Am J Transl Res 2025;17(4):3207-3218
www.ajtr.org /ISSN:1943-8141/AJTR0162912

Original Article

Predictive value of liver and kidney function and bone metabolism markers for postoperative outcomes in diabetic retinal surgery

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Received December 24, 2024; Accepted April 15, 2025; Epub April 15, 2025; Published April 30, 2025

Abstract: Objective: This study aimed to explore liver and kidney function as well as bone metabolism in patients undergoing diabetic retinal surgery, and to evaluate their clinical significance in predicting postoperative outcomes. Methods: A total of 150 patients (172 eyes) with proliferative diabetic retinopathy (PDR) who underwent retinal surgery were retrospectively analyzed and categorized into a vitrectomy group (n=78) and a photocoagulation group (n=72). Additionally, 50 healthy adults were included as the control group. Hepatic and renal function parameters, along with bone metabolism markers, were assessed before and after surgery. Logistic regression analysis was employed to evaluate their association with postoperative prognosis, while receiver operating characteristic (ROC) curves were used to assess the predictive performance of key indicators. Results: Compared to the control group, patients with PDR showed significantly elevated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (TBIL), urinary albumin-to-creatinine ratio (UACR), serum creatinine (Scr), and serum cystatin C (sCys-C), along with markedly reduced levels of glomerular filtration rate (GFR) and osteocalcin (all $P < 0.05$). When comparing treatment groups, the vitrectomy group exhibited a significantly higher overall improvement rate than the photocoagulation group (80.00% vs. 37.80%). Moreover, patients in the vitrectomy group demonstrated lower levels of AST, ALT, TBIL, UACR, Scr and sCys-C, and higher levels of GFR and osteocalcin (all $P<0.05$). Among all 150 surgical patients, the incidence of poor prognosis was 46.0%. Logistic regression analysis identified AST, ALT, TBIL, GFR, and surgical type as independent prognostic factors, irrespective of adjustment for confounding variables ($P<0.05$). ROC analysis showed that ALT and TBIL had moderate sensitivity (0.725 and 0.754, respectively), while AST and GFR exhibited high specificity (0.875 and 0.889, respectively) in predicting the prognosis of diabetic retinal surgery. Conclusion: In diabetic patients undergoing retinal surgery, hepatic and renal function, along with bone metabolism, are significantly altered and appear to improve following surgical intervention. Specifically, levels of AST, ALT, TBIL, and GFR are closely associated with postoperative prognosis and may serve as valuable predictors of clinical outcomes.

Keywords: Diabetic retinopathy, surgery, liver function, kidney function, bone metabolism

Introduction

Diabetes mellitus, a chronic metabolic disorder of the endocrine system, is associated with a wide range of complications, including diabetic retinopathy (DR), kidney disease, and diabetic foot [1]. More than 60% of patients with type 2 diabetes develop retinopathy within 15 to 20 years of disease onset [2]. Diabetic retinopathy, the leading cause of vision loss in working-age adults, is clinically classified into non-proliferative (NPDR) and proliferative diabetic retinopathy (PDR), based on the presence of retinal neovascularization. Beyond its ocular manifestations, DR has been increasingly recognized for its systemic implications, particularly its association with hepatic and renal dysfunction, as well as disturbances in bone metabolism. Severe forms of DR may cause progressive hepatic and renal impairment. Zhang et al. reported a significant association between liver fibrosis and the presence of DR [3], while Yao et al. identified abnormal liver and kidney function as independent risk factors for the develop-

https://doi.org/10.62347/MDVM6037

ment of DR [4]. Furthermore, clinical evidence supports DR severity as an independent predictor of diabetic nephropathy (DN) progression [5], with patients exhibiting a higher risk of nephropathy compared to the general population with type 2 diabetes [6]. Additionally, alterations in bone metabolism markers have been correlated with DR progression [7].

Conventional drug treatment of DR typically yields slow clinical improvement. Laser photocoagulation, which reduces oxygen demand in ischemic retinal areas by inducing local tissue atrophy, remains a widely adopted therapeutic approach. Although it can stabilize the ischemic state of retinal tissues, it carries a risk of complications such as vitreous hemorrhage and tractional retinal detachment, often necessitating surgical intervention [8]. Vitrectomy, primarily indicated for severe PDR, effectively removes vitreous hemorrhage, relieves retinal traction, restores anatomical structure, and suppresses pathological neovascularization, thereby improving visual acuity and reducing the risk of further complications [9]. Despite the clinical efficacy of vitrectomy, its potential systemic impact - particularly on liver and kidney function and bone metabolism - remains poorly understood. Whether the surgical procedure induces hepatic or renal damage or disrupts bone metabolism remains unclear. Moreover, its potential impact on the prognosis of DR surgery has yet to be established.

In this context, this study retrospectively analyzed clinical data from patients who underwent DR surgery to evaluate therapeutic outcomes and to investigate pre- and postoperative changes in liver and kidney function, as well as bone metabolism, thereby elucidating their potential roles in surgical prognosis.

Materials and methods

Case selection

This study included 150 patients with PDR, involving a total of 172 affected eyes, who were admitted to the First Affiliated Hospital of Xinxiang Medical University between May 2020 and December 2023. The cohort consisted of 62 males and 98 females, with a mean age of 41.36±5.25 years (range: 24-65 years). The duration of diabetes ranged from 3 to 20 years, with an average of 12.11±3.38 years.

