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RESEARCH ARTICLE

Xiao et al: LAP in glaucoma

Clinical significance of a novel inflammatory-nutritional index in glaucoma severity evaluation

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ABSTRACT

This study investigated the association between glaucoma and serum albumin (Alb), lymphocyte percentage (LYMPH%), and their combined index (LAP = LYMPH% × Alb), to evaluate their potential as biomarkers for systemic inflammation and disease progression in glaucoma. We enrolled 161 glaucoma patients and 181 healthy controls. Serum Alb and LYMPH% were measured using standard blood biochemistry and routine tests, and LAP was calculated accordingly. Statistical analyses were performed to compare these markers between groups and assess their correlation with disease severity. Both the median serum Alb level and peripheral blood LYMPH% were significantly lower in the glaucoma group compared to controls (Alb: 43.48 g/L vs. 44.63 g/L, $p < 0.001$; LYMPH%: 24.25% vs. 29.12%, $p < 0.001$). Correspondingly, LAP levels were also significantly reduced in glaucoma patients (1053 vs. 1298, $p < 0.001$).Lower LYMPH% and LAP levels were associated with more severe glaucomatous visual impairment (LAP, healthy controls vs. glaucoma: AUC = 0.7080, $p < 0.001$, Max Youden = 0.3621; early vs. severe glaucoma: AUC = 0.8061, $p < 0.001$, Max Youden = 0.5377). In summary, LAP may serve as a supportive biomarker of systemic inflammation in glaucoma. It demonstrates good accuracy in reflecting glaucoma severity and shows potential for monitoring disease progression.

Keywords: Glaucoma; albumin; Alb; lymphocyte rate; biomarker; systemic inflammation.

INTRODUCTION

Glaucoma, a group of diseases characterized by visual dysfunction and optic neuropathy (1), is projected to affect 100 million individuals globally by 2040 (2). The current challenges in early detection and prevention have prompted researchers to explore innovative diagnostic and therapeutic strategies using advanced biotechnological approaches (3, 4). While animal models have provided valuable insights into the biochemical pathways involved in glaucoma, their findings may not always translate seamlessly to non-invasive clinical applications (5, 6).

Growing evidence suggests that systemic inflammation plays a key role in the etiopathogenesis of glaucoma (7). Consequently, systemic inflammatory markers have emerged as promising tools for disease diagnosis and prognosis (8-10). Peripheral venous blood analysis, due to its cost-effectiveness, simplicity, and accessibility—even with minimal sample volumes (as little as a few milliliters)—offers a practical solution for screening and diagnosing high-risk individuals (11, 12). Our previous study found that two serum Alb and bilirubin, both of which have powerful anti-oxidant/anti-inflammatory properties, were significantly lower in patients with glaucoma than those in healthy controls (13). In addition, both of them were negatively associated with the clinical severity of visual impairment in glaucoma patients. Other groups have also reported the applications of systemic inflammatory indices in the clinical management of glaucoma, such as blood cell counts (neutrophils, lymphocytes)(14), complement C3 (15), uric acid (16), and platelets (17).

In addition to individual basic parameters, recent investigations have turned their attention towards the amalgamation of two parameters, emphasizing the potential value harbored by the neutrophil-to-lymphocyte ratio (NLR)(18), the platelet-to-lymphocyte ratio (PLR)(17), and the lymphocyte-to-monocyte ratio (LMR) as direct indicators of systemic inflammation (14). These biomarkers have exhibited exceptional promise as pioneering instruments for the early identification and individualized screening of glaucoma (19). In our earlier work, we unearthed a significantly positive correlation

between the neutrophil-to-albumin ratio (NAR) and the severity of visual impairment, demonstrating commendable accuracy in predicting the gravity of glaucoma (13).

To further optimize the utilization of serum Alb in the context of glaucoma, we developed a novel composite index, designated as the product of lymphocyte percentage multiplied by serum Alb concentrations (LAP). Our hypothesis posited that LAP might surpass Alb or lymphocyte levels alone as a superior means of monitoring disease severity in glaucoma patients.

To test this hypothesis, we conducted a single-center retrospective study involving glaucoma patients, analyzing LAP levels and their association with disease severity. Our findings highlight LAP's potential clinical utility in tracking glaucoma progression. As a biomarker that is non-invasive, cost-effective and simple to measure, LAP may serve as a useful tool for assessing disease progression and guiding personalized treatment strategies in glaucoma patients.

