SCINDEKS
Serbian Citation Index
J Med Biochem 2026; 45 (9) DOI: 10.5937/jomb0-65413

UDK 577.1 : 61 **ISSN 1452-8258**

J Med Biochem 45: 1970–1979, 2026

Original paper
Originalni naučni rad

CIRCULATING HOMOCYSTEINE, OXIDATIVE STRESS, AND IMMUNOGLOBULIN BIOMARKERS AS PREDICTORS OF POSTOPERATIVE OCULAR SURFACE DYSFUNCTION IN ELDERLY CATARACT PATIENTS

BIOMARKERI CIRKULIŠUĆEG HOMOCISTEINA, OKSIDATIVNOG STRESA I IMUNOGLOBULINA KAO PREDIKTORI POSTOPERATIVNE DISFUNKCIJE OČNE POVRŠINE KOD STARIJIH PACIJENATA SA KATARAKTOM

Yenan Wang, Xizhe Wang, Zhen Li, Lu Zhang, Huiqing Yang, Xuxiang Zhang*

Department of Ophthalmology, Xuanwu Hospital, Capital Medical University, Beijing, China

Summary

Background: Postoperative dry eye is a frequent complication following cataract surgery in elderly patients. Increasing evidence suggests that systemic metabolic imbalance, oxidative stress, and immune dysregulation contribute to ocular surface dysfunction. This study aimed to investigate the predictive value of circulating biochemical biomarkers, including homocysteine (Hcy), oxidative stress indicators, and immunoglobulin levels, for postoperative dry eye.
Methods: A total of 218 elderly patients undergoing phacoemulsification with intraocular lens implantation between January 2024 and November 2025 were retrospectively analyzed. Patients were divided into a postoperative dry eye group (n = 76) and a control group (n = 142). Preoperative serum levels of homocysteine (Hcy), superoxide dismutase (SOD), interleukin-6 (IL-6), and immunoglobulins (IgA, IgG, IgM) were measured. Univariate and multivariate logistic regression analyses were used to identify independent biochemical predictors of postoperative dry eye. Receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of individual and combined biomarkers.
Results: Patients who developed postoperative dry eye exhibited significantly higher serum Hcy and IL-6 levels and lower SOD, IgA, and IgG levels compared with controls ($P < 0.05$). Multivariate logistic regression identified elevated Hcy (OR = 1.325), elevated IL-6 (OR = 1.568), decreased SOD (OR = 0.972), and decreased IgG (OR = 0.856) as independent predictors of postoperative

Kratak sadržaj

Uvod: Postoperativni sindrom suvog oka je česta komplikacija nakon operacije katarakte kod starijih pacijenata. Sve više dokaza ukazuje na to da sistemski metabolički disbalans, oksidativni stres i imunološka disregulacija doprinose disfunkciji očne površine. Cilj ove studije bio je da se istraži prediktivna vrednost cirkulišućih biohemijskih biomarkera, uključujući homocistein (Hcy), indikatore oksidativnog stresa i nivoe imunoglobulina, za postoperativni sindrom suvog oka.
Metode: Retrospektivno je analizirano ukupno 218 starija pacijenta koji su podvrgnuti fakoemulzifikaciji sa implantacijom intraokularnog sočiva između januara 2024. i novembra 2025. godine. Pacijenti su podeljeni u postoperativnu grupu sa suvim okom (n = 76) i kontrolnu grupu (n = 142). Mereni su preoperativni serumski nivoi homocisteina (Hcy), superoksid dismutaze (SOD), interleukina-6 (IL-6) i imunoglobulina (IgA, IgG, IgM). Univarijantne i multivarijantne logističke regresione analize su korišćene za identifikaciju nezavisnih biohemijskih prediktora postoperativnog suvog oka. ROC krive su korišćene za procenu prediktivne efikasnosti pojedinačnih i kombinovanih biomarkera.
Rezultati: Pacijenti koji su razvili postoperativni sindrom suvog oka pokazali su značajno više nivoe serumskog Hcy i IL-6 i niže nivoe SOD, IgA i IgG u poređenju sa kontrolnom grupom ($P < 0,05$). Multivarijantna logistička regresija identifikovala je povišen Hcy (OR = 1,325), povišen IL-6 (OR = 1,568), smanjen SOD (OR = 0,972) i smanjen IgG (OR = 0,856) kao nezavisne

Address for correspondence:

Yenan Wang, MD. Department of Ophthalmology, Xuanwu Hospital, Capital Medical University, No. 45, Changchun Street, Xicheng District, Beijing 100053, China
Tel: 86013810300115
e-mail: wangyenan11@sina.cn

dry eye ($P < 0.05$). ROC analysis demonstrated that the combined biomarker model achieved superior predictive performance (AUC = 0.915) compared with individual biomarkers.

Conclusion: Circulating homocysteine, oxidative stress, and immune biomarkers are closely associated with postoperative dry eye in elderly cataract patients. Combined assessment of Hcy, SOD, IL-6, and IgG provides a promising biochemical approach for preoperative risk stratification and early identification of patients at high risk for postoperative ocular surface dysfunction.

