



OPEN Relationship between glucose to lymphocyte ratio and the first peritonitis episode in patients treated with peritoneal dialysis

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This study aimed to investigate the potential relationship between baseline glucose to lymphocyte ratio (GLR) levels and the first episode of peritonitis in patients treated with peritoneal dialysis (PD). A total of 314 patients treated with PD were included and divided into three groups based on GLR tertiles: tertile 1 ($\text{GLR} \leq 4.23$); tertile 2 ($4.23 < \text{GLR} \leq 5.96$), and tertile 3 ($\text{GLR} > 5.96$). The relationships between GLR and the first peritonitis episode were analyzed using Kaplan–Meier curves and multivariable Cox regression models. Competitive risk analysis, subgroup and sensitivity analyses were performed to validate the robustness of the findings. During a median follow-up of 27 months, 123 (39.17%) patients developed the first episode of peritonitis. The incidence of the first peritonitis episode increased with the higher GLR tertiles (tertile 1: 32.08%, tertile 2: 37.50%, tertile 3: 48.08%). Kaplan–Meier curves revealed significant differences in the cumulative incidence of the first peritonitis episode among the GLR tertiles (Log-Rank test, $P = 0.018$). After full adjustment for confounding factors, patients in tertile 3 remained at significantly higher risk for the first episode of peritonitis compared to those in tertile 1 (HR 2.633, 95% CI 1.223–5.668, $P = 0.013$). Competitive risk models and sensitivity analysis further confirmed this association. Our study suggests that elevated GLR is associated with an increased risk of the first peritonitis episode in patients with PD.

Keywords Glucose to lymphocyte ratio, Peritoneal dialysis, Peritonitis

Peritoneal dialysis (PD) is a widely utilized method of renal replacement therapy for patients with end-stage kidney disease (ESKD). Since 1985, Hong Kong has implemented the PD first policy, which had a positive impact on the promotion and application of PD therapy worldwide¹. However, PD-associated peritonitis remains a significant complication, leading to poor clinical outcomes² and posing a major challenge to the long-term treatment of PD. Therefore, to reduce the risk of peritonitis episodes, exploring novel biomarkers to identify patients at higher risk of peritonitis episodes is an important research direction.

Patients treated with PD commonly experience chronic inflammation³ and have an increased risk of developing disorders in glucose metabolism⁴ and immune function⁵. Both of these factors may be associated with the peritonitis episodes. The glucose to lymphocyte ratio (GLR) has emerged as a novel inflammatory biomarker, combining aspects of glucose metabolism and immune status. GLR has been shown to correlate with the development and prognosis of various diseases^{6,7}, but its specific role in predicting PD-associated peritonitis remains underexplored. A study has demonstrated a positive correlation between GLR and neutrophil to lymphocyte ratio (NLR)⁸, while NLR has been proven useful in predicting the risk of PD-associated peritonitis⁹. Based on these findings, we hypothesize that GLR could serve as a predictive marker for peritonitis episodes in patients treated with PD. This study aims to explore the potential relationship between baseline GLR levels and the first episode of peritonitis in patients treated with PD. By evaluating whether GLR is a reliable early biomarker for identifying high-risk individuals, our research findings may facilitate personalized medical decision-making and patient-centered care to reduce the incidence of peritonitis, prolong the technical survival of patients, and ultimately improve patients' quality of life and long-term outcomes.

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Materials and methods

Study population

In this retrospective cohort study, a total of 430 patients undergoing initial PD at the Second Affiliated Hospital of Anhui Medical University were identified from existing medical records between January 1, 2010, and December 31, 2022, for inclusion in the study. The exclusion criteria included: (1) younger than 18 years; (2) transferred from maintenance hemodialysis (HD); (3) PD less than 3 months; (4) active infection, hematological diseases, or use of glucocorticoids, as these may influence the GLR levels; (5) Missing GLR or follow-up data. All patients and caregivers received standardized PD training and passed operational assessments at the hospital after catheterization. All patients used glucose-based dialysis solution and no patients used the PD cyclers. All data were fully anonymized and all participants were signed informed consent. This study conforms to the Declaration of Helsinki and was approved by the ethics committee of the Second Affiliated Hospital of Anhui Medical University (No. KY201302).

