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Analysis of the relationship between VEGF, NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients with primary open-angle glaucoma

Qiming Zhang[1†], Liying Gu[1†] and Yujuan Xu[1*]

Abstract

Objective Our study aimed to investigate the relationship between vascular endothelial growth factor (VEGF), NOD-like receptor thermal protein domain associated protein 3 (NLRP3) inflammatory complex, erythropoietin (EPO) levels, and ocular hemodynamics in patients diagnosed with primary open-angle glaucoma (POAG).

Methods This is a prospective observational study. Patients diagnosed with POAG at The Sixth Hospital of Wuhan hospital between November 2022 and February 2023were enrolled.The patients were categorized into three groups based on the average visual field defect (mean deviation, MD) value: severe injury group (MD > 12 dB, 93 cases), moderate injury group (7 ≤ MD ≤ 12 dB, 89 cases), and mild injury group (MD < 7 dB, 85 cases). The levels of VEGF, NLRP3 inflammatory complex, EPO, and ocular hemodynamics were compared among the groups. Furthermore, the relationship between VEGF, NLRP3, EPO levels, and ocular hemodynamics in patients with POAG was analyzed using Pearson correlation analysis. After adjusting for confounding factors such as age and gender, multivariate Logistic regression analysis was performed with the ocular hemodynamics indexes being used as dependent variables, and VEGF, NLRP3, ASC, Caspase-1, and EPO being used as independent variables.

Results A total of267 patients with POAG were enrolled. There were no significant differences in sex, age, body mass index, systolic blood pressure, diastolic blood pressure, smoking, alcohol consumption, and blood glucose between the two groups ($P > 0.05$). The levels of NLRP3, ASC, Caspase-1, and EPO in the severe and moderate injury groups were higher than those in the mild injury group, whereas the VEGF levels were lower in the severe and moderate groups compared to the mild group, showing significant differences ($P < 0.05$). The severe group exhibited higher levels of NLRP3, ASC, Caspase-1, and EPO than the moderate group, while the VEGF levels were lower in the severe group compared to the moderate group, showing significant differences ($P < 0.05$). The peak systolic velocity(PSV) and resistance index (RI) were higher in the severe and moderate groups than in the mild group, whereas the EDV was significantly lower in the severe and moderate groups compared to the mild group ($P < 0.05$). The severe

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group exhibited higher PSV and RI values compared to the moderate group, while the EDV was lower in the severe group compared to the moderate group, showing significant differences ($P < 0.05$). Pearson correlation analysis was performed to examine the relationship between VEGF, NLRP3, EPO levels, and ocular hemodynamics in patients with POAG. VEGF, NLRP3, ASC, Caspase-1, and EPO showed positive correlations with PSV and RI, and negative correlations with EDV in patients with POAG. Regression analysis showed that VEGF, NLRP3, ASC, Caspase-1 and EPO were significantly correlated with ocular hemodynamics in POAG (all $P < 0.001$).

Conclusion We demonstrated that the levels of VEGF, NLRP3 inflammatory complex, and EPO were highly associated with ocular hemodynamics in patients diagnosed with POAG.

Keywords VEGF, NLRP3 inflammatory complex, EPO, Primary open-angle glaucoma, Ophthalmic hemodynamics

Introduction

According to statistics, the global population of middle-aged and elderly individuals with glaucoma currently exceeds 60 million, and it isexpected to surpass 100 million by 2040, with Asians comprising approximately 60% of these cases [1]. Among various types of glaucoma, primary open-angle glaucoma (POAG) is the most prevalent, with over 12 million affected individuals aged 40 and above in China. However, as the quality of life, scientific advancements, and medical technologies continue to improve, the incidence rate of POAG is also on the rise. Nevertheless, the diagnostic rate of POAG in China remains low, standing at only 10% [2]. Due to the insidious onset process of this condition, by the time most patients experience clinical symptoms, irreversible visual damage has already occurred to a certain extent [3]. Therefore, early detection and treatment of POAG are crucial in preventing further deterioration of visual function, preserving existing vision, and enhancing overall quality of life. The underlying mechanisms responsible for optic nerve damage in POAG have yet to be fully elucidated. For a long time, mechanical and ischemic theories have been predominant. However, growing evidence has suggested that abnormalities in hemodynamics and other factors can result in insufficient blood supply to the optic nerve, ultimately leading to impaired optic nerve function [1, 4].