Keywords: homocysteine, oxidative stress, immunoglobulin, interleukin-6, dry eye, cataract surgery

prediktore postoperativnog suvog oka ($P < 0,05$). ROC analiza je pokazala da je kombinovani model biomarkera postigao superiorne prediktivne performanse (AUC = 0,915) u poređenju sa pojedinačnim biomarkerima.

Zaključak: Cirkulišući homocistein, oksidativni stres i imuni biomarkeri su usko povezani sa postoperativnim suvim okom kod starijih pacijenata sa kataraktom. Kombinovana procena Hcy, SOD, IL-6 i IgG pruža obeć avajući biohemijski pristup za preoperativnu stratifikaciju rizika i ranu identifikaciju pacijenata sa visokim rizikom od postoperativne disfunkcije očne površine.

Ključne reči: homocistein, oksidativni stres, imunoglobulin, interleukin-6, suvo oko, operacija katarakte

Introduction

With the rapid progression of global population aging, age-related cataract has become the leading cause of blindness worldwide, exerting an increasingly profound negative impact on visual function and quality of life among older adults (1). According to the latest statistics from the World Health Organization (WHO), approximately 320 million people globally experience varying degrees of visual impairment due to cataract. The prevalence exceeds 65% among individuals over 60 years of age and rises to more than 80% in those aged over 80 (2, 3). In China, the aging population continues to expand, with the number of elderly patients with cataract increasing at an annual rate of approximately 12%. It is projected that by 2030, the number of cataract patients aged over 60 will surpass 30 million, posing a significant public health challenge for clinical ophthalmic care (4). Phacoemulsification combined with intraocular lens implantation has become the preferred surgical approach for age-related cataract, owing to its advantages of a small incision, minimal tissue trauma, rapid postoperative visual recovery, and a low rate of complications. This technique has markedly improved visual outcomes in the elderly population (3).

However, postoperative complications continue to limit improvements in patients' rehabilitation outcomes. As the most common complication following cataract surgery (5), dry eye has attracted considerable attention in clinical research because of its high incidence and long-term impact. Clinical evidence indicates that the incidence of postoperative dry eye in elderly cataract patients is substantially higher than that in younger and middle-aged populations, typically ranging from 30% to 50%, with some studies reporting rates exceeding 60%. Moreover, symptoms in elderly patients tend to persist longer, often requiring 3 to 6 months or more for relief and showing a tendency to recur, thereby significantly compromising postoperative visual comfort (6). The typical manifestations of postoperative dry eye include ocular surface dryness, foreign body sensation, burning, photophobia, visual fluctuation, and asthenopia. Patients with mild symptoms often depend on long-term use of artificial tears, which not only increases medical costs but may also disrupt the ocular surface microenvironment. In more severe cases, patients may develop corneal epithelial defects, erosion, ulcers, and even secondary infections or corneal opacity, leading to further deterioration of visual quality. In addition, severe ocular discomfort may impair daily activities and increase the risk of accidents such as falls and fractures, imposing a substantial burden on both families and the healthcare system (7–10). Therefore, early identification of high-risk factors for postoperative dry eye in elderly cataract patients, along with the development of accurate and efficient preoperative predictive models, is of great clinical and societal importance. Such efforts would enable effective risk stratification and individualized interventions, ultimately reducing the incidence and duration of postoperative dry eye and improving patients' visual outcomes and overall quality of life.

The pathogenesis of dry eye is complex and multifactorial, involving mechanisms such as reduced tear secretion, impaired tear film stability, ocular surface inflammation, abnormal neural regulation, and meibomian gland dysfunction (11). In recent years, advances in translational research have demonstrated that systemic metabolic disturbances, oxidative stress imbalance, and immune dysfunction are not independent processes; rather, they interact and synergistically drive the pathophysiological progression of dry eye, constituting a central mechanism underlying its development (12). Homocysteine (Hcy), a key intermediate in methionine metabolism, is normally maintained at low concentrations under physiological conditions. Elevated levels of Hcy (hyperhomocysteinemia) have been identified as an independent risk factor for a range of systemic disorders, including cardiovascular and cerebrovascular diseases, neurological conditions, and metabolic syndromes (13). In ocular tissues, increased Hcy levels can induce damage to the ocular surface through multiple pathways. On the one hand, Hcy activates the nuclear factor-κB (NF-κB) signaling

pathway, promoting the release of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8). This cascade triggers chronic inflammation in the lacrimal gland and ocular surface epithelium, leading to apoptosis of lacrimal acinar cells, reduced tear secretion, and disruption of epithelial tight junctions, thereby compromising tear film adhesion and stability (14). On the other hand, Hcy promotes excessive production of reactive oxygen species (ROS), exacerbating oxidative stress and inhibiting the expression of vascular endothelial growth factor (VEGF). This results in damage to ocular surface microvascular endothelial cells, impairing nutrient delivery and metabolic waste clearance, and ultimately further disrupting the ocular surface microenvironment (15).

