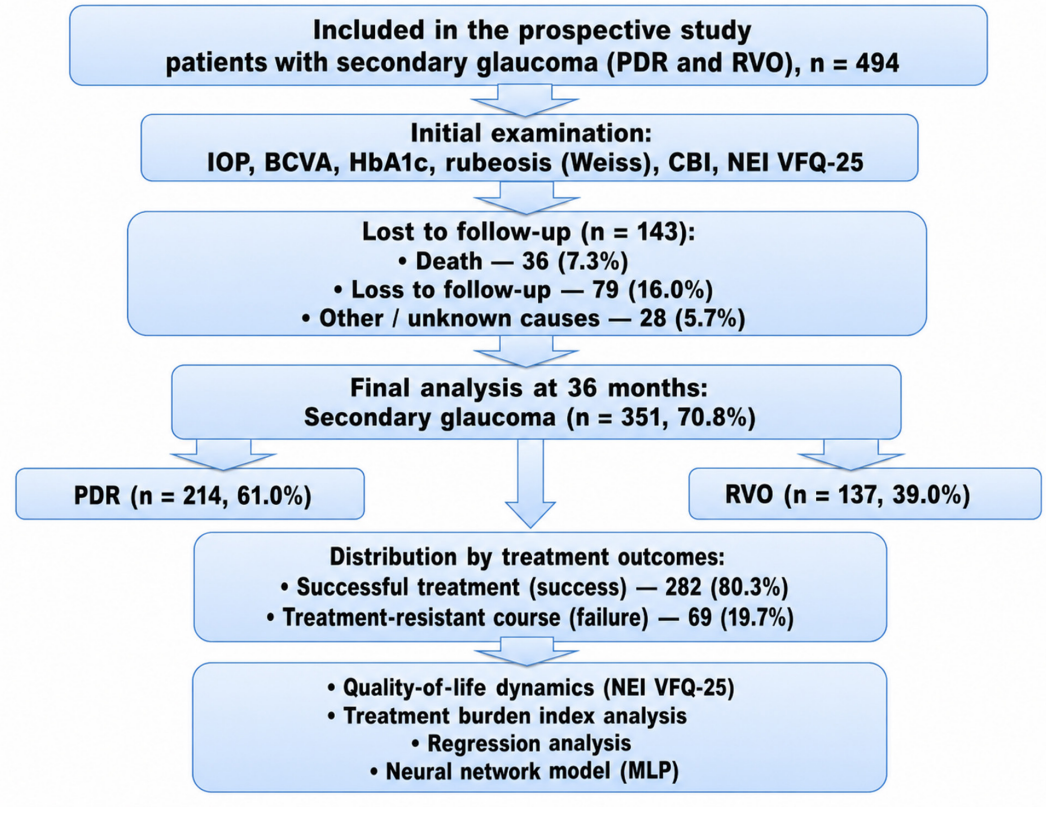


Fig. 1. Patient selection and study sample formation flowchart: PDR — proliferative diabetic retinopathy; RVO — retinal vein occlusion; BCVA — best-corrected visual acuity

and determination of the optimal cutoff value using the Youden index. No substantial missing data were identified. A complete-case analysis was performed. Differences were considered statistically significant at $p < 0.05$.

Results

The study included 351 patients (351 eyes) with secondary NVG who completed the 36-month follow-up period and the NEI VFQ-25 questionnaire. Treatment was successful in 282 patients (80.3%), whereas 69 patients (19.7%) demonstrated a treatment-resistant disease course.

Secondary NVG was associated with proliferative diabetic retinopathy in 214 patients (61.0%) and with retinal vein occlusion in 137 patients (39.0%).

At baseline, quality-of-life measures did not differ significantly between the successful-treatment and treatment-resistant groups ($p > 0.05$), indicating comparability between the groups with respect to patient-reported outcomes at the beginning of follow-up (***Table 1***).