All patients met the diagnostic criteria for PDR based on comprehensive clinical assessments, including blood glucose, lipid profile, renal function tests, clinical symptoms, and signs, in accordance with established diagnostic criteria [10]. The clinical manifestations included recurrent and extensive vitreous hemorrhage, marked retinal fibrovascular proliferation, and retinal detachment. All patients underwent retinal surgery, either vitrectomy or retinal photocoagulation, depending on the severity of the disease and clinical indication. Complete baseline data and surgical records were available for all participants. Patients with ocular disease unrelated to DR were excluded.

Inclusion Criteria: Diagnosis of PDR: All patients were diagnosed with PDR based on comprehensive clinical evaluation, including blood glucose levels, lipid profile, renal function tests, clinical signs and symptoms, and in accordance with established diagnostic criteria [10]. Characteristic manifestations included recurrent and extensive vitreous hemorrhage, severe fibrovascular proliferation, and retinal detachment. Indication for surgery: All patients met the clinical criteria for retinal surgery, including vitrectomy or photocoagulation. Complete clinical data: Only patients with complete baseline and surgical records were included to ensure data integrity and reliability of analysis. Age range: Eligible patients were between 24 and 65 years of age. Diabetes duration: Patients had a documented history of diabetes ranging from 3 to 20 years.

Exclusion Criteria: Presence of other ocular diseases: Patients with ocular diseases other than DR were excluded. This included, but was not limited to, glaucoma, advanced cataracts (that impaired assessment of PDR), uveitis, or other retinal diseases of non-diabetic origin. Patients with cognitive impairment, psychiatric illness, or other conditions were excluded from the study. Severe systemic diseases: Patients with severe systemic illnesses that could interfere with surgical tolerance or confound study outcomes were excluded. These included uncontrolled heart failure, severe liver cirrhosis (Child-Pugh Class C), end-stage renal disease requiring dialysis (except in cases directly related to diabetic nephropathy), and active malignancies. Pregnancy or lactation: Pregnant or lactating women were excluded due to potential

physiological changes due to potential study-related biomarkers and outcomes.

Grouping

The 150 PDR patients were designated as the PDR group. According to the type of surgical intervention received, patients were further categorized into two subgroups: those who underwent vitrectomy were assigned to the vitrectomy group, while those who received photocoagulation were included in the photocoagulation group. Additionally, a control group comprising 50 healthy adults undergoing routine physical examinations at the First Affiliated Hospital of Xinxiang Medical University during the same period was established for comparative analysis.

This study was carried out in strict accordance with the ethical principles outlined in the Declaration of Helsinki. Prior to enrollment, all patients were fully informed of the study's purposes, methods, potential risks, and anticipated benefits. Throughout the research process, the privacy and confidentiality of all participants were rigorously protected to safeguard their rights and personal data. Ethical approval for this study was granted by the Ethics Committee of the First Affiliated Hospital of Xinxiang Medical University.

Intervention method

Vitrectomy: All patients undergoing vitrectomy received retrobulbar block anesthesia. In cases with significant lens opacity, phacoemulsification was performed prior to vitrectomy. For patients with mild lens opacity but prominent fundus fibrovascular proliferation, tractional retinal detachment, or requiring silicone oil tamponade, phacoemulsification with preservation of the posterior capsule was conducted before initiating a standard three-port vitrectomy. For incomplete posterior vitreous detachment (PVD), complete PVD was induced prior to vitreous removal. In patients with an indistinct, transparent anterior retinal membrane, intraoperative triple acetate staining was employed to enhance visualization, followed by membrane peeling. For proliferative membranes densely adherent to the retina, dissection was performed using intraocular electrocoagulation and glass incision. To avoid iatrogenic holes, forceful traction or peeling was avoided. After successful detachment, air-liquid exchange was conducted, followed by intraocular photocoagulation and external scleral condensation of retinal hiatus. In case of extensive retinal proliferation, concurrent retinal detachment, or intraoperative retinotomy, silicone oil tamponade was administered. For eyes with limited proliferation and intraoperative hemorrhage, photocoagulation was completed to the greatest extent possible, followed by injection of 16% perfluoropropane (C3F8) gas for internal tamponade.

Panretinal photocoagulation: Panretinal photocoagulation was performed using the MD-960 laser system. Each session consisted of approximately 500 laser burns, with a total of 1500-2000 burns applied over three to four treatment sessions to achieve complete coverage.

Postoperative treatment: All patients received routine postoperative care, including hemostatic therapy and broad-spectrum antibiotics to prevent infection. For patients who received intraoperative tamponade with silicone oil or gas, a lower-body-dependent position was maintained for 10 days after surgery. Intraocular pressure and visual acuity were closely monitored during the operation.

Data collection and outcome measurement

Primary indicators: Clinical efficacy evaluation was conducted at six months postoperatively. Visual acuity was measured using a standard logarithmic visual acuity chart, compliant with national standards (GB11533-2011). An increase of ≥ 0.2 in the logarithm of the minimum angle of resolution (LogMAR) value was defined as a significant improvement in visual acuity. A change in LogMAR value of < 0.2 was categorized as a general improvement, whereas no change or deterioration was considered no improvement [11]. The total number of improved cases included both significantly and generally improved cases. The prognostic classification was defined as follows: a good prognosis referred to patients with significant or general improvement in vision (in both eyes for patients with bilateral involvement), while a poor prognosis was assigned if visual acuity failed to improve in at least one eye.

Laboratory assessments were performed at two time points: preoperatively and six months postoperatively. Fasting venous blood samples (5 ml) were collected in the morning, centrifuged at 3000 rpm for 10 minutes, and the serum was separated for analysis. The following indicators were evaluated.

(1) Liver function markers: Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL) were measured using an automatic biochemical analyzer (Model BS-350S, Mindray Medical International Co., LTD.).

