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Risk of visual impairment in patients with neovascular glaucoma and synechial closures of the iridocorneal corner after double transscleral cyclophotocoagulation

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Purpose: *To assess the risk of worsening of visual function at 12 months after diode transscleral cyclophotocoagulation (TSCPC) for neovascular glaucoma (NVG) secondary to diabetic retinopathy (DR) or retinal vein occlusion (RVO) performed at various durations of synechial angle closure.*
Material and Methods: *Two hundred and nine patients (209 eyes) with NVG secondary to DR or RVO were included in the study. In all patients, NVG was accompanied by active neovascularization, and patients varied in the duration of angle closure at the initiation of TSCPC. Median (interquartile (IQR) range) intraocular pressure (IOP) and best-corrected visual acuity (BCVA) at baseline were 36.0 (33; 40) and 0.03 (0.02; 0.06), respectively. Of 209 patients, 38% had prior panretinal photocoagulation (PRP) and antiangiogenic therapy. All patients had a modified diode TSCPC. Treatment success was assessed at 12 months and was defined as an IOP equal to or below 21 mmHg, an improvement in or preservation of preoperative BCVA, and a reduction in or stabilization of preoperative phosphene threshold current (PTC), in the absence of eye pain.*
Results: *At 12 months, 146 (70%) of patients showed no change or an improvement in median BCVA (IQR) to 0.06 (0.03; 0.1) ($p < 0.001$), and regression of angle and iris neovascularization. Of these, 69 (47%) had prior PRP and antiangiogenic therapy. Cox regression analysis showed that, in patients having no prior PRP or anti-VEGF therapy, the median hazard ratio (95% confidence interval) of a reduction in BCVA at 12 months was 1.1 (0.7; 1.73) for the 6 week duration of angle closure at the initiation of TSCPC, and 4.6 (2.8; 7.7) for the 14 week duration of angle closure at the initiation of TSCPC versus 1.09 (0.6; 1.97) for patients having prior PRP or anti-VEGF therapy.*
Conclusion: *In patients with NVG secondary to DR or RVO and active neovascularization and angle closure, early (≤ 6 weeks after an attack of angle closure) diode TSCPC and prior PRP and anti-VEGF therapy enable a significant reduction in the hazard of worsening of BCVA at 12 months.*

Keywords:
diabetes mellitus, retinal vein occlusion, neovascular glaucoma, iridocorneal angle, cyclophotocoagulation

Introduction

Neovascular glaucoma (NVG) is a severe form of refractory glaucoma which often manifests as terminal-stage disease, leading to either a significant loss of vision or blindness with potential loss of the eye. NVG may occur in patients with ocular and systemic diseases leading to retinal hypoxia and ischemia, with increased vascular endothelial growth factor (VEGF) secretion contributing to the neovascularization of the anterior segment, synechial angle closure, rise in intraocular pressue (IOP) and severe eye pain [1, 2]. Because an untimely reduction in IOP results in the loss of visual function [3], the search for improved treatment options for secondary NVG with active neovascularization and angle closure is still ongoing [4]. Drainage valve implantation (46.88%), cyclodestructive procedures (22.55%) and trabeculectomy (6.24%) were found to be the three most commonly selected treatment options for NVG [5, 6].

Other researchers, however, reported on risk factors for failure of, and high rate of ocular complications after, tube shunt surgery, and low long-term rates of surgery success for Ahmed glaucoma valve in patients with NVG [7-9].

In eyes with NVG, intravitreal anti-VEGF only caused the resolution of iris neovascularization but failed to lower the IOP [10]. Fourteen (93%) of 15 eyes required surgery by 2 months after initial intravitreal anti-VEGF alone and achieved IOP stabilization [10].

Glaucoma drainage device combined with preoperative anti-VEGF agents injection would help maintain residual visual acuity but not improve the long-term surgical success rate [11].

Cyclodestructive procedures have been found to be the second most commonly selected treatment option for NVG, the first being drainage valve implantation [5]. With the introduction of anti-VEGF therapy [12, 13] and new technologies for cyclodestructive procedures [14], new effective strategies are emerging for IOP reduction and maintaining useful (> 20/200) visual acuity in eyes with NVG with the neovascularization of the anterior segment and synechial angle closure.

Time from the diagnosis to treatment may have a decisive value for maintaining visual function in eyes with secondary NVG. Lee and colleagues [15] aimed to evaluate the visual outcomes of Ahmed glaucoma valve implantation (AGVI) in patients with NVG who underwent diabetic vitrectomy and suggest appropriate AGVI timing. They concluded that if IOP is not adequately controlled (< 30 mmHg) within a week from the time of NVG diagnosis, early AGVI within six days might be necessary to preserve use¬ful vision. Wang and colleagues [16] concluded that prompt primary slow-burn CPC with prior or concurrent anti-VEGF may be an effective strategy to immediately lower IOP in acute NVG eyes with active anterior segment NV and near-total synechial angle closure. If IOP becomes uncontrolled later, an aqueous shunt can be implanted in a controlled setting after active anterior segment NV has regressed [16].

Therefore, taking into account poor general condition of patients with NVG secondary to diabetic retinopathy (DR) or retinal vein occlusion (RVO), active neovascularization of the anterior segment, and the onset of ocular pain in the presence of synechial angle closure, it is in need to determine the optimal time for the treatment with diode transscleral cyclophotocoagulation (TSCPC) for reducing the IOP and maintaining visual function at late time points as much as possible.