Data collection

All baseline characteristics and clinical information were collected at the initiation of PD therapy from the electronic medical records of our center. Demographic data including sex, age, body mass index (BMI), and causes of ESKD; comorbidities including diabetes mellitus (DM) and history of cardiovascular disease (CVD); laboratory parameters including hemoglobin, white blood cell (WBC) count, lymphocyte count, platelet count, high-sensitive C-reactive protein (hs-CRP), serum creatinine, serum urea nitrogen, serum uric acid, serum corrected calcium, serum phosphorus, serum albumin, fasting blood glucose, and intact parathyroid hormone. GLR was calculated by fasting blood glucose/lymphocyte count. Dialysis-related data were collected at least 1 month after the initiation of PD therapy, including daily ultrafiltration, 24-hour urine volume, total weekly Kt/V, and glucose exposure. Glucose exposure was calculated by multiplying the glucose concentration by the prescribed infusion volume on a regular dialysis day. For example, in a patient who receives 2 exchanges of 2 L 1.5% glucose and 2 exchanges of 2 L 2.5% glucose, the total glucose exposure is calculated as $(2 \times 2 \times 15) + (2 \times 2 \times 25) = 160$ g of glucose/24 h. Additionally, the use of antidiabetic drugs was also recorded.

Study outcome

The study outcome was the first episode of peritonitis, transfer to HD therapy, renal transplantation, death, transfer to other centers, loss of follow-up, or censoring on December 31, 2023. Peritonitis was diagnosed when at least 2 of the following conditions were present¹⁰: (1) abdominal pain and/or cloudy dialysis effluent; (2) dialysis effluent WBC count $> 100/\mu\text{L}$ (after a dwell time of at least 2 h), with $> 50\%$ polymorphonuclear leukocytes; (3) positive dialysis effluent culture. When peritonitis was suspected, 5–10 mL effluent was injected into aerobic and anaerobic blood-culture bottles for microbiology tests. All peritonitis was treated using the recommended empirical antibiotic therapy and the medication regimen was adjusted based on the actual organism and antibiotic susceptibility. Dialysis effluent WBC count on day 1, causative organisms, and peritonitis outcomes were recorded.

Statistical analysis

The Shapiro-Wilk test was employed to assess whether the data conforms to a normal distribution. The results indicated that only albumin and daily ultrafiltration adhered to a normal distribution. Albumin and daily ultrafiltration were expressed as mean \pm standard deviation, while other skewness distribution data were expressed by median (interquartile range). Categorical variables were expressed as frequency (percentage). All participants were divided into three groups based on the tertiles of GLR. Group differences were compared using the “CBCgrps” package in R. The difference in cumulative incidence of the first peritonitis episode was analyzed using the Kaplan-Meier curve. Cox proportional hazard models were used to investigate the association between GLR and the first peritonitis episode. The proportional hazards assumption was evaluated using Schoenfeld residuals, and no violations were identified. The variance inflation factor (VIF) was used to assess potential collinearity among the covariables. The use of antidiabetic drugs was excluded from the Cox regression models due to strong collinearity with DM, as indicated by a VIF greater than 10. The performance of the models was assessed using the concordance index. To ensure the reliability of the finding, we constructed four models based on meaningful covariates identified in univariate Cox regression analysis and clinically significant factors: model 1, adjusted for age, sex, BMI; model 2, adjusted for model 1 covariates plus DM and history of CVD; model 3, adjusted for model 2 covariates plus hemoglobin, platelet count, serum creatinine, serum uric acid, serum corrected calcium, serum phosphorus, serum albumin, intact parathyroid hormone, and hs-CRP; model 4, adjusted for model 3 covariates plus daily ultrafiltration, 24-hour urine volume, total weekly Kt/V, and glucose exposure. Additionally, as transfer to HD therapy, renal transplantation, death, transfer to other centers, and loss of follow-up were considered competing risk events for the first peritonitis episode, cumulative incidence considering competing risks was depicted using Gray’s test, and the Fine-Gray subdistribution hazards model was employed. Considering the missing values in hs-CRP, total weekly KTV, daily ultrafiltration, 24-hour urine volume, and intact parathyroid hormone, we employed multiple imputation methods and subsequently re-conducted the multivariate Cox regression models as a sensitivity analysis. The time-dependent receiver operating characteristic (ROC) curves and their corresponding area under the curve (AUC) were used to assess the predictive ability of fasting blood glucose, lymphocyte count, and GLR for the first episode of peritonitis. The “compare” function of the “timeROC” package was applied to compare the AUC values. Subgroups were stratified by age (< 60 vs. ≥ 60 years), sex (male vs. female), DM (yes vs. no), and history of CVD (yes vs. no). Interactions between subgroup variables and GLR were examined by conducting a formal test of interaction. A forest plot was constructed to depict the result of the subgroup analyses and interaction test. Power analysis for

the study was performed using the “powerSurvEpi” package in R, yielding a power of 0.928. A 2-sided $P < 0.05$ was considered statistically significant. All statistical analyses were performed by R software (version 4.3.1).