MATERIALS AND METHODS

Patients

According to the Declaration of Helsinki, we recruited 161 glaucoma patients and 181 healthy controls of > 18 years of age. Patients in the study had their first eye exam, which included measurements of corrected distance sharpness, intraocular pressure, retinal nerve fiber layer (RNFL), spectral Optical coherence tomography and static visual field. Patients with pre-existing diabetes, chronic renal failure, rheumatism, hypertension, hyperlipidemia, anemia, cancer, and myocardial infarction were excluded. Meanwhile, we excluded all patients who were taking drugs known to affect blood cells or serum biochemistry.

We categorized the severity of the patients based on their visual field, which was mild, moderate, and severe. The field of view was divided into four concentric circles, and each field was given a score between 0 and 20. Where 0 indicates that the defect point is not measured, 20 indicates that at least two depressions are measured in the nasal area, and nine depressions are measured in each half field. Then the severity of visual

field injury was graded based on this score, finally, the visual field results obtained using the aforementioned method were utilized for Mean Deviation (MD) grading.

We recruited healthy controls who met the inclusion criteria from examination centers. The reference criteria were as follows; Daytime IOP less than 21 mmHg, mean RNFL within the standard range, no opening Angle, vertical cup/disk ratio less than 0.3 and/or cup/disk symmetry and/or large nipple area without atrophy, and absence of visual field defects. Patients were also questioned about a possible history of neurological disease, which was ruled out.

Clinical examination

Blood samples were collected from the anterior elbow vein of non-fasting patients. Blood image, CRP, and ESR analysis were performed immediately after sampling. Peripheral blood was collected using EDTA - anticoagulated Vacutainer CPT tubes (BD Biosciences), and serum was collected with serum - separator tubes (BD Biosciences). Samples were processed within half an hour. Blood cell counts were done on a Mindray BC - 5500 system, and serum albumin was analyzed on an Architect C 16000 (Abbott) in the hospital's biochemistry lab.

Ethical statement

This was a case-control study with the subjects derived from the outpatients and inpatients in the Sichuan Provincial People's Hospital, a provincial comprehensive hospital in Chengdu, China. All individuals provided their written, informed permission for the use of their clinical data in this study. Adhering strictly to the Declaration of Helsinki guidelines, this study received full approval from the Institutional Review Board for Clinical Research at the Sichuan Provincial People's Hospital (NO: 2024019).

Statistical analysis

GraphPad Prism was used for statistical analysis (version 9; GraphPad Prism Software, Inc.). All data were first determined to conform to a normal distribution using the Kolmogorov-smirnov test before the next analysis. The levels of lymphocytes, ALB, and LAP were compared between the two groups using a non-parametric rank-sum test.

The categorical variables were analyzed by chi-square test. Kolmogorov-smirnov was used to test the normality. Data conforming to the normal distribution were presented as mean ± standard deviation. The unpaired Student's T (two-tailed) test was used between the glaucoma patients and the healthy control group except for age. If the data did not conform to the normal distribution, the differences between the two groups were analyzed by Mann-Whitney test. Statistically significant, $p < 0.05$.

Receiver operating characteristic (ROC) analysis was used to determine the optimal cutoff values for predicting PACG, which were then used to calculate the sensitivity and specificity of LAP probabilities in predicting glaucoma. After verifying the predictive value of LAP as a continuous variable, we evaluated the correlation between LAP classifications.

RESULTS

Demographics of the participants

In this study, 161 glaucoma patients were enrolled, including 99 PACG and 62 POAG. The control group consisted of a population with a similar age and sex distribution (n = 181). The patients were divided into three groups according to the mean deviation of the visual field (MD) and the degree of visual field defect (Early, n = 34, > −6 dB; Moderate, n = 63, −12 ~ −6 dB; Severe, n = 64, not higher than −12dB). If the patient has glaucoma in both eyes, one eye is randomly selected to record data. Demographic information and descriptive statistics of glaucoma and healthy controls are shown in Table 1 in details.