The purpose of the study was to assess the risk of worsening of visual function at 12 months after TSCPC for secondary NVG performed at various durations of synechial angle closure.

Material and Methods

Study design

A prospective comparative interventional crossover single-center study was conducted at State Institution "The Filatov Institute of Eye Diseases and Tissue Therapy". The study was conducted in accordance with the standards expressed in the Helsinki Declaration and was approved by the Filatov Institute ethics committee (Minutes no. 4, 2024). Written informed consent was obtained from all study patients.

Two hundred and nine patients (209 eyes) with NVG secondary to DR or RVO were included in the study. Of these, 133 had DR, and 76 had RVO. In all patients, NVG was accompanied by active neovascularization, and patients varied in the duration of angle closure at the initiation of TSCPC.

Inclusion criteria included NVG secondary to DR or RVO, neovascularization of the iris or angle documented in clinical notes, synechial angle closure, ocular pain and an IOP ≥ 30 mmHg despite maximal hypotensive medication. Anterior chamber angle was assessed by gonioscopy. Ultrasound biomicroscopy was used for assessing the angle if gonioscopy was impossible in eyes with corneal edema and high IOP.

Exclusion criteria were NVG secondary to other disorder; systemic disease preventing TSCPC; no eye pain; or an open iridocorneal angle.

Data collection

The following data were included in the analysis: age at the beginning of treatment (V0), number of previous glaucoma operations, Goldmann IOP, best-corrected visual acuity (BCVA), phosphene threshold current (PTC), and the number of TSCPC procedures since angle-closure glaucoma onset. Angle-closure glaucoma onset was defined as the time of the onset of the acute condition with a sudden rise in IOP and the appearance of ocular pain. The time from glaucoma surgery to presentation exceeded 12 months for any patient.

The preoperative visit (V0) was carried out the day before TSCPC. Preoperatively, HbA1c level and counts of neutrophils, lymphocytes, platelets and monocytes were determined. Systemic immune inflammation index (SSI) defined as platelet (/μL) × neutrophil (/μL)/lymphocyte (/μL), and systemic inflammation response index (SIRI) defined as neutrophil count × monocyte count/lymphocyte count were calculated. Patients were checked for the presence of any cardiovascular disease.

They were followed up at 1 month and 3, 6 and 12 months (V1, V3, V6 and V12, respectively) after TSCPC. Repeat CPC or other treatment was used in case of lack of response to IOP lowering therapy or loss of the obtained hypotensive effect. After treatment, eyes were dichotomized into two groups based on whether their BCVA improved/ did not change (1) or worsened (0) postoperatively.

TSCPC procedure

Patients received the 820-nm diode laser TSCPC according to our modified methodology reported previously [17, 18].

Treatment success

Treatment success was assessed at 12 months (V12) and was defined as an IOP equal to or below 21 mmHg, an improvement in or preservation of preoperative BCVA, and a reduction in or stabilization of preoperative PTC, in the absence of eye pain. Treatment failure requiring a repeat TSCPC was defined as an IOP of ≥ 22 mmHg despite maximal hypotensive medication, the development of any complications, a reduction in preoperative BCVA, and/or an increase in preoperative PTC.

Statistical analysis

Data were analyzed using the open-source JASP software (version 0.19.2; the JASP Team, Amsterdam, the Netherlands).was used for statistical analysis. Descriptive statistics for categorical variables are presented as frequencies and percentages. Data were evaluated for normality using the Shapiro-Wilk test. Non-parametric data are presented as median (Me) and interquartile range (IQR). A comparative analysis was conducted between patients with a favorable visual outcome (an improvement in or preservation of preoperative BCVA) and those with an unfavorable visual outcome (worsening of preoperative BCVA). Chi-square test, Fischer's exact test and Mann-Whitney U-test were used for comparison between groups. Factors of possible influence on the clinical outcome are presented graphically [19]. The level of significance $p \leq 0.05$ was assumed. Cox regression analysis was used to determine long-term visual function in patients with NVG secondary to DR or RVO, given the duration of synechial closure at the initiation of TSCPC and the presence or absence of prior panretinal laser photocoagulation (PRP) and anti-VEGF therapy.

Results

Two hundred and nine patients (209 eyes) with NVG secondary to DR or RVO were included in the study. Of these, 133 had DR, and 76 had RVO.

Figure 1 shows a photograph of a patient with secondary neovascular glaucoma due to retinal vein occlusion before transscleral cyclophotocoagulation.

Table 1 shows demographic and clinical data before operation (V0).

Figure 2 demonstrates that SSI and SIRI significantly increased with the duration of synechial closure.

A longer than 8 week duration of angle closure at the initiation of TSCPC resulted in a visual acuity loss (worsening of preoperative BCVA) in eyes with NVG secondary to DR or RVO, especially in eyes with NVG secondary to DR (Fig. 3A). The presence of prior PRP and anti-VEGF therapy increased the odds of maintaining preoperative visual acuity with a shorter than a 12 week duration of angle closure at the initiation of TSCPC (Fig. 3B). At 12 months, 146 eyes (70%) with NVG showed an improvement or no change in BCVA and regression of angle and iris neovascularization. Of these, 69 (47%) had preoperative PRP and anti-VEGF therapy.