Results

Study participants and clinical characteristics

As shown in Fig. 1, a total of 314 patients treated with PD were included in the analysis. The patients were divided into three groups based on GLR tertiles: tertile 1 ($\text{GLR} \leq 4.23$); tertile 2 ($4.23 < \text{GLR} \leq 5.96$), and tertile 3 ($\text{GLR} > 5.96$). Baseline demographic and clinical characteristics are presented in Table 1. The median age of the patients was 52 (42, 61) years, with 145 males (46.18%) and 59 patients (18.79%) having diabetes. There were significant differences in age, hemoglobin, platelet count, serum creatinine, serum urea nitrogen, serum corrected calcium, serum albumin, intact parathyroid hormone, and 24-hour urine volume among the three groups. During a median follow-up of 27 months, 123 patients (39.17%) developed the first episode of peritonitis. The incidence of the first peritonitis episode increased with the higher GLR tertiles (tertile 1: 32.08%, tertile 2: 37.50%, tertile 3: 48.08%). The overall peritonitis rate was 0.13 episodes per year at risk. The causative organisms and outcomes of peritonitis are presented in Table 2. Gram-positive bacteria were the most common causative organisms in the first peritonitis episode, observed in 59 (47.97%) patients. Among other culture-positive organisms, 28 (22.76%) peritonitis episodes involved gram-negative bacteria, 5 (4.07%) peritonitis episodes involved fungus, and 1 (0.81%) peritonitis episode involved polymicrobial bacteria. Additionally, culture-negative peritonitis was observed in 30 (24.39%) patients. Of the total patients with peritonitis, 109 (88.62%) were completely cured, 10 (8.13%) transferred to HD therapy, and 4 (3.25%) died.

GLR and the first episode of peritonitis in patients treated with PD

The time-dependent ROC curves for predicting the first peritonitis episode using fasting blood glucose, lymphocyte count, and GLR were showed in Fig. 2. At 1 year, the AUC values were 0.576 for GLR, 0.557 for fasting blood glucose, and 0.553 for lymphocyte count. At 3 years, the AUC values were 0.605, 0.563, and 0.591, respectively. At 5 years, the AUC values were 0.596, 0.522, and 0.604. Although there were no statistically significant differences in AUC between GLR and fasting blood glucose or lymphocyte count, the AUC for GLR was higher than that for fasting blood glucose and lymphocyte count at 1 and 3 years, and the AUC for GLR was slightly lower than that for lymphocyte count but remained higher than that for fasting blood glucose at 5 years, indicating that the predictive ability of GLR may be superior to that of fasting blood glucose or lymphocyte count alone. The Kaplan-Meier curves for GLR tertiles was shown in Fig. 3. The results indicate significant differences in the cumulative incidence of the first peritonitis episode (Log-Rank test, $P = 0.018$). Further comparisons between groups revealed that the cumulative incidence of the first episode of peritonitis in