In recent years, significant attention has been focused on the relationship between VEGF, NLRP3 inflammatory complex, erythropoietin (EPO) levels, and patients with POAG. Among these factors, VEGF is a highly specific molecule that promotes the proliferation of vascular endothelial cells and stimulates capillary formation [5]. In conditions of ocular hypoxia, VEGF enhances the activity of plasminogen activator, modifies the extracellular matrix, promotes proteolysis, and induces the growth of new capillaries. The NLRP3 inflammatory complex is a protein complex comprising NLRP3, ASC, and caspase-1. It is expressed by macrophages, neutrophils, and endothelial cells during the process of blood circulation [6]. EPO, on the other hand, is a glycoprotein hormone that stimulates erythropoiesis. In the eye, hypoxia plays a significant role in stimulating EPO to bind with erythroid progenitor cell receptors, thus promoting the release of red blood cells [7].

Dimtsas et al. [8]. conducted a study highlighting the high expression of VEGF in patients with POAG, indicating its potential as a protective factor. Lai et al. [9]. reported the close relationship between EPO levels and glaucoma patients. Chen et al. [10]. demonstrated that NLRP3 could promote the apoptosis of ganglion cells in acute glaucoma. However, limited research exists on the association between VEGF, NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients with POAG. Therefore, this study aimed to explore the correlation between VEGF, NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients diagnosed with POAG.

Participants and methods

Participants

This is a prospective observational study.A total of 267 patients diagnosed with POAG, admitted to The Sixth Hospital of Wuhan between November 2022 and February 2023, were enrolledinto this study. The patients were categorized into three groups based on the average visual field defect (mean deviation, MD) value: severe injury group (MD > 12 dB, 93 cases), moderate injury group ($7 \leq MD \leq 12$ dB, 89 cases), and mild injury group (MD < 7 dB, 85 cases) [11]. This study was approved by the ethics committee of the Sixth Hospital of Wuhan[No.23–046 (2022)] and was conducted according to the principles of the Declaration of Helsinki. All patients provided written informed consent to use their data for analysis and publication.

Selection criteria

The following criteria were used to include participants in the study: 1)Patients were diagnosed in accordance with the diagnostic criteria for primary open-angle glaucoma outlined in the "Experts Consensus on the Diagnosis and Treatment of Primary Glaucoma in China (2014) [12]". 2) Patients were with age of35 to 78 years old; 3) Presence of glaucoma with visual field changes indicative

of glaucomatous damage, or characteristic morphological changes in the optic disc and retinal nerve fiber layer observed in fundus examination, or narrow angle opening, with intraocular pressure (IOP) measured to be >21 mmHg or ≤21 mmHg during the peak period of a 24-hour period.4) Patients with primary open-angle glaucomaand IOP at 18 mmHg or lower by medication or patients with normal tension glaucoma [11]. The following criteria were used to exclude individuals from the study: (1) Presence of uveitis, fundus vascular diseases, or other ocular diseases. (2) Patients who had factors such as mental or intellectual disabilities that hindered cooperation, as well as those who were unable to fix their vision due to impaired visual function. (3) Previous glaucoma surgery or laser treatment. (4) Pregnancy or lactation. (5) Participation in other clinical trials within the past three months. (6) Inability to adhere to treatment or follow-up. (7) History of previous eye surgery, radiotherapy, chemotherapy, or biological cell immunotherapy. (8) Patients with consciousness or mental disorders that hindered cooperation. (9) Patients with hematological, infectious, immunological, or other malignant tumor diseases.

Clinical data

(1) General information regarding the participants'sex, age, BMI, systolic blood pressure, blood sugar, etc., was collected.