Table 2 compares patients with an improvement or preservation of BCVA with those with a reduction of BCVA at 12 months after TSCPC compared to baseline with regard to important clinical characteristics. The presence of prior PRP and anti-VEGF therapy, duration of synechial closure by the time of TSCPC, PTC, SSI and SIRI had a significant effect on the visual function in eyes with NVG secondary to DR or RVI at 12 months after TSCPC (Table 2). No correlation was found between the improvement in pre-CPC BCVA at 12 months and the presence of history of glaucoma surgery.

Cox regression analysis showed that, in patients with secondary glaucoma having no prior PRP or anti-VEGF therapy, the cumulative hazard of BCVA loss at 12 months was 1.1 times increased for the 6 week duration of angle closure at the initiation of TSCPC, and 4.6 times increased for the 14 week duration of angle closure at the initiation of TSCPC. Additionally, in patients with secondary glaucoma having prior PRP and anti-VEGF therapy, the cumulative hazard of a reduction in BCVA at 12 months was only 1.09 times increased for the 14 week duration of angle closure at the initiation of TSCPC (Fig. 4).

Throughout the follow-up, corneal edema, ocular inflammation, and/or hyphema were found in 62% of patients with a reduction in BCVA, and in 23% of patients with an improvement or no change in BCVA at 12 months compared to baseline. No phthisis bulbi developed.

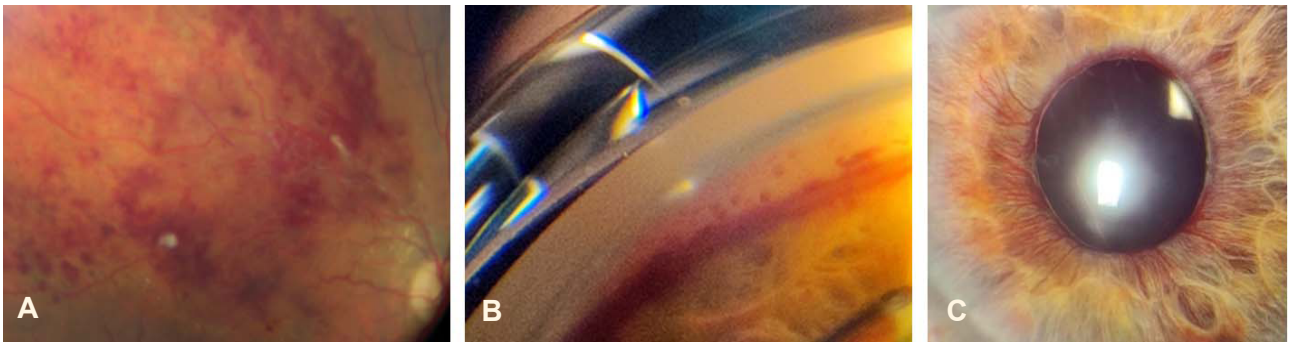

Fig. 1. Patient T., 62 years old. Secondary neovascular glaucoma due to retinal vein occlusion (visit V0): A - photo of the fundus with multiple hemorrhages and exudates in the retina; B - photo of the closed iridocorneal angle, its neovascularization; C - photo of the anterior segment - rubeosis iridis. Pseudophakia. BCVA(V0) = 0.06; IOP 32 mmHg, on maximum hypotensive therapy.

Table 1. Demographic and clinical characteristics of patients with neovascular glaucoma (NVG) secondary to diabetic retinopathy (DR) or retinal vein occlusion (RVO) at baseline (V0)

Baseline characteristics	Median (interquartile range) value or number (percentage)
Age, years	64.0 (61; 67)
Males / Females	93 (44%) / 116 (56%)
DR/ RVO	133 (64%) / 76 (36%)
IOP V0, mmHg	36.0 (33; 40)
BCVA	0.03 (0.02; 0.06)
PTC, μA	94 (86; 100)
History of glaucoma surgery, yes/no	62 (30%) / 147 (70%)
Duration of time after glaucoma surgery: DR/RVO, months	36 (33; 60) / 30 (15; 45)
Cataract/ Pseudophakia	122 (58%) / 87 (42%)
History of PRP + anti-VEGF therapy, yes / no	79 (38%) / 130 (62%)
Duration of time between synechial angle closure and TSCPC, weeks	4.0 (2; 10)
Duration of DR/RVO, months	132 (84; 168) / 11 (6; 15)
HbA1c, %	7.4 (6.9; 8.8)
SIRI *10^9/l	0.69 (0.54; 1.06)
SII *10^9/ l	434.1 (386; 671)
Presence of cardiovascular disease, yes/no	155 (74%) / 54 (26%)
Smoking, yes/no	58 (28%) / 151 (72%)

Note: Data are presented as median (interquartile range) value or number (percentage). Abbreviations: BCVA, best corrected visual acuity; CPC, cyclophotocoagulation; DM, diabetes mellitus; DR, diabetic retinopathy; HbA1c, glycosylated hemoglobin; IOP, intraocular pressure; NVG, neovascular glaucoma; PDR, proliferative diabetic retinopathy; PRP, panretinal photocoagulation; PTC, phosphene threshold current; RVO, retinal vein occlusion; SIRI, systemic inflammation response index; SSI, systemic immune inflammation index; TSCPC, transscleral cyclophotocoagulation