(2) Renal function markers: The urinary albumin-to-creatinine ratio (UACR) was calculated from urinary albumin (measured via radioimmunoassay using a HISCL-5000 automatic chemiluminescence immunoassay analyzer, Sysmex, Japan) and urinary creatinine (assessed using the picric acid assay with reagents from Aibixin Biotechnology Co., Ltd., Shanghai).

(3) Serum creatinine (Scr) was determined using the picric acid assay, and serum cystatin C (sCys-C) was determined by an immunoturbidimetric assay using a Hitachi 7180 automated biochemical analyzer. The glomerular filtration rate (GFR) was calculated as follows:

For males: $GFR = 1.86 \times Scr^{-1.154} \times age^{-0.203}$ [12].

For females: GFR = male GFR × 0.742.

(4) Bone metabolism markers: Fasting venous blood was anticoagulated with routine heparin and analyzed using an automated biochemical analyzer. Serum levels of calcium, phosphorus, and alkaline phosphatase (via high-performance liquid chromatography) were measured, as well as osteocalcin using enzyme-linked immunosorbent assay.

Secondary indicators: Secondary data included baseline demographics (gender, age), duration of diabetes, severity of eye disease, and the aforementioned clinical efficacy outcomes. Laboratory parameters also included liver function indicators (AST, ALT, TBIL), renal function indicators (UACR, Scr, sCys-C, GFR), and bone metabolic markers (calcium, phosphorus, alkaline phosphatase, osteocalcin).

Statistic analysis

All statistical analyses were conducted using SPSS 23.0. Measurement data with a normal distribution were expressed as mean ± standard deviation. Between-group comparisons were conducted using independent-sample t-tests, while within-group comparisons before and after surgery were analyzed using paired t-tests. Count data were presented as frequencies or percentages and analyzed using the chi-square test. Logistic regression analysis was subsequently performed to examine the relationship between preoperative indicators and postoperative prognosis. The predictive value of relevant indicators was assessed using receiver operating characteristic (ROC) curve analysis. A *P*-value of less than 0.05 was considered statistically significant.

Results

Preoperative hepatic, renal, and bone metabolism markers in PDR patients

Preoperative levels of AST, ALT, TBIL, UACR, Scr, and sCys-C were significantly higher in the PDR group than in the control group, whereas GFR and osteocalcin levels were significantly lower ($P<0.05$). No significant differences were observed in serum calcium, phosphorus, or alkaline phosphatase levels between the two groups ($P>0.05$) (**Table 1**).

Baseline data of the vitrectomy and photocoagulation groups

The vitrectomy group comprised 78 patients (90 affected eyes), and the photocoagulation group included 72 patients (82 affected eyes). All patients had T2DM. No statistically significant differences were found between the two groups in terms of gender, age, duration of diabetes, number of affected eyes, severity of retinal lesions, LogMAR visual acuity, fasting plasma glucose (FPG), or 2-hours plasma glucose (2h PG) ($P > 0.05$), indicating comparability between groups (**Table 2**).

Clinical efficacy

The total improvement rate in the vitrectomy group was 80.00%, significantly higher than that in the photocoagulation group (37.80%) ($P<0.05$) (**Table 3**).

Changes in liver function indicators pre- and postoperatively

No significant preoperative differences were noted in AST, ALT, or TBIL levels between the two groups ($P>0.05$). Postoperatively, all three

Table 1. Levels of liver and kidney function indicators and bone metabolism indicators in 150 patients with PDR before surgery

Indicator	PDR group (n=150)	Control group (n=50)	t	*P*
AST (U/L)	50.97±10.62	29.65±5.27	13.630	<0.001
ALT (U/L)	46.01±8.40	21.35±4.48	19.820	<0.001
TBIL (μmol/L)	26.31±3.29	12.25±3.21	26.330	<0.001
UACR (mg/g)	369.69±71.47	17.33±4.02	34.790	<0.001
Scr (μmol/L)	87.73±21.74	47.56±5.22	12.920	<0.001
sCys-C (mmol/L)	1.61±0.37	1.07±0.08	10.220	<0.001
GFR (mL/min)	67.54±16.90	105.36±14.18	14.240	<0.001
Calcium (mmol/L)	2.28±0.58	2.31±0.69	0.302	0.763
Phosphorus (mmol/L)	1.20±0.29	1.22±0.40	0.382	0.703
Alkaline phosphatase (U/L)	68.42±8.63	67.03±10.59	0.930	0.354
Osteocalcin (ng/mL)	15.30±2.34	21.18±1.65	16.440	<0.001

Note: PDR: proliferative diabetic retinopathy; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TBIL: total bilirubin; UACR: urinary albumin-creatinine ratio; Scr: serum creatinine; sCys-C: serum cystatin C; GFR: glomerular filtration rate.

Table 2. Baseline data of vitrectomy and photocoagulation groups [(n)%, $\bar{x}\pm s$]

Data	Vitrectomy group (n=78, 90 affected eyes)	Photocoagulation group (n=72, 82 affected eyes)	t/χ^2	*P*
Sex			0.525	0.469
Male	28 (35.90)	30 (41.67)		
Female	50 (64.10)	42 (58.33)		
Age (years)	41.35±5.22	41.38±5.39	0.035	0.972
Duration of diabetes (years)	11.95±3.31	12.30±3.51	0.177	0.860
Affected eye			1.339	0.237
Unilateral (ocellus)	64 (82.05)	64 (88.89)		
Bilateral (binoculus)	14 (17.95)	8 (11.11)		
Eye severity			-1.364	0.173
Stage IV	35 (38.89)	25 (30.49)		
Phase V	26 (28.89)	23 (28.05)		
Stage VI	29 (32.22)	34 (41.46)		
LogMAR	1.52±0.42	1.48±0.40	0.596	0.552
FPG	9.86±1.55	9.72±1.45	0.570	0.570
2h PG	14.28±2.37	14.41±2.16	0.350	0.727

Note: LogMAR: logarithm of the minimum angle of resolution; FPG: fasting plasma glucose; 2h PG: 2-hour plasma glucose.