Oxidative stress is a pathological state in which the balance between the body's oxidation system and antioxidant system is disrupted, ROS accumulates in large quantities, and causes oxidative damage to tissue cells. Its role in the elderly population and ocular diseases has been widely confirmed. Superoxide dismutase (SOD) is the core enzyme of the body's antioxidant defense system, which can specifically scavenge excess superoxide anion free radicals and maintain the oxidation-antioxidation balance (16, 17); interleukin-6 (IL-6) is an important pro-inflammatory cytokine that is closely related to oxidative stress and inflammatory response, and its serum level can reflect the degree of systemic and local inflammation associated with oxidative stress damage. With the increase of age, the activity of antioxidant enzymes in the elderly population naturally declines, and the level of oxidative stress is significantly higher than that in young and middle-aged groups. The occurrence of cataract is also closely related to oxidative damage of lens tissue. Previous studies have shown that abnormal oxidative stress is involved in the pathological process of dry eye. Oxidative damage of ocular surface tissue can destroy the barrier function of corneal epithelial cells, reduce tear mucin secretion, disrupt the metabolism of the tear film lipid layer, shorten the tear film break-up time, and induce or aggravate dry eye symptoms (18, 19). In addition, operations such as ultrasonic energy release, intraocular lens implantation, and mechanical stimulation of ocular surface tissue during cataract surgery will further induce the production of ROS, aggravating postoperative ocular surface oxidative stress damage. Patients with preoperative oxidative stress imbalance have a significantly increased risk of postoperative dry eye, which is not conducive to the repair of ocular surface tissue. Preoperative oxidative stress imbalance significantly reduces the ocular surface's capacity to resist oxidative damage caused by trauma associated with cataract surgery, thereby increasing the likelihood of developing postoperative dry eye.

Abnormal immune function is another important mechanism for the occurrence of dry eye. As an important part of the body's immune system, the ocular surface mucosal immune barrier plays a key role in resisting external stimuli and maintaining the stability of the ocular surface microenvironment. As the core component of the mucosal immune barrier, the change of immunoglobulin level directly affects the ocular surface immune function: immunoglobulin A (IgA) mainly exists in mucosal secretions, participates in local immune defense, and protects the ocular surface mucosa by neutralizing pathogens and inhibiting pathogen adhesion (20, 21); immunoglobulin G (IgG) is the most abundant immunoglobulin in serum, which maintains the ocular surface homeostasis by regulating the intensity of inflammation, promoting tissue repair, and activating the complement system (22); immunoglobulin M (IgM) plays a core role in the primary immune response, can quickly identify and eliminate pathogens, and participate in early immune defense (22). The elderly population has obvious immune senescence, with decreased B lymphocyte function and reduced immunoglobulin synthesis ability. The function of the ocular surface mucosal immune barrier is weakened. After external stimuli such as surgery, it is prone to chronic inflammation, and the ability to clear inflammation is insufficient. Inflammatory factors continue to accumulate, which further destroys the lacrimal gland secretion function and tear film stability, and induces dry eye.

Although some studies have explored the correlation between Hcy, oxidative stress, immunoglobulin and dry eye, the existing studies still have many limitations, which are difficult to meet the clinical needs of accurate prediction of postoperative dry eye in elderly cataract patients (12, 15, 17). Firstly, most studies focus on primary dry eye or dry eye secondary to Sjögren's syndrome, and there are few studies on the correlation between preoperative serum indicators and postoperative dry eye in elderly cataract patients. However, elderly patients have the characteristics of old age, frequent combination of underlying diseases, and decreased physiological function. The pathogenesis of postoperative dry eye is significantly different from that of primary dry eye, and the existing conclusions are difficult to be directly promoted and applied; secondly, previous studies mostly adopt single indicator analysis, and the predictive value of combined detection of metabolic, oxidative stress, and immune indicators has not been clarified. A single indicator is easily affected by individual differences, underlying diseases, diet structure, medication history and other factors, with limited prediction accuracy, and cannot fully reflect the overall state of patients; thirdly, elderly people often have underlying diseases such as hypertension and diabetes, which can increase the risk of postoperative dry eye by affecting systemic

metabolism, vascular function and immune status. However, most relevant studies do not include such confounding factors in multivariate analysis, resulting in limited clinical applicability and reliability of the conclusions; fourthly, some studies have small sample size, short follow-up time and single-center research, with selection bias and insufficient extrapolation of results.

Based on this, this study took elderly patients who underwent phacoemulsification combined with intraocular lens implantation as the research objects, retrospectively analyzed their clinical data, systematically explored the correlation between preoperative serum levels of Hcy, SOD, IL-6, IgA, IgG, IgM and postoperative dry eye, and included confounding factors such as age, gender, body mass index, history of hypertension, history of diabetes, and surgical-related indicators. Univariate and multivariate Logistic regression analyses were used to screen independent risk factors, and receiver operating characteristic (ROC) curves were used to evaluate the predictive efficacy of each single indicator and combined indicators. The innovation of this study lies in breaking through the limitation of single indicator research, constructing a multi-dimensional prediction model by combining metabolic indicators (Hcy), oxidative stress indicators (SOD, IL-6), and immune indicators (IgA, IgG, IgM) for the first time, and comprehensively evaluating the impact of preoperative systemic metabolism, oxidative stress, and immune status on the postoperative ocular surface microenvironment; at the same time, fully considering the physiological characteristics and underlying disease spectrum of elderly patients, excluding the interference of confounding factors, and improving the clinical applicability of the conclusions. This study aims to provide a scientific basis for clinical early identification of high-risk groups and formulation of individualized preoperative intervention plans, reduce the incidence of postoperative dry eye through preoperative targeted intervention, improve the quality of patients' postoperative rehabilitation, and provide new ideas for the precise diagnosis and treatment of senile cataract.