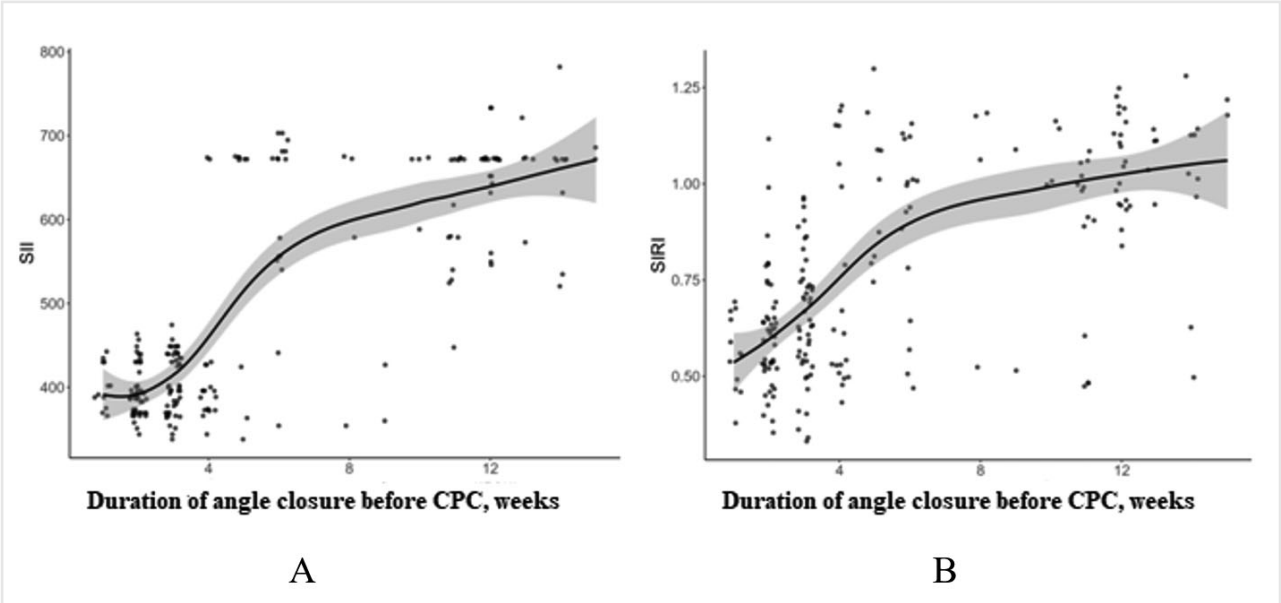

Fig. 2. Distribution of preoperative SII (A) and SIRI (B) values depending on the duration of synechal closure before TSCPC in patients with secondary NVG

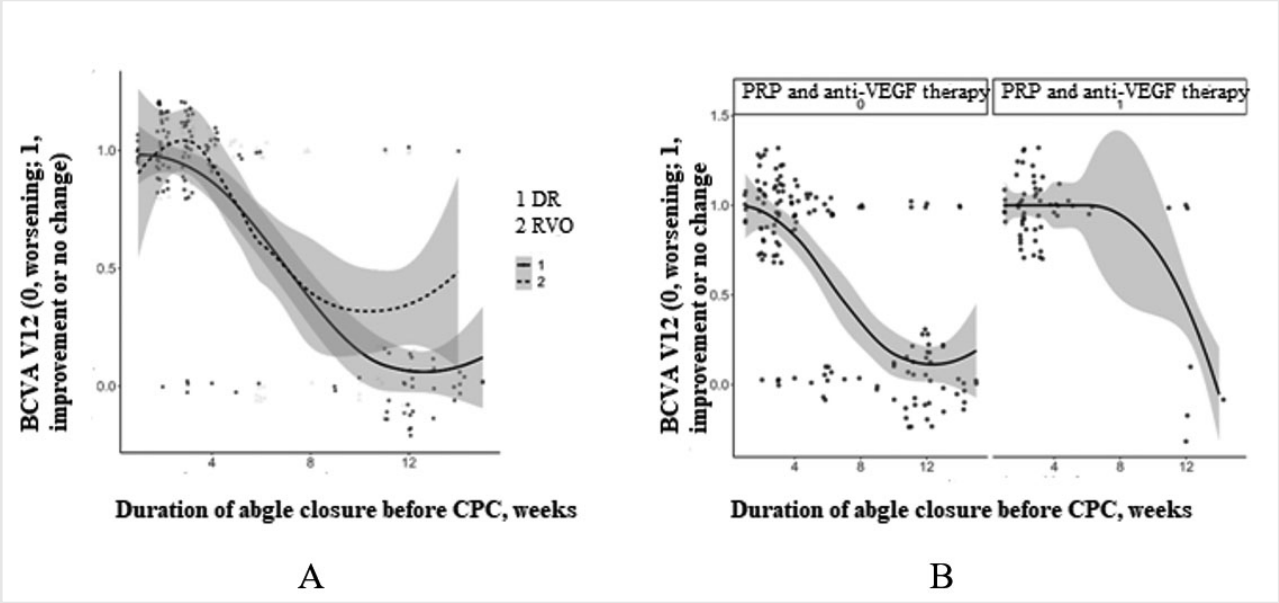

Fig. 3. Distribution of BCVA (worsening at 12 months, 0; improvement or no change at 12 months, 1) values depending on the duration of synechal closure at the initiation of TSCPC in patients with secondary NVG depending on disease etiology (A) and the presence of prior PRP and anti-VEGF therapy (0, no prior PRP or anti-VEGF therapy; 1, prior PRP + anti-VEGF therapy) (B)