Table 3. Clinical efficacy [(n)%]

Group	Vision significant improvement	Vision improvement	No improvement or improvement in vision	Overall improvement
Vitrectomy group (90 affected eyes)	56 (62.22)	16 (17.78)	18 (20.00)	72 (80.00)
Photocoagulation group (82 affected eyes)	25 (30.49)	6 (7.32)	51 (62.20)	31 (37.80)
χ^2		-5.135		31.800
P		<0.001		<0.001

indicators decreased in both groups, with the vitrectomy group showing significantly lower levels compared to the photocoagulation group ($P<0.05$) (**Table 4**).

Table 4. Changes in liver function indicators before and after surgery ($\bar{x}\pm s$)

Indicator		Vitrectomy group (n=78)	Photocoagulation group (n=72)	t	*P*
AST (U/L)	Before surgery	51.52±10.33	50.38±11.04	0.653	0.515
	After surgery	25.22±7.53[a]	36.27±8.82[a]	8.271	<0.001
ALT (U/L)	Before surgery	46.22±8.38	45.79±8.53	0.311	0.756
	After surgery	23.54±7.58[a]	31.26±7.36[a]	6.319	<0.001
TBIL (μmol/L)	Before surgery	26.35±3.27	26.27±3.34	0.148	0.882
	After surgery	16.38±2.83[a]	21.25±3.42[a]	9.530	<0.001

Note: AST: aspartate aminotransferase; ALT: alanine aminotransferase; TBIL: total bilirubin. [a]stands for preoperative comparison with this group, $P<0.05$.

Table 5. Changes in renal function indicators before and after surgery ($\bar{x}\pm s$)

Indicator		Vitrectomy group (n=78)	Photocoagulation group (n=72)	t	*P*
UACR (mg/g)	Before surgery	372.56±73.36	366.58±70.25	0.509	0.611
	After surgery	218.24±65.58[b]	280.56±61.28[b]	6.000	<0.001
Scr (μmol/L)	Before surgery	88.59±21.24	86.79±22.53	0.504	0.615
	After surgery	55.26±14.39[b]	68.53±15.47[b]	5.443	<0.001
sCys-C (mmol/L)	Before surgery	1.63±0.34	1.58±0.39	0.839	0.403
	After surgery	0.62±0.17[b]	1.03±0.21[b]	13.190	<0.001
GFR (mL/min)	Before surgery	68.27±15.67	66.75±18.32	0.547	0.585
	After surgery	92.16±10.18[b]	82.39±11.25[b]	5.584	<0.001

Note: UACR: urinary albumin-creatinine ratio; Scr: serum creatinine; sCys-C: serum cystatin C; GFR: glomerular filtration rate. [b]stands for preoperative comparison with this group, $P<0.05$.

Changes in renal function indicators pre- and postoperatively

Preoperative UACR, Scr, sCys-C, and GFR levels did not differ significantly between the vitrectomy group and the photocoagulation group ($P>0.05$). After surgery, UACR, Scr, and sCys-C levels decreased while GFR increased in both groups. Moreover, the levels of UACR, Scr, and sCys-C in the vitrectomy group were lower than those in the photocoagulation group, and the GFR level in the vitrectomy group was higher than that in the photocoagulation group ($P<0.05$) (**Table 5**).

Changes in bone metabolism indicators pre- and postoperatively

No significant differences were observed between the two groups in calcium, phosphorus, alkaline phosphatase, or osteocalcin levels before and after surgery ($P>0.05$). However, osteocalcin levels increased significantly in both groups, with higher levels observed in the vitrectomy group ($P<0.05$) (**Table 6**).

Correlation between preoperative indicators and surgical prognosis

Among the 150 patients who underwent retinal surgery, 69 had a poor prognosis, yielding a poor prognosis rate of 46.0%. Prognosis (coded as: 0 = good, 1 = poor) was treated as the dependent variable. Independent variables included surgical method (0 = vitrectomy, 1 = photocoagulation), and preoperative values of AST, ALT, TBIL, UACR, Scr, sCys - C, GFR, and osteocalcin (all entered based on measured values). These variables were incorporated into a logistic regression model to identify predictors of postoperative outcomes. The analysis revealed that, regardless of model adjustments, AST, ALT, TBIL, GFR, and surgical method remained independent prognostic factors for postoperative outcomes in diabetic retinal surgery ($P<0.05$) (**Table 7**).