Materials and Methods

Research Objects

Elderly patients who underwent phacoemulsification with intraocular lens implantation in our hospital's Ophthalmology Department (Jan 2024–Nov 2025) were enrolled.

Inclusion criteria: ① Aged ≥60 years, meeting age-related cataract criteria, with monocular/binocular cataract confirmed by ophthalmic examination; ② Preoperative Schirmerl test >10 mm/5 min, BUT >10 s, negative FL, no history of dry eye; ③ No medications interfering with tear secretion, oxidative stress or immune function (e.g., hormones) 3 months before surgery; ④ Complete clinical data, voluntary participation, and signed informed consent.

Exclusion criteria: ① Complicated with other ocular diseases (glaucoma, keratitis, etc.); ② Complicated with severe systemic diseases (hepatorenal insufficiency, tumors, etc.); ③ History of ocular surgery, trauma or long-term topical medications; ④ Intraoperative complications (posterior capsule rupture, etc.); ⑤ Incomplete follow-up data or loss to follow-up.

Patients were divided into case group (postoperative dry eye) and control group (no dry eye) based on dry eye diagnosis 1 month postoperatively. Referring to Expert Consensus on Dry Eye Diagnosis and Treatment in China (2023), dry eye was diagnosed when 2 of the following 3 criteria were met: Schirmer I test <=10 mm/5 min, BUT <=10 s, and positive FL.

Collection of General Data

Baseline data were collected from electronic medical records, covering age, gender, BMI, history of hypertension/diabetes, smoking/drinking history, surgical eye, intraocular lens type and operation duration.

Detection of Serum Indicators

Fasting elbow venous blood (5 mL) was collected from each patient 1 week before surgery into anticoagulant-free tubes. After standing at room temperature for 30 min, the samples were centrifuged at 3000 r/min for 15 min, and the serum supernatant was separated for testing.

Serum Hcy levels were measured using an enzymatic cycling method, SOD activity was determined by the xanthine oxidase method, and IL-6 levels were quantified using enzyme-linked immunosorbent assay (ELISA). Serum immunoglobulins (IgA, IgG, and IgM) were assessed using an immunoturbidimetric assay. All measurements were conducted strictly in accordance with the manufacturers' instructions. Each sample was analyzed in triplicate, and the mean value was used for statistical analysis. The evaluated serum biomarkers included Hcy, SOD, IL-6, IgA, IgG, and IgM.

Postoperative Follow-up and Dry Eye Evaluation

All patients were reexamined 1 month postoperatively, and dry eye indicators were measured by

the same ophthalmologist per standard protocols. ① Schirmerl test: Fold the filter paper 5 mm, place it at the middle-outer 1/3 of the lower eyelid margin, close eyes for 5 minutes, then measure the wetted length. ② BUT: Instill sodium fluorescein eye drops, blink several times, then observe the first tear film dry spot time under slit lamp cobalt blue light. ③ FL: Record the degree and range of corneal epithelium staining under cobalt blue light.

Statistical analysis

Data were analyzed using Statistic Package for Social Science (SPSS) 26.0 (IBM, Armonk, NY, USA). Normally distributed data were expressed as $\bar{x}\pm s$ (independent samples t-test for inter-group comparison); count data as rate (%) (chi-square test). Univariate analysis screened potential risk factors, and indicators with $P<0.05$ were included in multivariate Logistic regression to identify independent factors. ROC curves were plotted to calculate AUC, sensitivity, specificity and optimal cut-off value, to evaluate the predictive efficacy of each indicator. $P<0.05$ was statistically significant.

Results

Comparison of General Data between the Two Groups

A total of 218 elderly patients with cataract were enrolled in this study. At 1 month postoperatively, 76 patients were diagnosed with dry eye, yielding an incidence of 34.86%. These patients were assigned to the case group (n = 76), while the remaining 142 patients comprised the control group. There were no statistically significant differences between the two groups in terms of sex, body mass index (BMI), operated eye, type of intraocular lens, or surgical duration ($P > 0.05$). However, patients in the case group were older and had a higher prevalence of hypertension and diabetes compared with the control group, with statistically significant differences ($P < 0.05$). Detailed results are presented in *Table I*.

Comparison of Preoperative Serum Indicator Levels between the Two Groups

The preoperative serum levels of Hcy and IL-6 in the case group were significantly higher than those in the control group, with statistically significant differences ($P<0.001$); the preoperative serum levels of SOD, IgA, and IgG in the case group were significantly lower than those in the control group, with statistically significant differences ($P<0.05$); there was no statistically significant difference in preoperative serum IgM level between the two groups ($P>0.05$). See *Table II* for details.

Univariate and Multivariate Logistic Regression Analyses of Postoperative Dry Eye

Univariate analysis results showed that age, history of hypertension, history of diabetes, preoperative serum Hcy level, SOD level, IL-6 level, IgA level, and IgG level were all related to the occurrence of postoperative dry eye in elderly patients with cataract ($P<0.05$). The above indicators were included in multivariate Logistic regression analysis, and the results showed that elevated preoperative Hcy (OR=1.325, 95% CI: 1.156~1.518, $P<0.001$), decreased SOD (OR=0.972, 95% CI: 0.958~0.986, $P<0.001$), elevated IL-6 (OR=1.568,

Table I Comparison of general data between the two groups.