(2) Analysis of NLRP3 inflammatory complex, EPO, and VEGF: (1) Participants were instructed to lie on their backs on the operating table.The conjunctival sac was cleaned, and routine disinfection was performed.Tissue placement and anesthesia were administered. (2) An eyelid spreader was used to expose the eye, and a No. 25 needle was used to puncture the anterior chamber from the limbus.Approximately 0.5 mL of aqueous humor was collected for examination.The expression levels of EPO and VEGF in aqueous humorwere detected using an enzyme-linked immunosorbent assay (ELISA) kit from R&D Systems, USA. The detection procedure strictly followed the instructions provided with the kit. (3) A volume of 5 mL of peripheral venous blood was collected from patients to extract the levels of NLRP3 inflammatory complex in peripheral venous blood macrophages.White blood cells were separated and extracted through Ficoll density gradient centrifugation.The cells were washed twice with phosphate buffer and fixed with 50 $g{\cdot}L^{-1}$ paraformaldehyde for 30 min at room temperature.Blocking was performed using 10% goat serum for 1 h.Anti-human NLRP3 antibody (Epitomics, USA), apoptosis-associated speck-like protein containing a CARD (ASC) (Abcam, UK), and rabbit anti-human caspase-1 antibody (Cell Signaling Technology, USA) were added and incubated overnight at 4 °C.The cells were washed three times with Tris-HCl buffer containing Tween-20 and incubated with anti-rabbit secondary antibody (labeled with PE-Texas Red A) for 30 min at room temperature.The cells were washed three times with phosphate buffer containing Tween-20.The cells were resuspended in double distilled water before being transferred to flow cytometry.Macrophage subpopulations were screened using flow cytometry (BD Company, USA).The fluorescence intensity of NLRP3, ASC, and caspase-1 on the cell surface was measured with actin as the internal reference.Stripe grayscale analysis was performed using Image J software.

(3) Ocular Hemodynamics: Doppler ultrasound (GE) was used to measure ocular hemodynamicswith probe frequency being 5 ~ 12 MHz.The patient was placed in a supine position, the pupils looked directly, and both eyes closed naturally. The probe with adjusted frequency was gently placed on the patient's eyelids.The peak systolic velocity (PSV), end diastolic velocity (EDV), and resistance index (RI) of the ophthalmic artery were measured using color Doppler ultrasound (GE).

Statistical analysis

Data analysis was performed using SPSS 21.0 software, and a database was established using Excel. Measurement data that followed a normal distribution were expressed as mean±standard deviation ($\bar{x}\pm s$), and t-tests were used for paired comparisons between and within groups. Count data were presented as percentages (%), and chi-square (χ^2) tests were used for comparisons. Pearson correlation analysis was conducted to investigate the relationship between VEGF, NLRP3, EPO levels, and ocular hemodynamics in patients with POAG. After adjusting for confounding factors such as age and gender, multivariate Logistic regression analysis was performed with the ocular hemodynamics indexes being used as dependent variables, and VEGF, NLRP3, ASC, Caspase-1, and EPO being used as independent variables. $P<0.05$ was considered of significant difference.

Results

Comparison of general information among groups

The severe injury group consisted of 45 males and 48 females, aged between 38 and 75 years, with an average age of (50.09±13.19) years and a body mass index (BMI) range of 20–25 kg/m^2, with an average BMI of (23.03±2.17) kg/m^2. The moderate injury group comprised 46 males and 43 females, aged between 37 and 76 years, with an average age of (50.83±14.23) years and a BMI range of 20–25 kg/m^2, with an average BMI of (22.83±2.31) kg/m^2. The mild injury group included 42 males and 43 females, aged between 39 and 76 years, with an average age of (50.43±13.93) years and a BMI range of 20–25 kg/m^2, with an average BMI of (22.98±2.09) kg/m^2. No significant differences were observed in terms of general data between the threegroups, including gender,

Table 1 Comparison of general information among groups

Parameter	Severe injury group($n=93$)	Moderate injury group($n=89$)	Mild injury group($n=85$)	χ^2/t	*P*
Sex (male/female) (n)	45/48	46/43	42/43	0.206	0.902
Age (year)	50.09 ± 13.19	50.83 ± 14.23	50.43 ± 13.93	0.441	0.659
BMI (kg/m^2)	23.03 ± 2.17	22.83 ± 2.31	22.98 ± 2.09	0.283	0.778
SBP (mmHg)	120.98 ± 11.93	119.02 ± 12.39	121.29 ± 11.76	0.002	0.966
DBP (mmHg)	75.87 ± 7.19	76.09 ± 8.01	75.93 ± 7.38	0.198	0.719
Blood glucose (mmol/L)	5.18 ± 0.38	5.09 ± 0.31	5.12 ± 0.36	0.209	0.732
Alcohol consumption (n)	6	5	7	0.493	0.782
Tobacco use (n)	7	6	4	0.624	0.732