LAP levels are significantly decreased in patients with glaucoma

As reported in Table 1, serum Alb (43.48 ± 2.867 g/L) levels exhibited a significant reduction compared to the control group (Alb, 44.63 ± 2.514 g/L, $p < 0.001$), consistent with our prior findings. Furthermore, we directed our scrutiny towards the blood LYMPH%, which also manifested a decrease in glaucoma patients when compared to the control cohort (13). While previous studies have examined the absolute count of blood lymphocytes, LYMPH% has yet to be explored in the context of glaucoma. As

alluded to earlier, we formulated a novel amalgamated metric, LAP, designated as the product of LYMPH% and serum Alb concentrations. Intriguingly, LAP exhibited a discernible decline in glaucoma patients (1053 ± 313.5) compared to controls (1298 ± 333.3, $p < 0.001$). Meanwhile, considering that age and gender are also factors that can affect the level of systemic inflammation, we also conducted a multivariate analysis. The results showed that LAP also had significant differences between glaucoma patients and healthy people (LAP: OR 0.997, 95% CI: 0.996–0.998, $p < 0.001$) (Supplementary Table 1). However, when comparing LAP levels between patients with PACG and POAG, no significant differences were observed (PACG: 1067 ± 338.3, POAG: 1032 ± 270.7, $p = 0.491$, Supplementary Table 2).

Associations of LAP with disease severity of patients with glaucoma

Subsequently, our focus shifted towards exploring the clinical applicability of LAP in the context of glaucoma. To achieve this, we meticulously categorized glaucoma patients based on the severity of their visual condition. The ensuing investigation, as depicted in Figure 1, revealed a pronounced downward trajectory of LAP values as one traverses from the Early to the Severe group. Notably, this trend attained statistical significance when comparing the Early group to the Severe group, as well as when contrasting the Moderate group with the Severe group. This intriguing finding implies a potential correlation between LAP levels and the progressive nature of glaucoma. It suggests that LAP might serve as a discerning indicator of disease severity, exhibiting a gradual decline as the condition advances. Such a relationship underscores the potential clinical value of LAP as an invaluable tool for monitoring and assessing the progression of glaucoma.

The correlation between LAP and glaucoma analyzed by receiver operating characteristic (ROC) curve

Having established the diminished LAP levels in glaucoma patients compared to controls, our investigation progressed to a more comprehensive analysis of LAP's value through the use of ROC curves. Table 2 showcases the results, illustrating that LAP

(AUC = 0.7080, $p < 0.001$) exhibited commendable accuracy as a discriminatory marker for distinguishing glaucoma from controls, surpassing the individual abilities of ALB (AUC = 0.6151) or LYMPH% (AUC = 0.6894) (figure 2). Moreover, considering our previous findings that identified serum total bilirubin, indirect bilirubin, the neutrophil-to-albumin ratio, the neutrophil-to-total bilirubin ratio, and the neutrophil-to-indirect bilirubin ratio as discriminatory indices between glaucoma patients and controls, we conducted a comparative analysis of all these indices against LAP. (NAR, AUC = 0.6673; NTBR, AUC = 0.6338; NIBR, AUC = 0.6566), showing that LAP had the highest AUC in this particular scenario. Our inquiry delved deeper, aiming to ascertain LAP's potential in discerning glaucoma severity. Employing ROC analysis to compare the LAP levels across patient groups stratified by clinical severity, we observed LAP to outperform all other factors in distinguishing severe glaucoma from its early counterpart (Early vs Severe: AUC = 0.8061, $p< 0.001$, Max. Youden = 0.5377). Notably, this superior performance surpassed the previously reported abilities of Alb, LYMPH%, total bilirubin, indirect bilirubin, the neutrophil-to-albumin ratio, the neutrophil-to-total bilirubin ratio, and the neutrophil-to-indirect bilirubin ratio. Consequently, these data suggest that LAP could serve as a valuable indicator in stratifying patients based on the extent and progression of the disease (Table 3).

DISCUSSION

The pursuit of non-invasive methodologies for monitoring visual deterioration in glaucoma continues to pose a formidable clinical challenge, as existing techniques remain insufficient for definitive assessment of disease progression (19). There persists an urgent need for innovative, reliable tools capable of tracking visual functional changes without invasive intervention. Addressing this unmet need would substantially advance glaucoma management and patient care.