The median BCVA of the fellow eye was significantly higher in the successful-treatment group than in the treatment-resistant group (0.3 [0.08–0.6] vs. 0.03 [0.02–0.4], $p < 0.001$). In 14 cases, there was no vision in the fellow eye (visual acuity = 0), whereas in 81 patients, visual acuity in the fellow eye was lower than that in the study eye.

During the 36-month follow-up, substantial differences were observed in the trajectories of quality-of-life measures between the successful-treatment and treatment-resistant groups (***Table 2, Fig. 2***). Patients in the successful-treatment group demonstrated a gradual improvement in NEI VFQ-25 scores throughout the follow-up period, whereas patients in the treatment-resistant group showed a progressive decline.

Between-group differences were statistically significant at 12 and 36 months ($p < 0.001$).

To provide an integrated assessment of changes in quality of life, the ΔQoL measure was analyzed.

In the successful-treatment group, the mean ΔQoL was +(10.26 ± 6.18) points, indicating a clinically significant improvement in quality of life. In contrast, the treatment-resistant group demonstrated a decline in quality of life, with a ΔQoL of −(7.43 ± 6.97) points ($p < 0.001$).

The between-group difference corresponded to a very large clinical effect (Cohen's d **=** 2.77), confirming a substantial impact of treatment outcomes on patient-reported outcomes.

Analysis of the association between the CBI and quality-of-life measures demonstrated a significant negative association: higher CBI values were associated with lower NEI VFQ-25 scores (***Fig. 3***).

In the unadjusted analysis, each 1-point increase in the CBI was associated with a 2.67-point decrease in the quality-of-life score at 36 months ($p <$ 0.001).

After adjustment for age, HbA1c level, baseline IOP, and degree of iris neovascularization, the CBI remained an independent predictor of lower quality of life. In the multivariable linear regression model, each 1-point increase in the CBI was associated with a 1.42-point decrease in the NEI VFQ-25 score (95% CI, −2.49 to −0.34; $p =$ 0.009).

TTable 1. Baseline clinical characteristics of patients according to treatment outcome at 36 months

Parameter	Successful treatment (n = 282)	Treatment-resistant course (n = 69)	p
Age, years	64 (61–67)	66 (62–68)	<0,01
Sex (M/F)	159/123	33/36	0,18
HbA1c, %	6,4 (4,6–7,2)	8,8 (4,4–9,5)	<0,001
IOP, mmHg	33 (33–36)	40 (38–42)	<0,001
BCVA	0,03 (0,02–0,08)	0,02 (0,01–0,02)	<0,01
BCVA of the fellow eye	0,3 (0,08–0,6)	0,03 (0,02–0,4)	<0,001
QoL (NEI VFQ-25), score	42,0 (36,8–54,2)	46,0 (40,7–54,2)	>0,05

Note. Data are presented as median and interquartile range. Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and the χ^2 test for categorical variables.

Table 2. Changes in quality-of-life scores (NEI VFQ-25) in patients with neovascular glaucoma over the 36-month follow-up period (n = 351)

Follow-up time point	Successful treatment	Treatment-resistant course	p
Before treatment	42,0 (36,8–54,2)	46,0 (40,7–54,2)	0,07
At 12 months	47,4 (42,8–60,0)	42,0 (39,4–44,8)	<0,001
At 36 months	54,1 (50,4–69,3)	37,8 (35,0–42,8)	<0,001

Note. Data are presented as median and interquartile range. Between-group comparisons were performed using the Mann–Whitney U test.