Indicators	Case group (n=76)	Control group (n=142)	χ^2/t value	P value
Age (years, $\bar{x}\pm s$)	72.54±5.82	68.36±6.15	4.572	<0.001
Gender (male/female, case)	35/41	68/74	0.215	0.643
BMI (kg/m^2, $\bar{x}\pm s$)	23.12±2.05	22.85±1.98	0.924	0.357
History of hypertension (yes/no, case)	42/34	56/86	5.016	0.025
History of diabetes (yes/no, case)	30/46	27/115	10.251	0.001
Smoking history (yes/no, case)	18/58	32/110	0.102	0.749
Surgical eye (left/right, case)	39/37	75/67	0.078	0.779
Type of intraocular lens (hydrophobic/hydrophilic, case)	40/36	78/64	0.095	0.758
Surgical duration (min, $\bar{x}\pm s$)	15.26±3.12	14.85±2.96	0.987	0.325

Table II Comparison of preoperative serum indicator levels between the two groups ($\bar{x}\pm s$).

Indicators	Case group (n=76)	Control group (n=142)	t value	P value
Hcy (μmol/L)	16.85±3.26	12.34±2.85	10.235	<0.001
SOD (U/mL)	85.26±12.35	102.58±15.62	8.762	<0.001
IL-6 (pg/mL)	18.65±4.32	12.18±3.56	11.247	<0.001
IgA (g/L)	1.85±0.36	2.12±0.42	4.785	<0.001
IgG (g/L)	10.25±1.58	11.68±1.85	5.623	<0.001
IgM (g/L)	1.26±0.25	1.31±0.28	1.254	0.211

Table III Multivariate logistic regression analysis of postoperative dry eye in elderly patients with cataract.

Indicators	Regression coefficient	Standard error	Wald χ^2 value	OR value	95% CI	P value
Age	0.025	0.018	1.936	1.025	0.991~1.061	0.164
History of hypertension	0.856	0.452	3.562	2.354	0.968~5.721	0.059
History of diabetes	0.978	0.482	4.125	2.658	1.023~6.895	0.043
Preoperative Hcy level	0.281	0.072	15.362	1.325	1.156~1.518	<0.001
Preoperative SOD level	-0.028	0.007	15.875	0.972	0.958~0.986	<0.001
Preoperative IL-6 level	0.450	0.102	19.025	1.568	1.235~1.992	<0.001
Preoperative IgA level	-0.256	0.135	3.586	0.774	0.592~1.012	0.058
Preoperative IgG level	-0.156	0.042	13.852	0.856	0.785~0.934	<0.001

Table IV Efficacy indicators of each Indicator and combined indicators for predicting postoperative dry eye.

Detection indicators	AUC	Optimal cut-off value	Sensitivity (%)	Specificity (%)	95% CI
Hcy	0.785	14.62 μmol/L	78.95	72.54	0.721~0.849
SOD	0.752	93.85 U/mL	76.32	69.72	0.685~0.819
IL-6	0.802	15.36 pg/mL	80.26	74.65	0.740~0.864
IgG	0.726	10.96 g/L	73.68	67.60	0.658~0.794
Combined detection of four indicators	0.915	0.625	86.84	82.39	0.876~0.954

95% CI: 1.235~1.992, P<0.001), and decreased IgG (OR=0.856, 95% CI: 0.785~0.934, P<0.001) were independent risk factors for the occurrence of postoperative dry eye in elderly patients with cataract. History of diabetes was also an independent risk factor (OR=2.658, 95% CI: 1.023~6.895, P=0.043). See *Table III* for details.

Analysis of Predictive Efficacy of Each Indicator and Combined Indicators for Postoperative Dry Eye

ROC curve analysis showed that the area under the curve (AUC) for preoperative serum Hcy, SOD, IL-6, and IgG as individual predictors of postoperative dry eye were 0.785, 0.752, 0.802, and 0.726, respectively. The combined detection of these four biomarkers yielded an AUC of 0.915, which was significantly higher than that of any single indicator ($P < 0.05$). The optimal cut-off value for

the combined model was 0.625, corresponding to a sensitivity of 86.84% and a specificity of 82.39%. Detailed diagnostic performance metrics for each individual marker and the combined model are presented in *Table IV*.

Discussion

Correlation Mechanism between Core Indicators and Postoperative Dry Eye and Specificity in the Elderly Population

This study demonstrated that the incidence of dry eye at 1 month after surgery in elderly patients with cataract was 34.86%, which falls within the range reported in previous clinical studies (30%–50%), further confirming the high prevalence of this complication in the elderly population. Multivariate analysis identified elevated preoperative serum Hcy, reduced SOD activity, increased IL-6 levels, decreased IgG levels, and a history of diabetes as independent risk factors for postoperative dry eye ($P < 0.05$). These findings reflect more than simple associations between individual biomarkers; rather, they highlight a systemic imbalance involving metabolism, oxidative stress, immunity, and inflammation within the ocular surface microenvironment. This integrated network disruption is closely linked to age-related physiological degeneration and comorbid conditions in the elderly, underscoring both the mechanistic plausibility and population specificity of these risk factors.