Table 2 Comparison of NLRP3 inflammatory complex, EPO, and VEGF among groups

Index	Severe injury group($n=93$)	Moderate injury group($n=89$)	Mild injury group($n=85$)	t	*P*
NLRP3 inflammatory complex					
NLRP3 (%)	51.09 ± 10.76	43.87 ± 9.09	37.92 ± 9.17	47.913	< 0.001
ASC (%)	44.07 ± 8.93	38.02 ± 8.05	32.01 ± 8.17	35.093	< 0.001
Caspase-1 (%)	50.19 ± 8.17	44.69 ± 7.93	40.29 ± 7.54	26.198	< 0.001
EPO (U/L)	23.65 ± 3.08	17.38 ± 3.38	11.97 ± 2.16	18.761	< 0.001
VEGF (U/L)	138.01 ± 7.19	183.92 ± 6.65	229.91 ± 7.29	-37.971	< 0.001

Table 3 Comparison of ocular hemodynamics among groups

Index	Severe injury group($n=93$)	Moderate injury group($n=89$)	Mild injury group($n=85$)	t	*P*
PSV (cm·s^{-1})	32.98 ± 2.76	30.17 ± 2.65	28.03 ± 2.36	87.023	< 0.001
EDV (cm·s^{-1})	5.74 ± 0.87	7.73 ± 0.93	10.56 ± 0.98	-36.981	< 0.001
RI	0.92 ± 0.13	0.73 ± 0.09	0.52 ± 0.05	65.091	< 0.001

Table 4 Relationship between VEGF, NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients with POAG

Index	PSV		EDV		RI	
	r value	*P* value	*r* value	*P* value	*r* value	*P* value
VEGF	1.823	< 0.001	-4.981	< 0.001	3.281	< 0.001
NLRP3	7.914	< 0.001	-11.823	< 0.001	6.012	< 0.001
ASC	6.934	< 0.001	-7.043	< 0.001	4.113	< 0.001
Caspase-1	4.926	< 0.001	-5.981	< 0.001	1.023	< 0.001
EPO	12.198	< 0.001	-9.871	< 0.001	2.976	< 0.001

age, BMI, systolic and diastolic blood pressure, smoking, alcohol consumption, and blood glucose ($P>0.05$, Table 1).

Comparison of NLRP3 inflammatory complex, EPO, and VEGF amonggroups

The levels of NLRP3, ASC, Caspase-1, and EPO were significantly higher in the severe and moderate groups compared to the mild group, while the levels of VEGF were significantly lower in the severe and moderate groups compared to the mild group ($P<0.05$). Moreover, the severe group exhibited higher levels of NLRP3, ASC, Caspase-1, and EPO compared to the moderate group, while VEGF levels were lower in the severe group compared to the moderate group ($P<0.05$). Table 2.

Comparison of ocular hemodynamics among groups

The PSV and RI of the severe and moderate groups were significantly higher than those of the mild group, while the EDV was lower than that of the mild group, demonstrating significant differences ($P<0.05$). Additionally, the PSV and RI of the severe group were higher than those of the moderate group, whereas the EDV was lower than that of the moderate group, showing significant differences ($P<0.05$). Table 3.

Relationship between VEGF, NLRP3 inflammatory complex, EPO levels and ocular hemodynamics in patients with POAG

The results revealed that VEGF, NLRP3, ASC, Caspase-1, and EPO levels were positively correlated with PSV and RI in patients with POAG. Conversely, these factors showed a negative correlation with EDV. Detailed information can be found in Table 4.

Table 5 Relationship between VEGF, NLRP3 inflammatory complex, EPO levels, and PSV in patients with POAG

Index	β	SE	χ^2 value	OR (95%CI)	*P* value
VEGF	0.523	0.177	2.832	1.655(1.161–2.355)	0.003
NLRP3	0.389	0.172	2.456	1.462(1.032–2.019)	0.023
ASC	0.575	0.185	6.535	1.552(1.067–2.193)	0.001
Caspase-1	2.161	0.491	16.293	7.983(3.002–18.768)	< 0.001
EPO	0.287	0.205	6.359	1.309(1.002–1.829)	0.006

Table 6 Relationship between VEGF, NLRP3 inflammatory complex, EPO levels, and EDV in patients with POAG