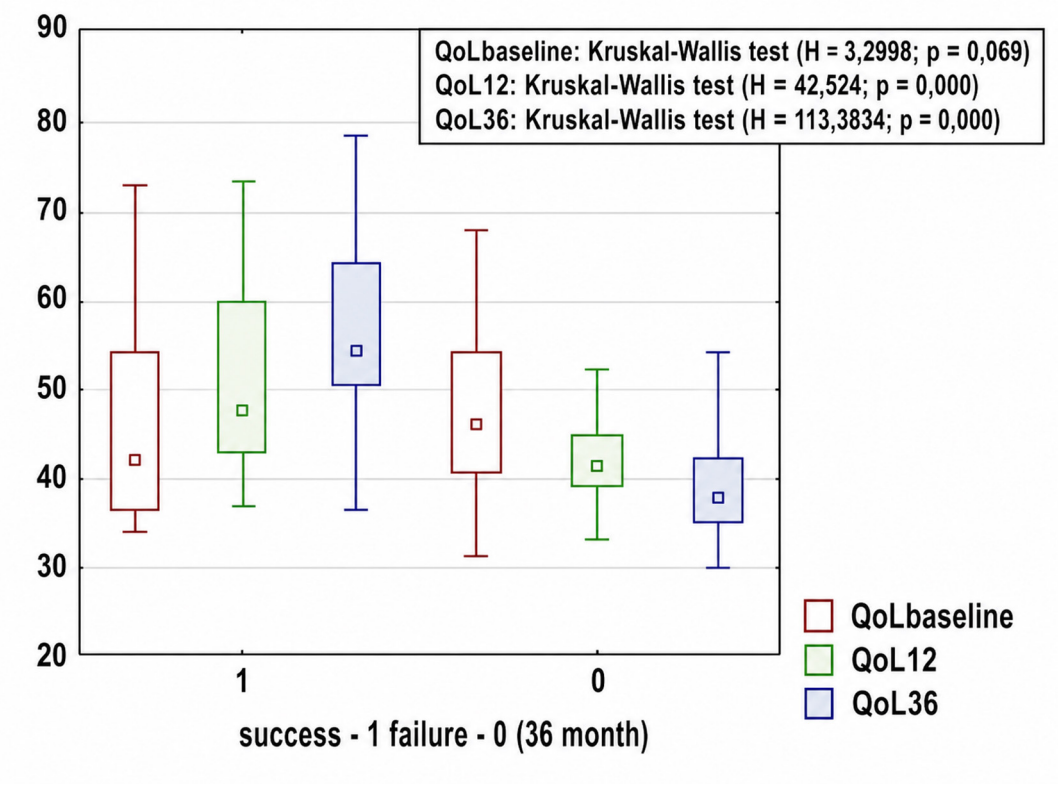


Fig. 2. Changes in the NEI VFQ-25 quality-of-life score over the 36-month follow-up period after transscleral cyclophotocoagulation