Building upon our prior demonstration of an inverse correlation between serum Alb levels and clinical severity of visual impairment in glaucoma patients (13), we herein propose a novel composite biomarker: the lymphocyte percentage multiplied by serum Alb concentration (LAP). This serological index integrates hematological (LYMPH%)

and biochemical (Alb) parameters to optimize the clinical utility of serum Alb in glaucoma evaluation. Our findings reveal two principal observations: first, glaucoma patients exhibit significantly reduced LAP levels compared to healthy controls; second, LAP demonstrates strong correlation with disease severity, substantiating its potential as a clinical assessment tool. The development of LAP as a composite index holds several advantages in evaluating glaucoma severity. By incorporating both LYMPH% and serum Alb concentrations, LAP offers a comprehensive and multifaceted approach to disease assessment. Lymphocyte percentage serves as a reflection of the immune response, which plays a crucial role in the pathogenesis of glaucoma. Serum Alb, on the other hand, serves as a surrogate marker for various physiological processes, including vascular integrity (20) and nutrition status (21). Combining these two parameters into a single index provides a more holistic representation of the underlying disease processes in glaucoma. By incorporating LAP into routine clinical practice, healthcare professionals can gain valuable insights into the progression of glaucoma and make well-informed decisions about treatment strategies. Furthermore, the non-invasive nature of LAP assessment adds an extra layer of convenience and patient comfort, making it a promising tool for long-term disease monitoring. Furthermore, the comprehensive nature of LAP allows for a more holistic assessment of disease severity, enabling personalized and targeted interventions.

Numerous research findings have highlighted the significant involvement of peripheral immunity in glaucoma. Specifically, we have observed that the circulating $CD4^+$ T cell response is enhanced in parallel with the stage of visual damage in glaucoma patients. Our data indicate a positive correlation between T cell activation and the severity of glaucoma. Additionally, we have identified an inverse relationship between serum Alb levels and the clinical severity of visual impairment in glaucoma patients. Furthermore, the redox state of vitreous Alb has been proposed as a biomarker for evaluating the oxidative environment in patients with primary open-angle glaucoma. Elevated levels of ischemia-modified albumin have also been documented in patients with primary angle-closure glaucoma, underscoring its potential as a biomarker for assessing

oxidative stress in this disease. Therefore, in the current study, we sought to enhance the utility of Alb and lymphocytes by combining these two parameters (through multiplication of serum Alb and peripheral blood lymphocyte ratio). We aimed to investigate whether this combined parameter, termed LYMPH%–Alb product (LAP), might be more effective in monitoring clinical activity and the progression of nerve injury in glaucoma patients compared to serum Alb and peripheral blood lymphocyte ratio individually.

The ROC analysis of LAP data from 161 patients and 181 healthy controls revealed an AUC of 0.7080, with a maximum cut - off value of 1141. At this level, sensitivity and specificity were 69.06% and 67.7%, respectively. Given the correlation between the disease and LAP from this and prior analyses, LAP shows diagnostic value. Further analysis of disease stages versus LAP found better diagnostic efficacy. Early vs. severe stage analysis gave an AUC of 0.8061, with a maximum cut - off of 1130, achieving sensitivity of 89.06% and specificity of 64.71%. These results are relatively satisfactory. Ultimately, multi-marker analyses integrating significantly correlated indicators may identify better supportive markers. Beyond its established role as a nutritional marker, serum Alb serves as a vital antioxidant in plasma, continuously combating oxidative stress (22). While the pathogenesis of glaucoma remains complex and largely enigmatic (23), the significance of disrupted oxidative/antioxidative balance has garnered attention in both patients and animal models. Alb acts as a "tramp steamer" in the circulation, capably scavenging various molecules, including transition metals (e.g., copper and iron) and polyunsaturated fatty acids (24-26). Upon reacting with oxygen, these molecules become potent generators of reactive oxygen species (ROS). The remarkable ligand-binding abilities of Alb confer numerous antioxidant activities (27). Despite previous notions dismissing impairments in Alb molecule and its antioxidant properties as "biologically insignificant," emerging evidence suggests that compromised antioxidant capacities of Alb may indeed be associated with various pathological conditions such as diabetes and chronic kidney diseases (28). Additionally, oxidized Alb has been suggested as an oxidative stress marker in neurodegenerative