Index	β	SE	χ^2 value	OR (95%CI)	*P* value
VEGF	1.004	0.406	6.112	0.366(0.165–0.812)	0.013
NLRP3	0.060	0.015	16.205	1.061(1.031–1.093)	< 0.001
ASC	0.015	0.004	14.087	1.015(1.007–1.023)	< 0.001
Caspase-1	1.378	0.309	19.86	3.966(2.164–7.269)	< 0.001
EPO	0.640	0.283	5.120	1.897(1.089–3.303)	0.024

Table 7 Relationship between VEGF, NLRP3 inflammatory complex, EPO levels, and RI in patients with POAG

Index	β	SE	χ^2 value	OR (95%CI)	*P* value
VEGF	1.042	0.242	17.565	2.863(1.692–3.883)	< 0.001
NLRP3	0.279	0.104	7.646	1.273(1.046–1.767)	0.004
ASC	1.365	0.369	12.178	3.868(1.761–6.324)	< 0.001
Caspase-1	0.837	2.219	9.872	2.198(1.531–2.876)	0.001
EPO	1.876	0.182	117.872	6.091(1.476–8.981)	< 0.001

Logistic regression analysis of VEGF, NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients with POAG

After adjusting for confounding factors such as age and gender, the results showed that VEGF, NLRP3, ASC, Caspase-1 and EPO were significantly correlated with ocular hemodynamics in patients with POAG (all $P<0.001$, Tables 5, 6 and 7).

Discussion

The treatment principle for primary open-angle glaucoma is to preserve visual function and protect the angle function. Specific measures include controlling elevated intraocular pressure (IOP) and safeguarding the optic nerve [13]. However, clinical observations have indicated that some patients may experience disease progression despite good IOP control or initially normal IOP levels. This may be attributed to insufficient perfusion resulting from vascular spasms.Hussain et al. [14]. identified the role of red blood cell oxidation barrier in the development of POAG. Specifically, upregulation of catalase in RBCs leads to lipid peroxidation, resulting in alterations in RBC surface properties. Although these changes may be subtle, they are sufficient to induce abnormalities in the morphology and function of retinal ganglion cells, ultimately leading to ischemia in POAG.Moreover, an earlier study demonstrated that inadequate blood supply to the optic nerve contributed to impaired blood circulation and could also lead to the onset of POAG [15]. Consequently, investigating ocular hemodynamics in patients with POAG has emerged as a significant area of focus in clinical research.

EPO is a glycoprotein hormone that plays a role in promoting angiogenesis. In the presence of retinal damage, EPO stimulates the differentiation and proliferation of erythroid progenitor cells, facilitating neurovascular growth and protecting retinal ganglion cells from damage. When local hypoxia occurs, along with insufficient blood flow perfusion in the optic disc and local ischemia, a reduction in intracellular hydrogen peroxide content triggers erythropoiesis, subsequently leading to an increase in EPO levels. This elevation in EPO can promote the formation of new blood vessels, potentially resulting in elevated intraocular pressure [16]. Furthermore, increased levels of EPO can cause adhesion of iris tissue, impacting hemodynamics and leading to disorders in eye microcirculation. Consequently, these effects can contribute to visual field defects and impairment of visual function. Lin et al.'s study provided evidence suggesting a close association between EPO levels and the condition of patients with POAG [17].Activation of the NLRP3 complex leads to the increase of downstream inflammatory factors, such as IL-1β and IL-18, enhancing the body's inflammatory response. Thisfurther influences abnormal changes in ET-1 levels, promotes leukocyte chemotaxis and aggregation, induces an increase in oxygen free radical lipid metabolites, releases proteolytic enzymes, and ultimately results in damage to eye tissue cells, increased permeability, and optic nerve function impairment [18]. Jassim et al.'s study highlighted the close

association between the NLRP3 inflammatory complex and glaucoma [18].VEGF, on the other hand, is a cytokine that promotes the mitosis of vascular endothelial cells, increases the permeability of venules and capillaries, and facilitates the proliferation of vascular endothelial cells. It also contributes to the exosmosis of protein macromolecules [19]. By increasing the permeability of blood vessels, VEGF allows blood proteins to penetrate into the extravascular space, leading to airway inflammation, edema, changes in the extracellular matrix, and the potential development of glaucoma [20]. Hussain et al.'s study highlighted the close relationship between VEGF and the occurrence and progression of glaucoma [14].The results of this study demonstrated that the levels of NLRP3, ASC, Caspase-1, and EPO were higher in the severe and moderate groups compared to the mild group, whereas VEGF levels were lower in the severe and moderate groups compared to the mild group ($P<0.05$). Additionally, the severe group exhibited higher levels of NLRP3, ASC, Caspase-1, and EPO compared to the moderate group, while VEGF levels were lower than the moderate group ($P<0.05$). These findings were consistent with the aforementioned research results, indicating that the levels of NLRP3, ASC, Caspase-1, EPO, and VEGF in patients with POAG varied with the severity of the condition.