Prognostic efficacy of preoperative AST, ALT, TBIL, and GFR levels in diabetic retinal surgery

ROC curve analysis was conducted to assess the prognostic value of AST, ALT, TBIL, and GFR

Table 6. Changes in bone metabolism indicators before and after surgery ($\bar{x} \pm s$)

Indicator		Vitrectomy group (n=78)	Photocoagulation group (n=72)	t	*P*
Calcium (mmol/L)	Before surgery	2.25±0.64	2.31±0.50	0.161	0.872
	After surgery	2.31±0.42	2.28±0.55	0.377	0.707
Phosphorus (mmol/L)	Before surgery	1.22±0.31	1.19±0.28	0.414	0.680
	After surgery	1.18±0.28	1.20±0.35	0.388	0.699
Alkaline phosphatase (U/L)	Before surgery	68.22±8.84	68.64±8.52	0.296	0.768
	After surgery	68.32±7.69	67.11±9.15	0.879	0.381
Osteocalcin (ng/mL)	Before surgery	15.39±2.28	15.21±2.43	1.092	0.277
	After surgery	20.13±4.26[c]	18.63±4.26[c]	2.155	0.033

Note: [c]stands for preoperative comparison with this group, $P<0.05$.

in diabetic retinopathy surgery. The results showed that ALT and TBIL had relatively high sensitivity (0.725 and 0.754, respectively), whereas AST and GFR demonstrated relatively high specificity (0.875 and 0.889, respectively). The area under the curve (AUC) for the combined model incorporating all four indicators was 0.780, outperforming each individual indicator. The combined model had a sensitivity of 0.522 and a specificity of 0.937 (**Table 8**; **Figure 1**).

Discussion

Pathophysiology of PDR and surgical efficacy

The pathophysiology of PDR is complex and multifactorial. Key characteristics include endothelial cell proliferation, thickening of the retinal capillary basement membrane, increased capillary permeability, capillary occlusion, and neovascularization. These pathological changes result in localized blood vessel stenosis and occlusion, leading to retinal ischemia and hypoxia [13]. Moreover, bleeding from newly formed vessels can disrupt the retinal barrier and compromise the integrity of the vitreous body. The exposure of the retinal pigment epithelium, coupled with the ingrowth of neovascular tissue into the vitreous cavity, promotes the infiltration of leukocytes, proteins and growth factors from the bloodstream into the vitreous through the compromised vascular wall, significantly impairing visual function [14].

In advanced stages of PDR, severe retinal ischemia triggers extensive neovascularization, which can lead to vitreous hemorrhage, macular edema, neovascular membranes, and tractional retinal detachment, all contributing to considerable visual impairment. Additionally, retinal vascular occlusion and optic nerve atrophy can ultimately result in blindness [15]. Most patients with PDR experience progressive and irreversible visual loss, with some leading to complete blindness. Vitrectomy, a widely used surgical intervention for PDR, has been shown to restore vision in many patients. In this study, statistical analysis revealed that the overall rate of visual improvement in patients undergoing vitrectomy was significantly higher compared to those treated with photocoagulation, corroborating with the findings of Lin et al. [16]. In conclusion, advanced PDR severely impairs vision, even causing blindness. Our study shows that vitrectomy offers a superior visual improvement over photocoagulation in PDR patients. These findings are crucial for informing surgical decisions and align with previous research, including the work of Lin et al. Further investigation into the underlying mechanisms driving the differential effectiveness of these surgeries is warranted to optimize treatment strategies and enhance visual outcomes.

Dysfunction of liver, kidney, and bone metabolism in PDR patients

The findings of this study indicate that PDR patients display varying degrees of dysfunction in liver, kidney, and bone metabolism. Specifically, levels of AST, ALT, TBIL, UACR, Scr, and sCys-C were elevated, while GFR and osteocalcin levels were significantly lower compared to healthy individuals. These results are consistent with previous research [17].

Research has highlighted that DR predominantly affects the liver and kidneys and is often associated with a syndrome of liver-kidney Yin

Table 7. Correlation between indicators and prognosis of diabetic patients undergoing retinal surgery

Model	Variables	B	SE	Wals	*P*	OR (95% CI)
Model 1	AST	0.052	0.019	7.187	0.007	1.053 (1.014-1.094)
	ALT	0.063	0.024	6.761	0.009	1.065 (1.016-1.117)
	TBIL	0.144	0.065	4.881	0.027	1.155 (1.016-1.313)
	GFR	-0.042	0.012	11.708	0.001	0.958 (0.935-0.982)
Model 2	AST	0.085	0.025	11.649	0.001	1.089 (1.037-1.143)
	ALT	0.078	0.030	6.754	0.009	1.081 (1.019-1.146)
	TBIL	0.164	0.077	4.552	0.033	1.178 (1.013-1.370)
	GFR	-0.050	0.015	11.118	0.001	0.951 (0.923-0.980)
	Operative method	3.069	0.542	32.044	<0.001	21.512 (7.434-62.245)
Model 3	AST	0.092	0.027	11.132	0.001	1.096 (1.039-1.157)
	ALT	0.081	0.034	5.829	0.016	1.084 (1.015-1.158)
	TBIL	0.200	0.085	5.571	0.018	1.221 (1.035-1.442)
	GFR	-0.049	0.017	8.469	0.004	0.953 (0.922-0.984)
	Operative method	3.619	0.642	31.770	<0.001	37.314 (10.600-131.358)
	UACR	0.008	0.004	4.435	0.035	1.008 (1.001-1.015)
	Scr	-0.009	0.012	0.554	0.457	0.991 (0.968-1.015)
	sCys-C	0.599	0.741	0.654	0.419	1.820 (0.426-7.770)
	Calcium	-0.337	0.454	0.551	0.458	0.714 (0.293-1.739)
	Phosphorus	1.154	1.019	1.283	0.257	3.172 (0.430-23.380)
	Alkaline phosphatase	-0.021	0.030	0.496	0.481	0.979 (0.923-1.039)
	Osteocalcin	0.115	0.117	0.976	0.323	1.122 (0.893-1.411)
Model 4	AST	0.106	0.030	12.195	<0.001	1.112 (1.048-1.181)
	ALT	0.075	0.036	4.328	0.037	1.078 (1.004-1.158)
	TBIL	0.236	0.093	6.404	0.011	1.266 (1.055-1.519)
	GFR	-0.045	0.020	5.108	0.024	0.956 (0.920-0.994)
	Operative method	3.785	0.693	29.793	0.000	44.043 (11.313-171.457)
	UACR	0.008	0.004	3.256	0.071	1.008 (0.999-1.016)
	Scr	-0.010	0.013	0.538	0.463	0.991 (0.966-1.016)
	sCys-C	0.876	0.812	1.165	0.280	2.402 (0.489-11.793)
	Calcium	-0.323	0.484	0.447	0.504	0.724 (0.280-1.867)
	Phosphorus	2.071	1.228	2.844	0.092	7.936 (0.715-88.125)
	Alkaline phosphatase	-0.024	0.033	0.499	0.480	0.977 (0.915-1.043)
	Osteocalcin	0.073	0.123	0.353	0.553	1.076 (0.845-1.370)
	Sex	-0.348	0.573	0.369	0.544	0.706 (0.230-2.170)
	Age	-0.008	0.064	0.015	0.903	0.992 (0.876-1.125)
	Duration of diabetes	0.030	0.077	0.153	0.696	1.031 (0.886-1.198)
	Affected eye	-0.667	0.933	0.511	0.475	0.513 (0.082-3.195)
	LogMAR	-1.862	0.806	5.339	0.021	0.155 (0.032-0.754)
	FPG	-0.149	0.192	0.602	0.438	0.861 (0.591-1.256)
	2h PG	-0.093	0.124	0.571	0.450	0.911 (0.715-1.161)