The promotive effect of hyperhomocysteinemia on postoperative dry eye essentially reflects the combined impact of ocular surface inflammation and microvascular injury driven by metabolic disturbances. As an intermediate product of methionine metabolism, elevated Hcy disrupts ocular surface homeostasis through two principal pathways. First, it directly activates the NF-κB signaling pathway, enhancing the release of pro-inflammatory cytokines such as TNF-α and IL-6. In the elderly population, diminished B-lymphocyte function and insufficient anti-inflammatory responses predispose to prolonged inflammation, leading to apoptosis of lacrimal acinar cells, reduced tear secretion, and disruption of corneal epithelial tight junctions, thereby compromising tear film stability.

Second, elevated Hcy promotes excessive production of reactive oxygen species (ROS), forming a vicious cycle consistent with the observed increase in IL-6 and decrease in SOD in this study, which further exacerbates oxidative stress and inflammatory damage. Notably, elderly patients frequently present with comorbidities such as hypertension and diabetes—both of which were significantly more prevalent in the case group in this study—and are already associated with vascular endothelial dysfunction. Elevated Hcy can further aggravate microvascular endothelial injury on the ocular surface by inhibiting vascular endothelial growth factor (VEGF) expression, thereby impairing nutrient supply, metabolic waste clearance, and postoperative tissue repair capacity (13, 14).

In addition, insufficient intake of B vitamins is common in the elderly. Folic acid and vitamins B6 and B12 serve as essential cofactors in Hcy metabolism; their deficiency leads to impaired Hcy clearance, forming a pathological cascade of »nutritional deficiency–metabolic disturbance–ocular surface damage.« This mechanism may partly explain both the high prevalence of hyperhomocysteinemia in the elderly and its close association with postoperative dry eye (13).

Oxidative stress imbalance coupled with an abnormal inflammatory response represents a central pathological mechanism of postoperative dry eye in elderly patients, with clear age-dependent features. SOD, a key antioxidant enzyme, scavenges superoxide anion radicals, and its reduced activity directly reflects diminished systemic antioxidant capacity. IL-6, a pivotal pro-inflammatory cytokine, plays an essential role in coordinating oxidative stress and inflammatory responses; elevated IL-6 levels indicate activation of both systemic and local ocular surface inflammation associated with oxidative injury.

With advancing age, mitochondrial function declines, the synthesis of antioxidant enzymes is reduced, and baseline oxidative stress levels become significantly higher than those in younger populations. Consequently, ocular surface epithelial cells and lacrimal gland cells exhibit decreased tolerance to oxidative and inflammatory insults. During cataract surgery, procedures such as ultrasonic energy application and intraocular lens implantation inevitably trigger a surge in reactive oxygen species (ROS) production and the release of pro-inflammatory mediators, including IL-6, leading to secondary damage of ocular surface tissues (16).

In patients with preoperatively decreased SOD activity and elevated IL-6 levels, the capacity to neutralize excess ROS and regulate inflammatory responses is impaired. This results in lipid peroxidation of the corneal epithelium, reduced mucin secretion, and disruption of tear film lipid layer metabolism, ultimately contributing to the development of dry eye (18). Furthermore, the negative correlation observed between SOD and IL-6 in this study ($r = -0.62$, not shown in the table) supports the notion that the degree of imbalance between oxidative–antioxidative systems and inflammatory regulation is positively associated with the risk of postoperative dry eye. This relationship is particularly pronounced in the elderly due to their diminished baseline antioxidant and

immune regulatory capacities, highlighting potential targets for preoperative antioxidant and anti-inflammatory interventions.

The impact of decreased IgG level on postoperative dry eye is essentially the weakening of ocular surface mucosal barrier function caused by immune senescence in the elderly (20). As the main immunoglobulin in serum, IgG can not only clear damaged cells by activating the complement system, but also regulate the intensity of inflammatory response and promote tissue repair. Its decreased level directly impairs the ocular surface immune defense and repair ability. The elderly population has decreased proliferation and differentiation ability of B lymphocytes, insufficient IgG synthesis, and the ocular surface mucosal immune barrier is inherently fragile. The secondary inflammation caused by surgical stimulation is difficult to be effectively regulated. The continuous accumulation of inflammatory factors will further destroy the lacrimal gland secretion function and tear film stability, forming a chronic dry eye state (21, 22). In this study, IgA was correlated in univariate analysis but not included in the multivariate model, and there was no inter-group difference in IgM. This result is consistent with the functional positioning of immunoglobulins: IgA is mainly aimed at pathogen invasion, but this study strictly excluded infected patients, so its defensive effect cannot be manifested; IgM dominates the primary immune response, while postoperative ocular surface inflammation is a secondary response, so its role is not significant. This suggests that IgG is a specific immune indicator for evaluating the risk of postoperative dry eye in elderly cataract patients, which can better reflect the core state of ocular surface immune repair ability.

History of diabetes being identified as an independent risk factor ($P=0.043$) is consistent with the clinical consensus that diabetes is a key influencing factor for postoperative dry eye. Diabetes can cause systemic metabolic disorders, microvascular lesions, and immune function abnormalities, which in turn affect lacrimal gland secretion function, tear film stability, and ocular surface epithelial cell repair ability, increasing the susceptibility to postoperative dry eye. This result further improves the clinical applicability of the prediction model by supplementing the influence of key underlying diseases.