diseases like Alzheimer's and Parkinson's (29, 30). Researchers have diligently explored the redox state of Alb in glaucoma patients, aiming to uncover its implications. For instance, the redox state of vitreous Alb has been proposed as a biomarker for assessing the oxidative milieu in patients with primary open-angle glaucoma (POAG)(31). Moreover, elevated levels of ischemia-modified Alb have been observed in patients with primary angle-closure glaucoma (PACG), underscoring its potential as a biomarker for assessing oxidative stress in this disease (32). Therefore, we speculate that the up regulation of oxidative stress response in patients with glaucoma leads to increased consumption of Alb, which could be one of the reasons for the decreased levels of serum Alb (33). Furthermore, there are reports suggesting that glaucoma patients may experience an increase in proteinuria, which may further contribute to the decline in serum Alb levels (34).

The alterations in the levels of C-reactive protein (CRP) and interleukin-6 (IL-6) in glaucoma, as well as their associations with the disease, warrant further investigation. In patients with primary angle-closure glaucoma (PACG), serum levels of IL-6, IL-8, and high-sensitivity C-reactive protein (hs-CRP) were significantly elevated compared to those in the normal control group. Moreover, IL-6 levels were positively correlated with the degree of visual field defect and the cup-to-disc ratio (VCDR). Additionally, in patients with primary open-angle glaucoma (POAG), aqueous humor IL-6 levels were significantly and positively correlated with intraocular pressure. Collectively, these findings suggest that changes in CRP and IL-6 levels may be closely related to the pathological processes of glaucoma, including inflammatory responses, optic nerve injury, and vascular lesions. Detection of these biomarkers may provide valuable references for clinical diagnosis and treatment. However, we are currently seeking more accessible biomarkers that do not impose additional economic burdens. To this end, we have explored the combined use of lymphocyte rate and serum Alb as potential indicators. We are also actively investigating other meaningful biomarkers. Future research may focus on conducting combined analyses to achieve the goal of auxiliary diagnosis in clinical practice. This approach is relatively more economical and simple,

although some challenges remain. We will continue to address these issues in subsequent in-depth studies.

However, several study limitations warrant consideration. Firstly, lymphocyte rate and serum albumin are general indicators reflecting systemic inflammation or nutritional status and are not specific to glaucoma. Currently, the sample size is relatively small. It is necessary to further verify their efficacy in a larger cohort and design multicenter and cross-regional studies to determine the universal applicability of LAP as a marker of disease severity. Secondly, the cross-sectional retrospective nature of this study limits our ability to draw definite conclusions about the causal relationship between LAP levels and the severity of glaucoma. In order to explore the temporal relationship between LAP and disease progression, it is necessary to enrich data collection and conduct long-term regular follow-up studies with large sample sizes. As well, future studies should consider the influence of more potential confounding factors, such as comorbidities and medication, for improve the accuracy and robustness of LAP as a clinical tool. Finally, there have been many studies in the field of non-invasive optic nerve injury biomarkers for glaucoma that have integrated hematological and biochemical parameters such as NLR, NAR, PLR and NIBR, with the aim of identifying nerve injury indicators for early detection and intervention. The existing indicators usually rely on the combination of two indicators. Our goal is to develop multi-level composite markers to assist in diagnosis through in-depth research, combining multiple indicators, integrating hematological and biochemical parameters.

CONCLUSION

In conclusion, our study successfully developed and evaluated the clinical utility of a novel lymphocyte- and Alb- based index, LAP, in the assessment of disease severity in glaucoma patients. The diminished LAP levels observed in glaucoma patients, coupled with the close correlation between LAP and clinical severity, highlight the potential of LAP as a valuable tool in glaucoma management. The comprehensive assessment capabilities of LAP, surpassing numerous previously investigated markers, offer a more accurate evaluation of disease severity. While additional research is required to

establish LAP's reliability in routine practice, this non-invasive biomarker shows promise for transforming glaucoma management and improving patient outcomes.

Conflicts of interest: Authors declare no conflicts of interest.

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Data availability: The datasets generated and/or analysed during the current study are not publicly available. Due to privacy protection and data security concerns, the data cannot be shared. However, upon reasonable request, the data may be made available from the corresponding author.