Note: A logistic regression model was used to analyze the relationship between various preoperative indicators and the prognosis of diabetic retinopathy surgery. Model 1 explored the association between each indicator and prognosis without controlling for any confounding variables. Model 2 adjusted for the surgical method to analyze the relationship between other indicators and the prognosis while accounting for the influence of the surgical method. Model 3 further incorporated adjustments for variables such as UACR, Scr, sCys-C, calcium, phosphorus, alkaline phosphatase, and osteocalcin, allowing for a more comprehensive evaluation of the combined effects of multiple factors. Model 4 included additional adjustments for confounders such as gender, age, duration of diabetes, affected eyes, LogMAR, FPG, and 2h PG, providing a deeper insight into the true relationship between each indicator and the prognosis of diabetic retinopathy surgery. AST: aspartate aminotransferase; ALT: alanine aminotransferase; TBIL: total bilirubin; UACR: urinary albumin-creatinine ratio; Scr: serum creatinine; sCys-C: serum cystatin C; GFR: glomerular filtration rate; LogMAR: logarithm of the minimum angle of resolution; FPG: fasting plasma glucose; 2h PG: 2-hours plasma glucose. SE: standard error; OR: odds ratio; CI: confidence interval.

Table 8. Receiver operating characteristic (ROC) curve analysis

Variables	AUC	*P*	95% CI	Sensitivity	Specificity
AST	0.692	<0.001	0.603-0.780	0.522	0.875
ALT	0.643	0.003	0.555-0.732	0.725	0.562
TBIL	0.646	0.002	0.557-0.736	0.754	0.512
GFR	0.683	<0.001	0.596-0.770	0.435	0.889
Combined forecasting	0.780	<0.001	0.705-0.856	0.522	0.937

Note: AST: aspartate aminotransferase; ALT: alanine aminotransferase; TBIL: total bilirubin; GFR: glomerular filtration rate; AUC: area under the curve; CI: confidence interval.

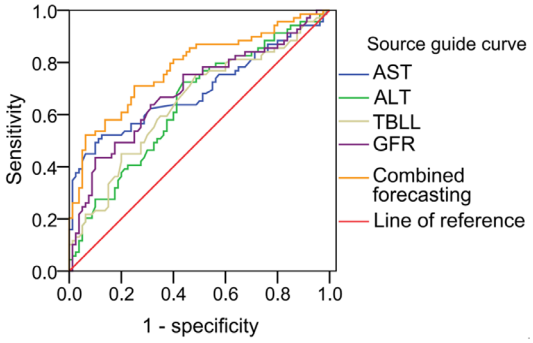

Figure 1. Receiver operating characteristic (ROC) curve of AST, ALT, TBIL, and GFR in predicting the prognosis of diabetic retinal surgery. *Note*: AST: aspartate aminotransferase; ALT: alanine aminotransferase; TBIL: total bilirubin; GFR: glomerular filtration rate.

deficiency [18]. Insulin resistance, a key factor in T2DM, induces metabolic stress and liver injury. For instance, Liu et al. demonstrated that insulin resistance exacerbates alcohol-induced liver damage by promoting oxidative stress and upregulating CYP2E1 [19]. Both DR and DN share common mechanisms of microvascular injury through immune and inflammatory pathways [20], while also influencing each other [21]. A meta-analysis by Li et al. suggested that DR could serve as an early predictor of secondary DN in T2DM patients [22]. As an indicator of active microvascular disease, DR can adversely affect renal microvessels, leading to renal insufficiency. Osteocalcin, a non-collagenous protein secreted by osteoblasts, is positively correlated with bone activity. In T2DM, defects in insulin receptors or insulin deficiency impair osteoblast activity and bone remodeling, resulting in decreased osteocalcin synthesis and secretion [23]. In summary, DR shows a distinct predisposition to liver and kidney dysfunction, linked to liver-kidney Yin deficiency. Insulin resistance in T2DM impacts both liver function and DR development. DR and DN share a common microvascular injury mechanism and influence each other, with DR potentially predicting DN. In addition, T2DM impairs osteoblast function, reducing osteocalcin synthesis. These intricate relationships between DR, liver and kidney function, and bone metabolism warrant further exploration to enhance our understanding and management of diabetes related complications.