Clinical Value of Combined Detection and Evidence-Based Basis for Individualized Intervention

ROC curve analysis showed that the AUC (0.915) of the combined detection of the four indicators (Hcy, SOD, IL-6, IgG) was significantly higher than that of a single indicator, with sensitivity and specificity reaching 86.84% and 82.39% respectively. Its advantage lies in breaking through the limitations of a single indicator and constructing a multi-dimensional risk assessment system. A single indicator is easily interfered: Hcy level may be affected by diet and gene polymorphism, SOD and IL-6 are easily interfered by liver function and drugs, and decreased IgG may be related to systemic malnutrition. Individual detection is difficult to accurately reflect the overall state of the ocular surface microenvironment. The combined detection can integrate information from three dimensions of metabolism, oxidative stress-inflammation, and immunity, comprehensively capture abnormal signals of the preoperative physical state of elderly patients, and accurately identify high-risk groups. For example, for elderly patients with diabetes, even if the Hcy level is at the critical value, if there are simultaneous decreases in SOD and IgG and elevation of IL-6, the risk of postoperative dry eye is still significantly increased. Combined detection can avoid missed judgment of a single indicator and provide quantitative basis for preoperative risk stratification.

Individualized intervention based on the results of this study should closely focus on the physiological characteristics and underlying disease spectrum of elderly patients to achieve »precision prevention«. For patients with high Hcy, those without underlying diseases can supplement folic acid (0.8 mg/d) + vitamins B6/B12 to promote Hcy metabolism; those with combined diabetes/hypertension need to adjust the dosage of nutrients while controlling the underlying diseases, and monitor Hcy levels regularly. For patients with oxidative stress imbalance and elevated IL-6, antioxidants such as vitamins C/E and glutathione can be taken orally before surgery, and appropriate anti-inflammatory interventions can be performed under the guidance of doctors to reduce preoperative inflammatory response; at the same time, guide the intake of foods rich in polyphenols and carotenoids to improve the body's antioxidant reserve. For patients with low IgG, potential diseases such as autoimmune diseases and malignant tumors should be excluded first. Those with simple immune senescence can supplement high-quality protein and immunomodulators to enhance B lymphocyte function. For patients with a history of diabetes, strict control of blood glucose before surgery is the key, including adjusting hypoglycemic drugs, optimizing diet and exercise plans, to reduce the impact of hyperglycemia on ocular surface microenvironment. For high-risk patients with multiple abnormal indicators, the surgical plan also needs to be optimized: select microincisions below 2.2 mm, control ultrasonic energy and duration, and use intraocular lenses with good biocompatibility to reduce ocular surface stimulation; combine anti-inflammatory and antioxidant eye drops in the early postoperative period, dynamically monitor dry eye indicators, and realize a closed-loop prevention and control of »pre-

operative intervention + intraoperative optimization + postoperative management«.

Objective Analysis of Research Innovations and Limitations

The principal innovation of this study lies in the construction of a multidimensional predictive model integrating metabolism, oxidative stress, inflammation, and immunity, with a specific focus on the elderly population. Previous studies have largely been limited to single biomarkers or younger and middle-aged cohorts. In contrast, the present study incorporated key confounding factors, such as diabetes, into a multivariate analysis tailored to the clinical characteristics of elderly patients, who often present with multiple comorbidities and age-related physiological decline. Furthermore, IL-6 was used in place of MDA to more accurately capture the interplay between oxidative stress and inflammatory responses, thereby enhancing the clinical relevance of the findings. Importantly, this study identified the independent predictive value of five factors—Hcy, SOD, IL-6, IgG, and a history of diabetes—thereby providing a practical and clinically applicable panel for routine risk screening, while avoiding the barriers associated with overly complex testing strategies.

This study has clear limitations, which need to be objectively faced and pointed out the direction for subsequent research: first, the single-center retrospective design leads to selection bias, and the extrapolation of research results is limited by the diagnosis and treatment level and patient structure of our hospital, so multi-center prospective studies are needed for verification; second, the follow-up time is only 1 month, which cannot reflect the correlation between indicators and the long-term prognosis of postoperative dry eye. The dry eye symptoms of elderly patients may last more than 6 months. Extending the follow-up to 1 year can clarify the long-term predictive value of indicators; third, the correlation between indicators and the severity of dry eye is not explored, and only grouped by »occurrence/non-occurrence«. Subsequent stratified analysis can be combined with dry eye symptom scores and corneal staining degrees to clarify the correlation between indicator levels and the severity of the disease; fourth, gene polymorphism analysis is not included. For example, MTHFR C677T gene polymorphism can affect Hcy metabolism, and SOD2 gene polymorphism is related to antioxidant capacity. These factors may indirectly affect the risk of postoperative dry eye, which can be further explored in future studies.

Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

References

1. Chen SP, Woreta F, Chang DF. Cataracts: A Review. Jama-J Am Med Assoc 2025; 333(23): 2093–103.
2. Jhori A, Bhargava M, Bera D. Cataract surgery with coexisting corneal degeneration. Indian J Ophthalmol 2025; 73(3): 464.
3. Macarie SS, Macarie DM. Macular changes after cataract surgery. Romanian Journal of Ophthalmology 2024; 68(3): 233-5.
4. Augustin VA, Friedrich M, Son H, Yildirim TM, Auffarth GU, Khoramnia R. Cataract Surgery and DMEK: Decision-making and the Timing of the Respective Interventions. Klin Monatsbl Augenh 2025; 242(8): 807–12.
5. Garg P, Gupta A, Tandon N, Raj P. Dry Eye Disease after Cataract Surgery: Study of its Determinants and Risk Factors. Turkish Journal of Ophthalmology 2020; 50(3): 133–42.
6. Villani E, Catania AG, Luccarelli SV, Magnani F, Martone G, Zanzottera E, et al. Dry eye and cataract surgery: Narrative review and recommendations for management. Eur J Ophthalmol 2023: 11206721231174060.
7. Graae Jensen P, Gundersen M, Nilsen C, Gundersen KG, Potvin R, Gazerani P, et al. Prevalence of Dry Eye Disease Among Individuals Scheduled for Cataract Surgery in a Norwegian Cataract Clinic. Clinical Ophthalmology (Auckland, N.Z.) 2023; 17(1233–43.
8. Son H, Yildirim TM, Khoramnia R, Poompokawat P, Knorz MC, Auffarth GU. Semi-fluorinated Alkane Eye Drops Reduce Signs and Symptoms of Evaporative Dry Eye Disease After Cataract Surgery. Journal of Refractive Surgery (Thorofare, N.J. : 1995) 2020; 36(7): 474–80.
9. Yu Y, Hua H, Wu M, Yu Y, Yu W, Lai K, et al. Evaluation of dry eye after femtosecond laser-assisted cataract surgery. J Cataract Refr Surg 2015; 41(12): 2614–23.
10. Bista B, Bista PR, Gupta S, Byanju R, Khadka S, Mishra S. Comparative Study of Dry Eye Indices Following Cataract Surgery. Nepalese Journal of Ophthalmology: A Biannual Peer-Reviewed Academic Journal of the Nepal Ophthalmic Society: NEPJOPH 2021; 13(25): 104–11.
11. Gundersen M, Nilsen C, Jensen P, Yazdani M, Utheim Ø, Sand ES, et al. Tear Global Metabolomic

Differences in Pre-Operative Cataract Patients With and Without Dry Eye Disease. Curr Eye Res 2025; 50(6): 579–89.

12. Guo B, Lu P, Chen X, Zhang W, Chen R. Prevalence of dry eye disease in Mongolians at high altitude in China: the Henan eye study. Ophthal Epidemiol 2010; 17(4): 234–41.
13. Sekeryapan B, Oner V, Kirbas A, Turkyilmaz K, Durmus M. Plasma homocysteine levels in dry eye patients. Cornea 2013; 32(5): e94–6.
14. Roedl JB, Bleich S, Schlötzer-Schrehardt U, von Ahsen N, Kornhuber J, Naumann GOH, et al. Increased homocysteine levels in tear fluid of patients with primary open-angle glaucoma. Ophthalmic Res 2008; 40(5): 249–56.
15. Cardoso R, Gonçalo M, Tellechea O, Maia R, Borges C, Silva JAP, et al. Livedoid vasculopathy and hypercoagulability in a patient with primary Sjögren's syndrome. Int J Dermatol 2007; 46(4): 431–4.
16. Seen S, Tong L. Dry eye disease and oxidative stress. Acta Ophthalmol 2018; 96(4): e412–20.
17. Mousa AM, Aldebasi YH. L-carnosine mitigates interleukin-1α-induced dry eye disease in rabbits via its antioxidant, anti-inflammatory, antiapoptotic, and antifibrotic effects. Cutan Ocul Toxicol 2021; 40(3): 241–51.
18. Hu R, Shi J, Xie C, Yao X. Dry Eye Disease: Oxidative Stress on Ocular Surface and Cutting-Edge Antioxidants. Glob Chall 2025; 9(7): e00068.
19. Choi W, Lian C, Ying L, Kim GE, You IC, Park SH, et al. Expression of Lipid Peroxidation Markers in the Tear Film and Ocular Surface of Patients with Non-Sjogren Syndrome: Potential Biomarkers for Dry Eye Disease. Curr Eye Res 2016; 41(9): 1143–9.
20. Shields C, Donthineni PR, Muralidhar R, Bhatt S, Karakoleva EV, Baer A, et al. Serological Influences on Dry Eye: Insights from the Sjögren's International Collaborative Clinical Alliance. Ophthalmology Science 2025; 5(6): 100843.
21. Alhalwani AY, Abudawood K, Qadizadah ABEA, Jambi S, Sannan NS. Immunoglobulin A levels and its correlation with neutrophil-to-lymphocyte ratio as inflammatory biomarkers for dry eye disease in type 2 diabetes: a retrospective study. Front Immunol 2023; 14: 1184862.
22. Parodis I, Lagutkin D, Lindblom J, Idborg H, Beretta L, Borghi MO, et al. New IgG and IgA autoantibody specificities against DNA-binding and RNA-binding proteins discriminate systemic lupus erythematosus from health and non-lupus autoimmunity-could anti-LIN28A enhance precision in diagnostics? Ann Rheum Dis 2025; 84(7): 1180–94.

Received: February 21, 2026
Accepted: March 24, 2026