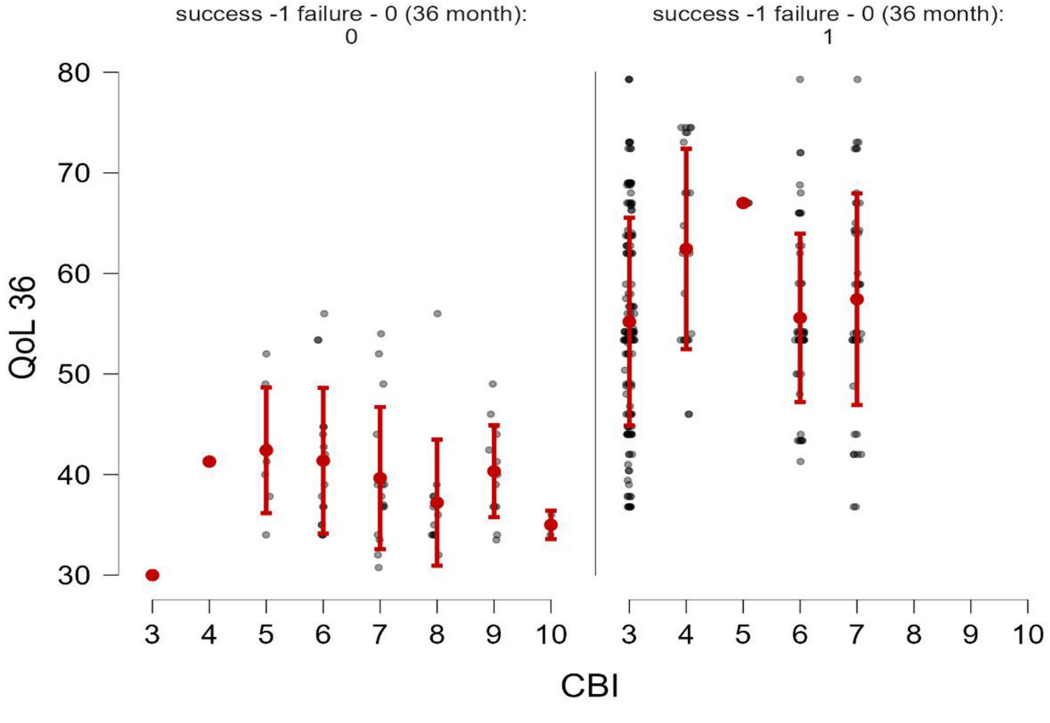


Fig. 3. Association between the Cumulative Burden Index (CBI) and the NEI VFQ-25 quality-of-life score at 36 months: success — successful-treatment group; failure — treatment-resistant group.

A similar association was observed for change in quality of life: each 1-point increase in the CBI was associated with a 1.78-point decrease in ΔQoL (95% CI, −2.57 to −0.99; p < 0.001), further supporting the negative association between the CBI and patient-reported treatment outcomes.

These findings suggest a dose-dependent relationship between cumulative treatment and clinical burden and quality-of-life measures in patients with secondary NVG.

The observed effect was characterized not only by statistical significance but also by substantial clinical relevance: the effect of the CBI on change in quality of life corresponded to a large effect size, indicating that the CBI may represent a key determinant of patient-reported outcomes in secondary NVG.

To identify factors associated with achieving a successful treatment outcome at 36 months, a multivariable logistic regression model was constructed, including the CBI, baseline IOP, degree of iris neovascularization, patient age, baseline quality of life ($QoL_{baseline}$), and NVG etiology.

The model demonstrated good predictive performance (Nagelkerke $R^2 = 0.74$, AUC = 0.96, p < 0.001). Multicollinearity diagnostics revealed no significant correlations among the predictors (VIF < 1.2 for all variables).

In the multivariable model, the CBI remained an independent predictor of treatment outcome: each 1-point increase in the CBI was associated with a lower likelihood of achieving a successful treatment outcome (odds ratio [OR] = 0.48), indicating an unfavorable prognostic effect of a higher CBI (p < 0.001). Similarly, higher baseline IOP and a greater degree of iris neovascularization were significantly associated with an unfavorable disease course (p < 0.001 for both variables).

Patient age, baseline quality-of-life score, and NVG etiology did not demonstrate statistically significant associations with treatment outcome ($p > 0.05$) (***Table 3***).

The model demonstrated good calibration (Hosmer–Lemeshow test, $p > 0.05$).

To further assess the prognostic value of the clinical parameters, a MLP artificial neural network model was applied using the following variables: CBI, baseline IOP, degree of iris neovascularization, patient age, and baseline quality-of-life score.

Analysis of the distribution of variables across the training, validation, and test datasets revealed no significant differences between the subgroups, indicating adequate representativeness and an appropriate distribution of the data.

The developed neural network model demonstrated good predictive performance for treatment outcomes in secondary neovascular glaucoma (***Table 4***).

The area under the receiver operating characteristic curve (AUC) was 0.83 (95% CI, 0.78–0.88), indicating high discriminative ability of the model (***Fig. 4***). The optimal classification threshold was 0.18. These findings are consistent with the results of the regression analysis and further support the significance of integrated clinical measures for predicting disease course.

At the optimal classification threshold of 0.18, determined using the Youden index, the model demonstrated a sensitivity of 81.2% and a specificity of 73.5%, indicating a balanced ability to identify both patients with successful treatment outcomes and those with a treatment-resistant course.