Table 2. Comparison of patients with secondary NVG showing worsening and those showing an improvement or no change in BCVA at 12 months after TSCPC by clinical characteristics

Clinical characteristics	Worsening versus an improvement or no change in BCVA at 12 months, median (interquartile range) or value (percentage)		P-value
	Worsening	Improvement or no change	
Number of eyes	63 (30%)	146 (70%)	<0.001[2]
IOP	24 (22; 26)	19 (18; 21)	<0.1[1]
BCVA	0.01 (0; 0.03)	0.06 (0.03; 0.1)	<0.001[1]
History of PRP + anti-VEGF therapy, yes/no	10 (16%)	69 (47%)	0.003[2]
Duration of time between synechial angle closure and TSCPC, weeks	11 (9; 12)	3 (2;4)	<0.001[1]
PTC, μA (V12)	135 (98.5; 143.8)	86 (80; 94)	<0.001[1]
SIRI*10^9/l (V0)	1.09 (0.99; 1.13)	0.62 (0.53; 0.78)	0.04[1]
SII*10^9/l (V0)	672 (545; 673)	400 (374; 447)	<0.001[1]

Note: Data are presented as median (interquartile range) value or number (percentage). Abbreviations: BCVA, best corrected visual acuity; CPC, cyclophotocoagulation; IOP, intraocular pressure; NVG, neovascular glaucoma; PRP, panretinal photocoagulation; PTC, phosphene threshold current; RVO, retinal vein occlusion; SIRI, systemic inflammation response index; SSI, systemic immune inflammation index; TSCPC, transscleral cyclophotocoagulation.

[1] - P-value, P-value for difference between baseline and 12 months as assessed by Wilcoxon test (median (interquartile range) or [2] - Fischer exact test (value (percentage))

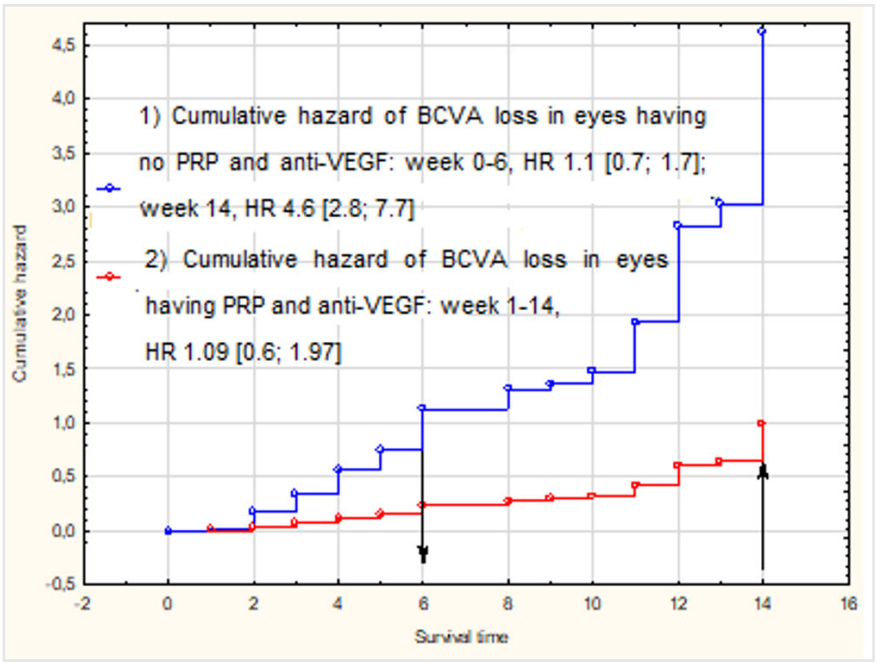

Fig. 4. Cumulative hazard of BCVA loss at 12 months in eyes with neovascular glaucoma (1) having no prior PRP and anti-VRGF therapy, with a 6-week or 14-week duration of angle closure at the time of TSCPC (HR 1.1 [95% CI 0.7; 1.73] or HR 4.6 [95% CI 2.8; 7.7], respectively) and (2) having prior PRP and anti-VRGF therapy, with a 14-week duration of angle closure at the initiation of TSCPC (HR 1.09 [95% CI 0.6; 1.97]).

Discussion

NVG is characterized by progressive neovascularization of the iris or angle. Based on its histological and clinical characteristics, NVG can be divided into three stages: rubeosis iridis, open-angle NVG, and angle-closure NVG [20]. Fibrotic contraction of neovascular vessels in the angle and peripheral anterior synechia results in the blockage of aqueous outflow. The latter is usually accompanied by a rapid IOP increase, causing intense pain that may be localized to the eye or may follow the trigeminal distribution [21].

IOP rise due to NVG can accelerate the progression of glaucomatous optic neuropathy and DR. IOP elevation in NVG may hasten the progression of glaucomatous optic neuropathy. Additionally, sustained extremely increased IOP may restrict the retinal blood flow through the optic disc and inner retinal circulation. Since the blood flow autoregulation is effective over only a narrow critical range normally, under the high IOP, the retinal blood flow restriction may not be compensated. Perfusion pressure decrease and retinal blood flow autoregulation failure due to prolonged IOP rise inhibit blood flow in the optic disc [22, 23], contributing to ischemic retinal damage [15].