Impact of surgical treatments on function, metabolism, and prognosis

The results of this study indicate that surgical treatment for DR leads to varying degrees of improvement in liver and kidney function, as well as bone metabolism. Notably, apart from calcium, phosphorus, and alkaline phosphatase, significant differences were observed in the degree of improvement across other functional and metabolic indicators between vitrectomy and photocoagulation groups. Vitrectomy was associated with greater enhancement of liver and kidney function and bone metabolism compared to photocoagulation. As a commonly employed technique for treating complex eye diseases - particularly in patients with PDR complicated by vitreous hemorrhage - vitrectomy enables the direct removal of vitreous hemorrhage, relieves retinal traction caused by proliferative membranes, and restores normal retinal anatomical structure. Additionally, vitrectomy facilitates the clearance of vascular endothelial growth factor from the vitreous, thereby contributing to improved therapeutic outcomes in PDR patients [24]. In conclusion, patients undergoing diabetic retinal surgery show improvements in liver, kidney, and bone metabolism. Among the surgical options, vitrectomy demonstrates superior efficacy in correcting these functions and metabolic parameters. By directly addressing vitreous hemorrhage,

relieving retinal traction, and clearing vascular endothelial growth factor, vitrectomy offers significant advantages over photocoagulation in the treatment of PDR and its related systemic changes.

We further explored the influence of these functional and metabolic indicators on the prognosis of diabetic retinal surgery. Among the 150 patients who underwent retinal surgery, 46.0% experienced a poor prognosis, which was higher than the rate reported by Gross et al. This discrepancy may be attributed to disparities in treatment methods and follow-up durations. Logistic regression analysis revealed that AST, ALT, TBIL, GFR, and the type of surgery were independent prognostic factors for diabetic retinal surgery, regardless of adjustments for other variables. The predictive sensitivity and specificity of these indicators exhibited distinct characteristics. Specifically, ALT and TBIL demonstrated higher sensitivity, whereas AST and GFR showed higher specificity. The AUC for the combined prediction using these four indicators was 0.780, surpassing the AUC for any single indicator. The sensitivity and specificity of the combined prediction were 0.522 and 0.937, respectively. These results suggest that the choice of surgical method, along with liver and kidney dysfunction, are crucial factors affecting the prognosis of retinal surgery in PDR patients. Therefore, we conclude that both the type of surgery and preoperative abnormalities in AST, ALT, TBIL, GFR, and other indicators can impact the surgical prognosis for PDR patients. Clinicians should tailor the surgical approach according to each patient's condition and closely monitor these indicators before surgery, remaining vigilant to any fluctuations. Rigorous and individualized preoperative interventions aimed at optimizing levels of AST, ALT, TBIL, GFR, and other key indicators may help mitigate the risk of poor postoperative outcomes. Such targeted management has the potential to improve clinical outcomes in patients undergoing PDR.

Study limitations and future perspectives

This study has several limitations. First, the sample size was limited by time and regional factors, which may have introduced bias and overlooked significant impact indicators. Second, while we compared two different surgical procedures (vitrectomy and photocoagulation), we did not fully explore the long-term effects of these surgeries on liver and kidney function, as well as bone metabolism. There may be other surgical-related factors not accounted for that could influence these outcomes. Additionally, we did not consider the potential impact of different postoperative care regimens, which could also affect the interpretation of our results.

For future research, we intend to significantly increase the sample size by including multiple regions and extending the study period. This will allow us to obtain more comprehensive data and reduce potential biases. Moreover, future studies should not only focus on the two surgical procedures explored here but also systematically assess the long-term effects of different surgical approaches and postoperative care regimens on liver and kidney function, bone metabolism, and overall prognosis. This will provide more precise and detailed guidance for the clinical treatment of PDR patients.

Conclusion

In conclusion, the metabolic functions of the liver, kidney and bone in diabetic patients undergoing retinal surgery showed noteble improvement. Additionally, the levels of AST, ALT, TBIL, and GFR were found to be closely associated with surgical prognosis, providing valuable insights for guiding preoperative interventions.

Disclosure of conflict of interest

None.

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References

[1] Kaštelan S, Orešković I, Bišćan F, Kaštelan H and Gverović Antunica A. Inflammatory and angiogenic biomarkers in diabetic retinopathy. Biochem Med (Zagreb) 2020; 30: 030502.

[2] Klein R, Knudtson MD, Lee KE, Gangnon R and Klein BE. The Wisconsin epidemiologic study of diabetic retinopathy: XXII the twenty-five-year progression of retinopathy in persons with