Table 3. Multivariable logistic regression analysis of predictors of treatment success at 36 months

Predictor	Odds ratio	95% CI	p
CBI	0,48	0,34–0,68	<0,001
Baseline IOP*	0,70	0,61–0,80	<0,001
Iris neovascularization (Weiss)	0,14	0,08–0,28	<0,001
Age	0,96	0,86–1,06	0,41
$QoL_{baseline}$	1,00	0,95–1,05	0,86
Etiology (PDR/RVO)	1,13	0,42–3,02	0,80

Note.
* — Before treatment.
PDR — proliferative diabetic retinopathy; RVO — retinal vein occlusion.

Table 4. Performance characteristics of the neural network model for predicting treatment outcomes in secondary neovascular glaucoma

Model architecture	Training set, %	Validation set, %	Test set, %	Training algorithm	Error function	Activation function	
						Hidden neurons	Output neurons
MLP 7-29-2	87,80	86,54	75,00	BFGS 45	Entropy	Hyperbolic	Softmax

Note: BFGS — quasi-Newton optimization algorithm; Softmax — activation function of the output layer.
The values represent classification accuracy in the respective datasets.

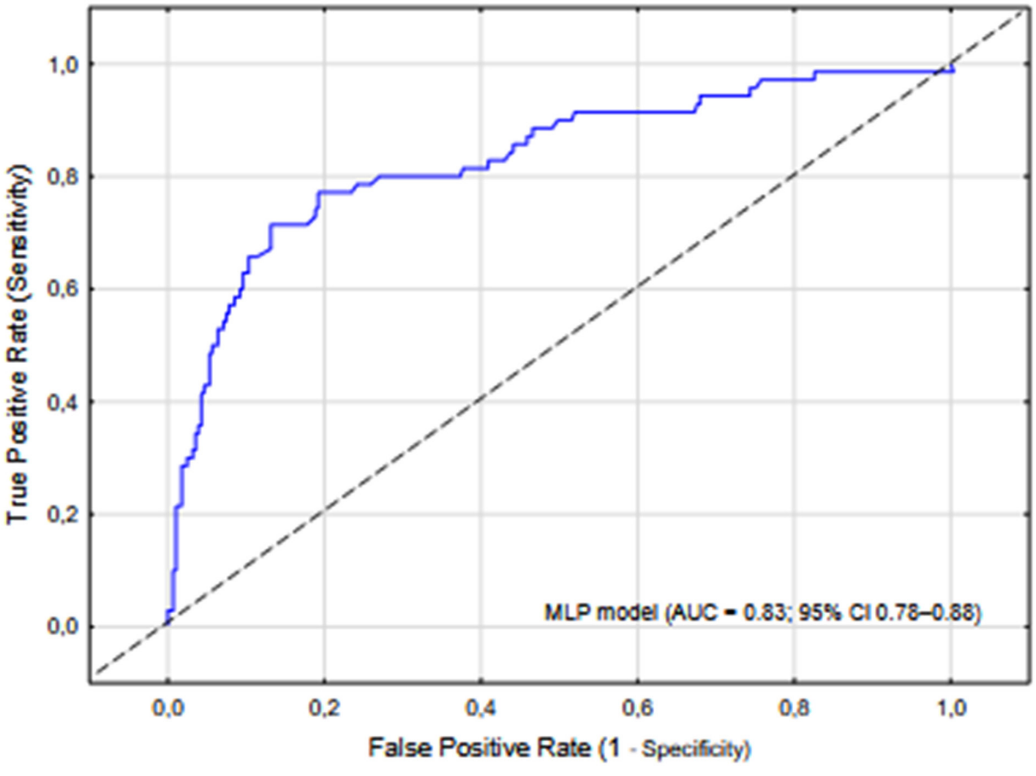


Fig. 4. ROC curve of the MLP neural network model for predicting treatment outcomes in secondary neovascular glaucoma (AUC = 0.83, 95% CI, 0.78–0.88)

These findings support the potential use of machine-learning methods as an additional tool for risk stratification in patients with secondary neovascular glaucoma.