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TABLES AND FIGURES WITH LEGENDS

Table 1. Demographics and parameters of glaucoma patients and healthy controls

	Glaucoma	Healthy controls	*p* value
n	161	181	-
Age (year)	61.4(±13.1)	70.0(±9.2)	<0.001
Gender			
Female	87	69	0.003
Male	74	112	
PACG/POAG	99/62	-	
Glaucoma severity			
Early	34	-	-
Moderate	63	-	-
Severe	64	-	-
LYMPH%	24.25 (±7.098)	29.12 (±7.455)	<0.001
Alb (g/L)	43.48 (±2.867)	44.63 (±2.514)	<0.001
LAP	1053 (±313.5)	1298 (±333.3)	<0.001

All data were expressed as median (IQR) or mean ± SD

Abbreviations: IQR, quartile range; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; LYMPH%, lymphocyte rate; Alb, serum albumin; LAP, lymphocyte rate-albumin index.

Kolmogorov-smirnov was used to test the normality. Data conforming to the normal distribution were presented as mean ± standard deviation. The unpaired Student's T (two-tailed) test was used between the glaucoma patients and the healthy control group

except for age. If the data did not conform to the normal distribution, the differences between the two groups were analyzed by Mann-Whitney test. Statistically significant, $p < 0.05$.

Table 2. The discriminative abilities of variables between patients with glaucoma and healthy controls

	GL vs. HC				
	AUC	*p*	Max. Youden	95% CI	Cut-off（Sensitivity%，Specificity%）
ALB	0.6151	<0.001	0.2028	0.5556 to 0.6746	42.85 (76.8%, 43.48%)
LYMPH%	0.6894	<0.001	0.3214	0.6333 to 0.7455	26.15 (66.3%, 65.84%)
LAP	0.7080	<0.001	0.3676	0.6531 to 0.7630	1141 (69.06%, 67.7%)

Receiver operating characteristics (ROC) curve analysis.

Youden index: sensitivity+specificity-1.

Statistically significant, $p < 0.05$.

Abbreviations: AUC, area under the ROC curve; Max. Youden, the Youden index maximum.

Table 3. The discriminative abilities of variables in patients with glaucoma, stratified according to disease severity.

	Early vs. Moderate					Early vs. Severe					Moderate vs. Severe				
	AUC	*P*	Max. Youden	95% CI	Cut-off（Sensitivity%, Specificity%）	AUC	*p*	Max. Youden	95% CI	Cut-off（Sensitivity%, Specificity%）	AUC	*p*	Max. Youden	95% CI	Cut-off（Sensitivity%, Specificity%）
Alb	0.5532	0.397	0.1761	0.4311 to 0.6735	45.15 (79.37%, 38.24%)	0.5409	0.507	0.1480	0.4212 to 0.6606	45.15 (76.56%, 38.24%)	0.5166	0.747	0.0741	0.4158 to 0.6175	44.75 (32.81%, 74.6%)
LYMPH%	0.6256	0.042	0.2246	0.5132 to 0.7379	18.65 (25.4%, 97.06%)	0.7813	<0.001	0.4770	0.6803 to 0.8822	26.05 (85.94%, 61.76%)	0.6360	0.008	0.3207	0.5360 to 0.7361	24.3 (79.69%, 52.38%)
LAP	0.6382	0.025	0.3198	0.5271 to 0.7492	864.4 (34.92%, 97.06%)	0.8061	<0.001	0.5377	0.7119 to 0.9002	1130 (89.06%, 64.71%)	0.6352	0.009	0.3373	0.5337 to 0.7366	1019 (75.00%, 58.73%)

Youden index: sensitivity+specificity-1. The severity of glaucoma was determined based on the mean deviation (MD) of visual field and the degree of visual field defect Statistically significant, $p < 0.05$.