High IOP can cause mechanical stress and strain on the posterior structures of the eye, with consequent mechanical axonal damage and disruption of axonal transport that interrupts retrograde delivery of essential trophic factors to retinal ganglion cells (RGC) from their brainstem target [24]. How mechanical stimuli are sensed and affect cellular physiology in the eye is unclear. Studies have shown that mechanosensitive ion channels are expressed in many ocular tissues relevant to glaucoma and may influence IOP regulation and RGC survival [25]. Although the angle closure stage is the terminal stage of the disease, a considerable number of patients retain some visual function at this stage. Patients usually suffer from sustained severe eye pain, photophobia, high IOP above 60 mmHg, accompanied by persistent hyperemia, corneal edema, mydriasis and uveal ectropion [20].

Studies on the efficacy of TSCPC in NVG have been reported [26], particularly those using infrared visualization of ciliary body structures for targeted laser-probe positioning during TSCPC [27]. Fong et colleagues [28] concluded that TSCPC alone is a safe and effective in lowering IOP in NVG, but the addition of intravitreal bevacizumab to TSCPC did not statistically advantage treatment outcomes [28]. In patients with open-angle NVG secondary to ocular ischemic syndrome, serial monthly anti-VEGF injections may be necessary combined with PRP to regress anterior segment neovascularization and prevent synechial angle closure [12]. Most previous studies have focused only on IOP normalization when assessing surgery success. The results regarding visual function have not been duly considered due to generally poor baseline vision of participants, and only the percentage of visual acuity loss after TSCPC has been calculated. In the current

study, we analyzed BCVA at baseline and at 12 months after surgery, and took into account the factors influencing visual prognosis.

Rotchford and colleagues [29] investigated the effect of diode laser TSCPC for glaucoma on central visual function in patients with pre-operative VA 20/60 or better. After a mean duration of follow-up of 5.0 years, IOP was ≤ 16 in 73.5% of patients, and median visual acuity was 20/60 with a ≥2 line loss recorded in 15 eyes (30.6%) [29]. In cases experiencing a 2 line loss in acuity, the main causes were glaucoma progression (9 cases) and macula edema (4 cases). Visual loss was unrelated to total treatment dose (mean 99.7J), initial acuity or initial IOP level [29].

In the current study, the presence of prior PRP and anti-VEGF therapy, duration of synechial closure by the time of TSCPC, and PTC, had a significant effect on the visual function in eyes with NVG secondary to DR or RVI at 12 months after TSCPC, possibly due to prolonged and severely elevated IOP and low retinal blood flow through the optic disc and inner retinal circulation.

Moreover, SSI and SIRI also had a significant effect on the visual function in eyes with NVG secondary to DR or RVI at 12 months after TSCPC. Others [30, 31, 32] also have stressed the activity of inflammatory factors capable of influencing the efficacy of CPC [33, 34] in patients with DR, which lays the ground for using anti-inflammatory therapy in these patients before CPC [31].

A retrospective study by Wang and colleagues [16] stressed that prompt primary slow-burn CPC with prior or concurrent anti-VEGF may be an effective strategy to immediately lower IOP in acute NVG eyes with active anterior segment NV and near-total synechial angle closure [16]. They advocated for a new algorithm of treatment (slow-burn CPC with prior or concurrent anti-VEGF) for secondary NVG based on the iridocorneal angle anatomy [6, 16].

Our analysis stressed the necessity of performing TSCPC early after synechial closure for maintaining visual function, especially in eyes with secondary NVG having no prior PRP or anti-VEGF therapy. However, in eyes with secondary NVG having prior PRP and anti-VEGF therapy, TSCPC may be performed 12 weeks after synechial angle closure with small odds of a reduction in BCVA over 12 months. Hong and colleagues [35] found that a triple therapy combining anti-VEGF therapy, trabeculectomy and PRP had a higher preservation rate of the visual function than TSCPC in the treatment of angle-closure NVG. Their study, however, was limited by a small number of cases and a relatively short follow-up time, and they did not determine the duration of angle closure at the initiation of treatment. Our study was limited by the fact that only 79 (38%) patients had prior PRP and anti-VEGF therapy, which could affect treatment results for the entire sample. Additionally, the time of onset of angle-closure glaucoma was determined during history taking (based on the patient self-reported time of eye pain onset), which could affect the accuracy of results. Of note that the time of onset of angle-closure glaucoma does not always coincide with the time of onset of eye pain due to some variation in the pain threshold among individuals.

In spite of the above limitations, we analyzed the risk of visual acuity worsening at 12 months after TSCPC depending on the duration of synechial closure at the initiation of TSCPC. Further research is warranted on the efficacy of treatment for NVG, with due consideration given to the pathophysiology of the pathological process and requirements for neuroprotective, antioxidative and anti-inflammatory therapy [36].

Conclusion

Early (≤ 6 weeks after synechial angle closure) diode TSCPC and prior PRP and anti-VEGF therapy enable a significant reduction in the cumulative hazard of visual acuity worsening at 12 months.