Discussion

Our findings indicate that the CBI is an independent factor associated with quality-of-life outcomes in patients with secondary NVG after TSCPC. An increase in the CBI was associated with a statistically and clinically significant decline in NEI VFQ-25 scores: each 1-point increase in the index was associated with a 1.7-point decrease in ΔQoL ($p < 0.001$).

These findings are consistent with the concept of treatment burden, according to which the complexity and intensity of therapy influence patients' daily functioning [16,17]. Importantly, the CBI reflects not only the extent of therapeutic interventions but also the severity of the clinical course, including the presence and progression of complications. The observed association between the CBI and quality of life suggests an integrated effect encompassing both treatment burden and the pathophysiological aggressiveness of secondary NVG, providing a rationale for considering the CBI as a clinical surrogate of disease burden.

Transscleral cyclophotocoagulation remains one of the key treatment modalities for refractory forms of glaucoma, including neovascular glaucoma, providing effective IOP reduction [9,10]. According to the literature, its long-term efficacy ranges from 55% to 65%, and a substantial proportion of patients require repeat interventions [11,12]. In our study, treatment success was achieved in 80.3% of patients, which may be attributable to a comprehensive management strategy and intensive longitudinal follow-up, consistent with contemporary approaches to optimizing glaucoma treatment [23, 24].

However, even when target IOP is achieved, the cumulative intensity of treatment may adversely affect quality of life. This finding highlights the limitations of the traditional biomedical paradigm focused primarily on IOP control and underscores the need to incorporate patient-reported outcomes into the assessment of treatment effectiveness [13, 14]. Glaucoma is known to be associated with a substantial functional and social burden that does not necessarily correlate solely with IOP levels [15, 18].

The clinical relevance of our findings is further supported by the magnitude of the observed effect: the between-group difference in ΔQoL exceeded 17 points, substantially surpassing the threshold for clinically meaningful change in the NEI VFQ-25. This finding indicates that treatment burden is not merely a statistically significant factor but may represent a clinically important determinant of patient-reported outcomes [19].

An important observation is that baseline quality of life did not demonstrate prognostic significance, whereas cumulative treatment characteristics played a determining role. This finding is consistent with the contemporary view that dynamic measures may have greater prognostic value in predicting the course of chronic diseases [16].

The findings are consistent with the current understanding of the complex pathophysiology of secondary NVG, including retinal ischemia, VEGF-

mediated angiogenesis, and structural changes in the anterior segment of the eye [1, 3]. The role of systemic factors and inflammatory mechanisms has also been demonstrated in recent studies [2]. Morphometric changes in the ciliary body may reflect a more aggressive disease course and may correlate with systemic factors [25]. In this context, the CBI integrates clinical, morphological, and functional aspects of the disease. Our findings indicate that vision-related quality of life is determined primarily by disease severity rather than by any specific treatment modality.

The findings also indicate that visual acuity in the fellow eye is an important factor influencing quality-of-life outcomes in patients with NVG. The substantially lower BCVA of the fellow eye observed in the treatment-resistant group (0.03 [0.02–0.4] vs. 0.3 [0.08–0.6], $p < 0.001$), together with the high proportion of patients with critically reduced or absent vision in the fellow eye, indicates greater dependence on the visual function of the study eye. This may amplify the impact of even moderate changes in the functional status of the affected eye on overall vision-related quality of life.

Treatment adherence and the effectiveness of physician–patient communication may also play an important role [19,20], potentially modifying patients' perception of treatment burden and influencing final outcomes.

The results of the neural network analysis further support the potential application of machine-learning methods for predicting treatment outcomes. The model demonstrated good discriminative ability (AUC = 0.83), while its concordance with the regression analysis supports the stability of the identified associations. These findings highlight the potential for implementing digital clinical decision-support tools in the management of patients with secondary NVG.