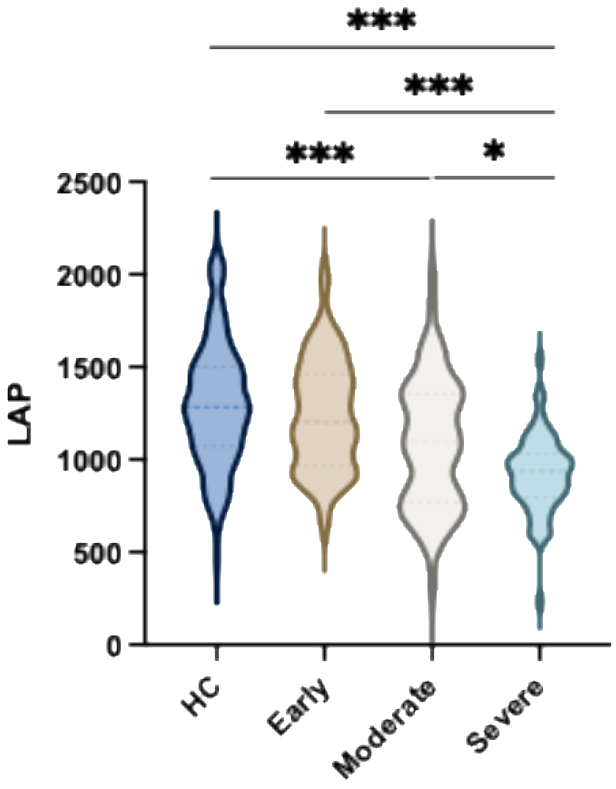

Figure 1. Relationship between serum albumin, lymphocyte rate, LAP and severity of disease

Different groups of glaucoma patients stratified by disease severity (A) LYMPH%, (B) Alb, and (C) LAP levels. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

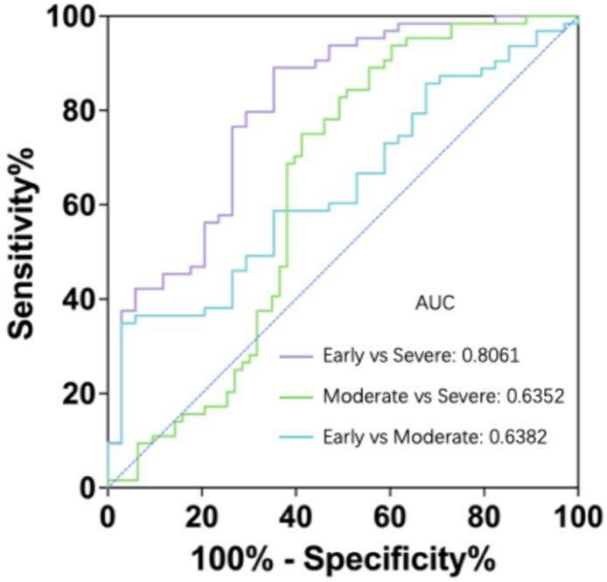

Figure 2. Receiver operating characteristic curve analysis of LAP in glaucoma patients with different severity. The severity of glaucoma was determined based on the mean deviation (MD) of visual field and the degree of visual field defect. AUC, area under the curve. Early vs. Severe, $p < 0.001$, Moderate vs. Severe, $p = 0.009$, Early vs. Moderate, $p = 0.025$.

SUPPLEMENTAL DATA

Table S1. Comparison of the glaucoma group and the control after multivariate logistic regression analysis

Characteristics	Glaucoma	Control	*OR* (95%*CI*)	*P* value
Age, M(SD)	61.4(±13.1)	70.0(±9.2)	0.950(0.929-0.972)	<0.001
Sex (Male), n (%)	74(46.0%)	112(61.9)	2.058(1.266-3.347)	0.004
LAP	1053 (±313.5)	1298 (±333.3)	0.997(0.996-0.998)	<0.001

n (%) indicates the number of constituents (n) and the composition ratio (%).

Table S2. Demographics and parameters of PACG and POAG.

	PACG	POAG	P value
n	99	62	-
Age, y	64(55-70)	58.5(53.75-72.25)	<0.001
Glaucoma severity			
Early	20	14	
Moderate	39	24	
Severe	40	24	
Alb (g/L)	43.20(41.90-45.20) ↓	44.00(41.98-45.20)	<0.001
LYMPH%	23.40(19.50-30.10) ↑	22.85(19.48-28.35)	<0.001
LAP	1067(±338.3)	1032(±270.7)	0.491

All data were expressed as median (IQR) or mean ± SD

Kolmogorov-smirnov was used to test the normality. Mann-Whitney test was used for differences in all indicators except LAP in PACG and POAG patients. Statistically significant, $p < 0.05$.