type 1 diabetes. Ophthalmology 2008; 115: 1859-68.
[3] Zhang GH, Yuan TH, Yue ZS, Wang L and Dou GR. The presence of diabetic retinopathy closely associated with the progression of non-alcoholic fatty liver disease: a meta-analysis of observational studies. Front Mol Biosci 2022; 9: 1019899.
[4] Yao X, Pei X, Fan S, Yang X, Yang Y and Li Z. Relationship between renal and liver function with diabetic retinopathy in patients with type 2 diabetes mellitus: a study based on cross-sectional data. Sci Rep 2022; 12: 9363.
[5] Hsing SC, Lee CC, Lin C, Chen JT, Chen YH and Fang WH. The severity of diabetic retinopathy is an independent factor for the progression of diabetic nephropathy. J Clin Med 2020; 10: 3.
[6] Luo WM, Su JY, Xu T and Fang ZZ. Prevalence of diabetic retinopathy and use of common oral hypoglycemic agents increase the risk of diabetic nephropathy-a cross-sectional study in patients with type 2 diabetes. Int J Environ Res Public Health 2023; 20: 4623.
[7] Zhao X, Huo L, Yu X and Zhang X. Association of bone metabolism indices and bone mineral density with diabetic retinopathy in elderly patients with type 2 diabetes mellitus: a cross-sectional inpatient study in China. J Diabetes Res 2021; 2021: 8853622.
[8] Schreur V, Brouwers J, Van Huet RAC, Smeets S, Phan M, Hoyng CB, de Jong EK and Klevering BJ. Long-term outcomes of vitrectomy for proliferative diabetic retinopathy. Acta Ophthalmol 2021; 99: 83-89.
[9] Ricca A, Boone K, Boldt HC, Gehrs KM, Russell SR, Folk JC, Zimmerman MB, Wilkinson ME and Sohn EH. Attaining functional levels of visual acuity after vitrectomy for retinal detachment secondary to proliferative diabetic retinopathy. Sci Rep 2020; 10: 15637.
[10] Saini DC, Kochar A and Poonia R. Clinical correlation of diabetic retinopathy with nephropathy and neuropathy. Indian J Ophthalmol 2021; 69: 3364-3368.
[11] Everett LA and Paulus YM. Laser therapy in the treatment of diabetic retinopathy and diabetic macular edema. Curr Diab Rep 2021; 21: 35.
[12] Moriya T, Hayashi A, Matsubara M, Suzuki A and Ouchi M. Glucose control, diabetic retinopathy, and hemodialysis induction in subjects with normo-microalbuminuric type 2 diabetic patients with normal renal function followed for 15 years. J Diabetes Complications 2022; 36: 108080.
[13] Chen DY, Sun NH, Chen X, Gong JJ, Yuan ST, Hu ZZ, Lu NN, Körbelin J, Fukunaga K, Liu QH, Lu YM and Han F. Endothelium-derived semaphorin 3G attenuates ischemic retinopathy by coordinating β-catenin-dependent vascular remodeling. J Clin Invest 2021; 131: e135296.
[14] Glassman AR, Beaulieu WT, Maguire MG, Antoszyk AN, Chow CC, Elman MJ, Jampol LM, Salehi-Had H and Sun JK; DRCR Retina Network. Visual acuity, vitreous hemorrhage, and other ocular outcomes after vitrectomy vs aflibercept for vitreous hemorrhage due to diabetic retinopathy: a secondary analysis of a randomized clinical trial. JAMA Ophthalmol 2021; 139: 725-733.
[15] Martinez-Zapata MJ, Salvador I, Martí-Carvajal AJ, Pijoan JI, Cordero JA, Ponomarev D, Kernohan A, Solà I and Virgili G. Anti-vascular endothelial growth factor for proliferative diabetic retinopathy. Cochrane Database Syst Rev 2023; 3: CD008721.
[16] Lin TZ, Kong Y, Shi C, Eric Pazo E, Dai GZ, Wu XW, Xu L and Shen LJ. Prognosis value of Chinese Ocular Fundus Diseases Society classification for proliferative diabetic retinopathy on postoperative visual acuity after pars plana vitrectomy in type 2 diabetes. Int J Ophthalmol 2022; 15: 1627-1633.
[17] Prakash J, Patel PS, Iqbal M, Sharma SS, Singh S, Agrawal NK and Singh U. Histological spectrum of clinical kidney disease in type 2 diabetes mellitus patients with special reference to nonalbuminuric diabetic nephropathy: a kidney biopsy-based study. J Assoc Physicians India 2022; 70: 11-12.
[18] Zhang S, Ma P and Chen Q. The correlation between the level of skin advanced glycation end products in type 2 diabetes mellitus and the stages of diabetic retinopathy and the types of traditional Chinese medicine syndrome. Evid Based Complement Alternat Med 2022; 2022: 5193944.
[19] Liu J, Kong D, Ai D, Xu A, Yu W, Peng Z, Peng J, Wang Z, Wang Z, Liu R, Li W, Hai C, Zhang X and Wang X. Insulin resistance enhances binge ethanol-induced liver injury through promoting oxidative stress and up-regulation CYP2E1. Life Sci 2022; 303: 120681.
[20] Hui Z, Chen YM, Gong WK, Lai JB, Yao BB, Zhao ZJ, Lu QK, Ye K, Ji LD and Xu J. Shared and specific biological signalling pathways for diabetic retinopathy, peripheral neuropathy and nephropathy by high-throughput sequencing analysis. Diab Vasc Dis Res 2022; 19: 14791641221122918.
[21] Yang J and Liu Z. Mechanistic pathogenesis of endothelial dysfunction in diabetic nephropathy and retinopathy. Front Endocrinol (Lausanne) 2022; 13: 816400.
[22] Li Y, Su X, Ye Q, Guo X, Xu B, Guan T and Chen A. The predictive value of diabetic retinopathy on subsequent diabetic nephropathy in patients with type 2 diabetes: a systematic re-

view and meta-analysis of prospective studies. Ren Fail 2021; 43: 231-240.

[23] Zeng H, Ge J, Xu W, Ma H, Chen L, Xia M, Pan B, Lin H, Wang S and Gao X. Type 2 Diabetes is causally associated with reduced serum osteocalcin: a genomewide association and mendelian randomization study. J Bone Miner Res 2021; 36: 1694-1707.

[24] Martinez-Zapata MJ, Salvador I, Martí-Carvajal AJ, Pijoan JI, Cordero JA, Ponomarev D, Kernohan A, Solà I and Virgili G. Anti-vascular endothelial growth factor for proliferative diabetic retinopathy. Cochrane Database Syst Rev 2023; 3: CD008721.