The findings provide a rationale for considering the CBI as a clinical surrogate of disease burden, integrating both treatment intensity and disease severity. The CBI may serve as a useful tool for identifying patients at high risk of quality-of-life deterioration and for optimizing therapeutic strategies. This may be particularly relevant in the context of the increasing prevalence of glaucoma and its associated global disease burden [26]. The findings are also consistent with previous studies demonstrating the role of systemic inflammation, endothelial activation, and microcirculatory disturbances in determining the severity of secondary NVG and treatment effectiveness [27].

Of particular interest is the finding that vision-related quality of life is determined primarily by disease severity rather than by a specific treatment modality. In particular, a study by N. Edupuganti *et al*. (2026) found no significant difference in overall quality of life among patients receiving different treatment modalities, whereas the severity of the glaucomatous process was identified as the key determinant [28]. This finding is consistent with our results. The integrated CBI, which reflects the complexity of the disease course, demonstrated a strong association with quality of life regardless of individual therapeutic interventions.

Assessment of quality of life using the NEI VFQ-25 is a validated and sensitive approach, as supported by recent psychometric studies. In particular, Chen *et al*. (2025), using Rasch analysis, demonstrated the high sensitivity of the questionnaire to clinically meaningful changes [29]. This supports the interpretation that the changes in NEI VFQ-25 scores observed in our study reflect actual functional changes rather than random fluctuations.

The decline in NEI VFQ-25 scores among patients with a high treatment burden may reflect not only local ophthalmic changes but also progressive neurodegeneration of the visual pathway. In this context, vision-related quality of life may be considered an integrated functional surrogate of chronic neurosensory impairment.

From a clinical perspective, our findings suggest that patients at high risk of a treatment-resistant course and with an increased likelihood of developing complications should be considered for early reassessment of the therapeutic strategy, with possible use of alternative or more intensive treatment approaches aimed at reducing treatment burden and preserving quality of life.

The study has several limitations. The proposed CBI does not account for all components of treatment, particularly pharmacological therapy and the frequency of outpatient visits. In addition, quality-of-life assessment was based on patient-reported questionnaires, which may introduce subjectivity into the responses. Furthermore, the models developed in this study have not undergone external validation. Multicenter studies are warranted to validate these findings in independent patient populations.

Conclusions

1. Vision-related quality of life in patients with secondary NVG after transscleral cyclophotocoagulation is significantly associated with the CBI. Higher CBI values were associated with statistically and clinically significant reductions in NEI VFQ-25 scores (ΔQoL = −1.7 points for each 1-point increase in CBI, $p < 0.001$).

2. Patients with a treatment-resistant disease course demonstrated a marked deterioration in vision-related quality of life compared with those who achieved successful treatment outcomes (ΔQoL −7.43 vs. +10.26 points, respectively; Cohen's $d = 2.77$), indicating a substantial impact of chronic neurovascular and treatment burden on the functional status of the visual system.

3. The CBI reflects the integrated burden of disease, including treatment intensity, the frequency of repeat interventions, and the complexity of the clinical course, and may serve as a practical tool for risk stratification and personalized management of patients with NVG.

4. Patients with high CBI values and evidence of a treatment-resistant course may benefit from early reassessment of the therapeutic strategy, with consideration of alternative or more intensive treatment approaches aimed at reducing neurovascular injury and preserving vision-related quality of life.

5. The combination of conventional statistical methods with machine-learning algorithms confirmed the prognostic significance of the CBI as a key integrated predictor, together with baseline clinical parameters, including IOP, degree of iris neovascularization, and the functional status of the visual system. The findings also support the potential utility of digital predictive models (AUC = 0.83) for clinical decision-making in patients with secondary NVG.

Disclosure

Conflict of interest

The authors declare no conflict of interest.

Ethical standards

All procedures performed in this study involving human participants were conducted in accordance with the ethical standards of the institutional and national ethics committees and with the principles of the Declaration of Helsinki of 1964 and its subsequent amendments or comparable ethical standards.

Informed consent

Written informed consent was obtained from all patients for participation in the study and publication of the study data.

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