References

1. Călugăru D, Călugăru M. Etiology, pathogenesis, and diagnosis of neovascular glaucoma. Int J Ophthalmol. 2022 Jun 18;15(6):1005-1010. https://doi.org/10.18240/ijo.2022.06.20.
2. Barac IR, Pop MD, Gheorghe AI, Taban C. Neovascular secondary glaucoma, etiology and pathogenesis. Rom J Ophthalmol. 2015; 59(1): 24–28.
3. Mannina A, Olivier M, Patrianakos T. Neovascular glaucoma. Dis Mon. 2021 May;67(5):101137. doi: 10.1016/j.disamonth.2021.101137.
4. Shchomak Z, Cordeiro Sousa D, Leal I, Abegão Pinto L. Surgical treatment of neovascular glaucoma: a systematic review and meta-analysis. Graefes Arch Clin Exp Ophthalmol. 2019 Jun;257(6):1079-1089.doi: 10.1007/s00417-019-04256-8.
5. Lin H, Gao X, Wu Z, Tam W, Huang, W, Dong Y.et al. Treatment modalities and trends for hospitalized patients with neovascular glaucoma: A retrospective study of 10 years. Asia Pac J Ophthalmol (Phila). 2025 Jan-Feb;14(1):100136. doi: 10.1016/j.apjo.2025.100136.
6. Urbonavičiūtė D, Buteikienė D, Janulevičienė I. A Review of Neovascular Glaucoma: Etiology, Pathogenesis, Diagnosis, and Treatment. Medicina (Kaunas, Lithuania). 2022; 58(12): 1870. https://doi.org/10.3390/medicina58121870.
7. Bowden EC, Choudhury A, Gedde SJ, Feuer WJ, Christakis PG, Savatovsky E, et al. Risk Factors for Failure of Tube Shunt Surgery: A Pooled Data Analysis. Am J Ophthalm. 2022; 240: 217–224. https://doi.org/10.1016/j.ajo.2022.02.027.
8. Kang YK, Shin JP, Kim DW. Long-term surgical outcomes of Ahmed valve implantation in refractory glaucoma according to the type of glaucoma. BMC ophthalmology. 2022; 22(1): 270. https://doi.org/10.1186/s12886-022-02493-w.
9. Netland PA, Ishida K, Boyle JW. The Ahmed Glaucoma Valve in patients with and without neovascular glaucoma. J Glaucoma. 2010; 19(9): 581–586. https://doi.org/10.1097/IJG.0b013e3181ca7f7f.
10. Wakabayashi T, Oshima Y, Sakaguchi H, Ikuno Y, Miki A, Gomi F, et al. Intravitreal bevacizumab to treat iris neovascularization and neovascular glaucoma secondary to ischemic retinal diseases in 41 consecutive cases. Ophthalmology. 2008; 115(9): 1571–1580.e15803. https://doi.org/10.1016/j.ophtha.2008.02.026.