Hemodynamics plays a crucial role in evaluating the aggregation and deformability of blood components, as well as the fluidity and viscosity of circulating blood. Hemorheology can undergo changes depending on the disease status of the human body. Abnormal blood flow and viscosity can lead to slow or stagnant blood flow, and in some cases, even blockages, ultimately resulting in local or systemic circulatory disorders. These circulatory disorders can lead to pathological changes in tissues and organs.Color Doppler ultrasound is a non-invasive technique used to evaluate live blood flow by quantitatively measuring blood flow parameters, including PSV, RI, and EDV. It provides an objective and accurate assessment of the hemodynamic information of the eye [21]. Research suggested that PSV, RI, and EDV, as blood flow parameters, could reflect the local blood supply status of the optic disc [21]. Duan et al.'s study asserted that patients with POAG exhibited hemodynamic disorders [22]. Additionally, Lindemann et al. [23]. noted that the severity of hemodynamic disorders corresponded to the severity of POAG. Based on our study, the PSV and RI in the severe and moderate groups were higher compared to the mild group, while the EDV was lower compared to the mild group ($P<0.05$). Moreover, the severe group exhibited higher PSV and RI values than the moderate group, whereas the EDV was lower than the moderate group ($P<0.05$). These results were consistent with the aforementioned research findings, indicating that the PSV, RI, and EDV in patients with POAGchanged in accordance with the severity of the condition.

Mou et al.'s study highlighted the close association between the NLRP3 inflammatory complex and the severity of optic nerve injury in primary glaucoma [24]. Similarly, another study indicated that abnormal levels of EPO and VEGF in the serum and aqueous humor of glaucoma patients were linked to increased resistance in ocular blood flow [25].The results of this study, utilizing Pearson correlation analysis, demonstrated that VEGF, NLRP3, ASC, Caspase-1, and EPO levels were positively correlated with PSV and RI in patients with POAG, while they were negatively correlated with EDV. Further multivariate Logistic regression analysis showed that VEGF, NLRP3, ASC, Caspase-1 and EPO were significantly correlated with ocular hemodynamics in patients with POAG. These findings suggested a close relationship between VEGF, the NLRP3 inflammatory complex, EPO levels, and ocular hemodynamics in patients with POAG. However, there were several limitations that should be acknowledged in the present study. The mechanism underlying the relationship between VEGF, NLRP3, EPO levels, and ocular hemodynamics in patients with POAG remains unclear in clinical research. Further studies should be conducted to elucidate the relevant mechanisms of their relationship in such patients.

Taken together, the levels of NLRP3, ASC, Caspase-1, EPO, and VEGF exhibited variations that corresponded to the severity of POAG. Similarly, the blood flow parameters of PSV, RI, and EDV also varied based on the severity of the condition. As the condition progressed, the abnormal levels of NLRP3, ASC, Caspase-1, EPO, VEGF, PSV, RI, and EDV became more prominent. Additionally, VEGF, NLRP3, ASC, Caspase-1, and EPO exerted a positive correlation with PSV and RI in patients with POAG, while demonstrating a negative correlation with EDV.

Abbreviations

EDV	End Diastolic Velocity
ELISA	Enzyme-Linked Immunosorbent Assay
EPO	Erythropoietin
IOP	Intraocular Pressure
POAG	Primary Open-Angle Glaucoma
PSV	Peak Systolic Velocity
RI	Resistance Index

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Author contributions

QZ conceptualized, collected the clinical data and drafted the manuscript. LG and YX collected the clinical data and revised the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets generated and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the ethics committee of the Sixth Hospital of Wuhan[No.23–046 (2022)] and was conducted according to the principles of the Declaration of Helsinki. All patients provided written informed consent to use their data for analysis and publication.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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