11. Yang H, Yu X, Sun X. Neovascular glaucoma: Handling in the future. Taiwan J Ophthalmol. 2018; 8(2): 60–66. https://doi.org/10.4103/tjo.tjo_39_18.
12. Asif H, Si Z, Quan S, Amin P, Dao D, Shaw L, et al. Neovascular Glaucoma from Ocular Ischemic Syndrome Treated with Serial Monthly Intravitreal Bevacizumab and Panretinal Photocoagulation: A Case Report. Case Rep Ophthalmol Med. 2022 Jul 28:2022:4959522. https://doi.org/10.1155/2022/4959522.
13. Rittiphairoj T, Roberti, G, Michelessi, M. Anti-vascular endothelial growth factor for neovascular glaucoma. Cochrane Database Syst Rev. 2023; 4(4): CD007920. https://doi.org/10.1002/14651858.CD007920.pub4.
14. Dastiridou AI, Katsanos A, Denis P, Francis BA, Mikropoulos DG, Teus MA, et al. Cyclodestructive Procedures in Glaucoma: A Review of Current and Emerging Options. Adv Ther. 2018; 35(12): 2103–2127. https://doi.org/10.1007/s12325-018-0837-3.
15. Lee JS, Lee YB, Kim TW, Park KH. Visual prognosis and surgical timing of Ahmed glaucoma valve implantation for neovascular glaucoma secondary to diabetic vitrectomy. BMC ophthalmology. 2023; 23(1): 107. https://doi.org/10.1186/s12886-023-02846-z.
16. Wang J, Chun LY, Qiu M. Cyclophotocoagulation in Neovascular Glaucoma with Near-Total Synechial Angle Closure. Case Rep Ophthalmol Med. 2023 Oct 26:2023:5719002. https://doi.org/10.1155/2023/5719002.
17. Guzun OV, Zadorozhnyy OS, Nasinnyk IO, Chargui W, Korol AR. Duration of the hypotensive effect of modified transscleral cyclophotocoagulation in patients with diabetic neovascular glaucoma. J Ophthalmol (Ukraine). 2025; 2: 9–16. https://doi.org/10.31288/oftalmolzh20252916.
18. Guzun O, Zadorozhnyy O, Nasinnyk I, Korol A. Efficacy of modified diode transscleral cyclophotocoagulation in patients with painful neovascular glaucoma secondary to retinal vein occlusion. J Ophthalmol (Ukraine). 2025;3: 3–10. https://doi.org/10.31288/oftalmolzh20253310.
19. Fife D. Flexplot: Graphically-based data analysis. Psychological methods. 2022; 27(4): 477–496. https://doi.org/10.1037/met0000424.
20. Tang Y, Shi Y, Fan Z. The mechanism and therapeutic strategies for neovascular glaucoma secondary to diabetic retinopathy. Frontiers in endocrin. 2023; 14: 1102361. https://doi.org/10.3389/fendo.2023.1102361.
21. Morgan J. Pathogenesis of glaucomatous optic neuropathy. In: Shaarawy TM, Sherwood MB, Crowston JG, Hitchings RA, eds. Glaucoma: Medical Diagnosis & Therapy. Vol. 1. Philadelphia: Saunders–Elsevier; 2009:45–54.
22. Hayreh SS. Blood flow in the optic nerve head and factors that may influence it. Prog Retin Eye Res. 2002; 20(5): 595–624. https://doi.org/10.1016/s1350-9462(01)00005-2.
23. Hayreh SS. Ischemic optic neuropathy. Prog Retin Eye Res. 2009; 28(1): 34–62. https://doi.org/10.1016/j.preteyeres.2008.11.002.
24. Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA. 2014; 311(18): 1901–1911. https://doi.org/10.1001/jama.2014.3192.
25. Garcia-Sanchez J, Lin D, Liu WW. Mechanosensitive ion channels in glaucoma pathophysiology. Vis Res. 2024; 223, 108473. https://doi.org/10.1016/j.visres.2024.108473.
26. Alabduljabbar K, Bamefleh DA, Alzaben KA, Al Owaifeer AM, Malik R. Cyclophotocoagulation versus Ahmed Glaucoma Implant in Neovascular Glaucoma with Poor Vision at Presentation. Clin Ophthalmol (Auckland, N.Z.). 2025; 18: 163–171. https://doi.org/10.2147/OPTH.S424321.
27. Zadorozhnyy O, Guzun O, Kustryn T, Nasinnyk I, Chechin P, Korol A. Targeted transscleral laser photocoagulation of the ciliary body in patients with neovascular glaucoma. J Ophthalmol (Ukraine). 2019;4:3-7.https://doi.org/10.31288/oftalmolzh2019437.
28. Fong AW, Lee GA, O'Rourke P, Thomas R. Management of neovascular glaucoma with transscleral cyclophotocoagulation with diode laser alone versus combination transscleral cyclophotocoagulation with diode laser and intravitreal bevacizumab. Clin & Exp Ophthalmol. 2011; 39(4): 318–323. https://doi.org/10.1111/j.1442-9071.2010.02449.x
29. Rotchford AP, Jayasawal R, Madhusudhan S, Ho S, King AJ, Vernon, SA. Transscleral diode laser cycloablation in patients with good vision. Br J Ophthalmol. 2010; 94(9): 1180–1183. https://doi.org/10.1136/bjo.2008.145565.
30. Si Y, Chen Q, Xiong X, Zheng M. The association of inflammatory biomarkers with clinical outcomes in diabetic retinopathy participants: data from NHANES 2009-2018. Diabetol Metab Syndr. 2024; 16(1): 181. https://doi.org/10.1186/s13098-024-01419-4
31. Sun C, Zhang H, Tang Y, Chen Y, Li Y, Nie C, et al. Aqueous Inflammation and Ischemia-Related Biomarkers in Neovascular Glaucoma with Stable Iris Neovascularization. Current Eye Res. 2025; 45(12): 1504–1513. https://doi.org/10.1080/02713683.2020.1762226
32. Sun C, Zhang H, Jiang J, Li Y, Nie C, Gu J, et al.Angiogenic and inflammatory biomarker levels in aqueous humor and vitreous of neovascular glaucoma and proliferative diabetic retinopathy. Intern Ophthalm. 2020; 40(2): 467–475. https://doi.org/10.1007/s10792-019-01207-4
33. Guzun OV, Zadorozhnyy OS, Vychuzhanin VV, Khramenko NI, Velichko LM, Korol AR. Et al. A neural network model for predicting the effectiveness of treatment in patients with neovascular glaucoma associated with diabetes mellitus. Rom J Ophthalm. 2024; 68(3): 294–300. https://doi.org/10.22336/rjo.2024.53
34. Hwang YH, Lee S, Kim M, Choi J. Comparison of treatment outcomes between slow coagulation transscleral cyclophotocoagulation and micropulse transscleral laser treatment. Sci Rep. 2024; 14(1): 23944. https://doi.org/10.1038/s41598-024-75246-y
35. Hong, Y, Hu Y, Dou H, Wang C, Zhang C, Ma Z. Comparison of the safety and efficacy of triple sequential therapy and transscleral cyclophotocoagulation for neovascular glaucoma in the angle-closure stage. Sci Rep. 2018; 8(1): 7074. https://doi.org/10.1038/s41598-018-25394-9
36. La Rosa LR, Pepe V, Lazzara F, Romano GL, Conti F, Giuffrida E, et al. Retinal Protection of New Nutraceutical Formulation. Pharmaceutics. 2025; 17(1): 73. https://doi.org/10.3390/pharmaceutics17010073.

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Abbreviation. *BCVA, best corrected visual acuity; CPC, cyclophotocoagulation; DM, diabetes mellitus; DR, diabetic retinopathy; IOP, intraocular pressure; NVG, neovascular glaucoma; PDR, proliferative diabetic retinopathy; PRP, panretinal photocoagulation; PTC, phosphene threshold current; RVO, retinal vein occlusion; TSCPC, transscleral cyclophotocoagulation.*