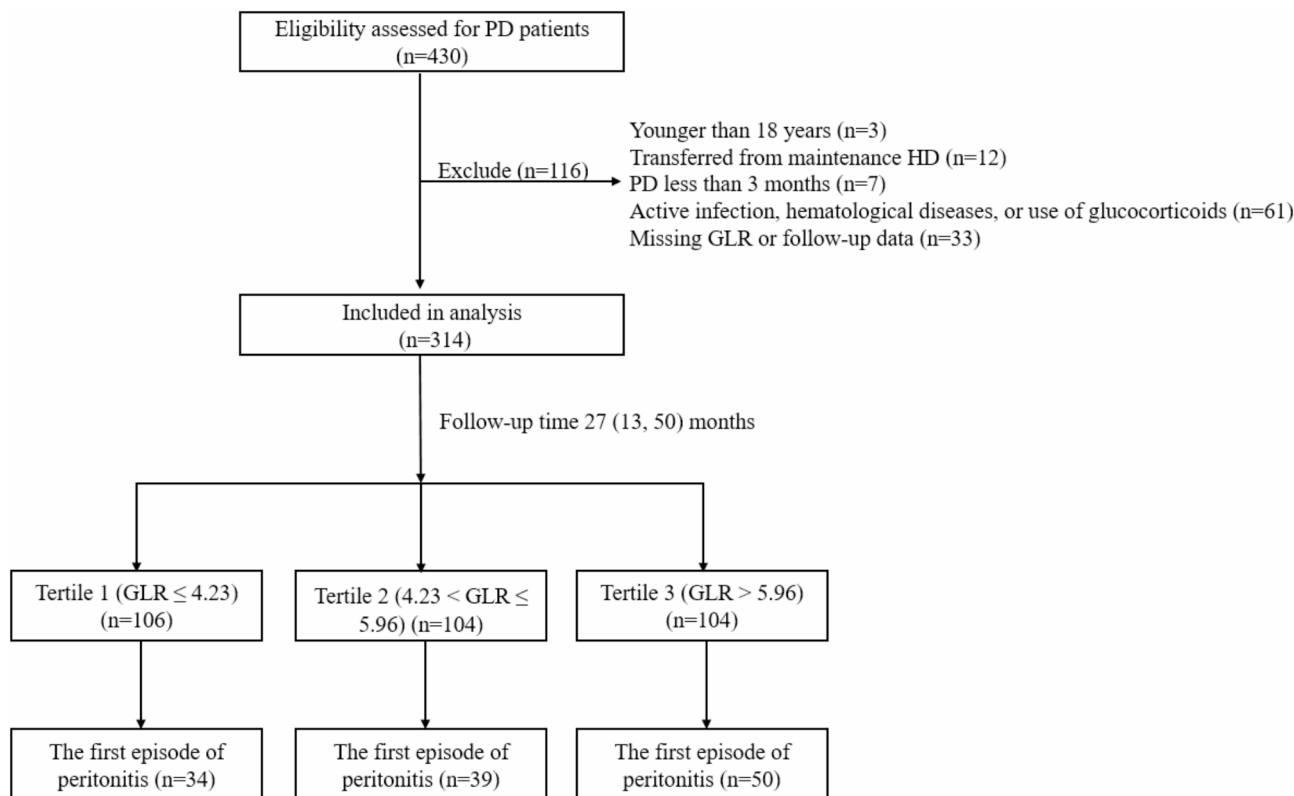


Fig. 1. Flowchart for patient selection. PD: peritoneal dialysis; HD: hemodialysis; GLR: glucose to lymphocyte ratio.

	Total (n=314)	Tertile 1 (n=106)	Tertile 2 (n=104)	Tertile 3 (n=104)	P value
Demographics					
Age (year)	52 (42, 61)	51 (37, 59)	50 (41, 60)	56 (45, 63)	0.027
Male n (%)	145 (46.18)	44 (41.51)	53 (50.96)	48 (46.15)	0.389
Body mass index (kg/m ²)	21.72 (19.72, 23.95)	21.69 (19.22, 24.17)	22.58 (20.08, 24.04)	21.31 (19.13, 23.65)	0.101
Causes of end-stage kidney disease					
Chronic glomerulonephritis n (%)	190 (60.51)	62 (58.49)	66 (63.46)	62 (59.62)	
Diabetic nephropathy n (%)	51 (16.24)	20 (18.87)	12 (11.54)	19 (18.27)	
Hypertensive nephropathy n (%)	41 (13.06)	13 (12.26)	15 (14.42)	13 (12.50)	
Others n (%)	32 (10.19)	11 (10.38)	11 (10.58)	10 (9.62)	
Comorbidities					
Cardiovascular disease n (%)	46 (14.65)	18 (16.98)	13 (12.50)	15 (14.42)	0.654
Diabetes n (%)	59 (18.79)	22 (20.75)	15 (14.42)	22 (21.15)	0.377
Use of antidiabetic drugs n (%)	51 (16.24)	18 (16.98)	13 (12.50)	20 (19.23)	0.407
Laboratory variables					
Hemoglobin (g/L)	76 (63, 90)	79 (66, 96)	78 (65, 91)	68 (56, 84)	<0.001
White blood count (10 ⁹ /L)	5.45 (4.47, 7.01)	5.68 (4.83, 7.19)	5.28 (4.37, 7.02)	5.47 (4.13, 6.91)	0.103
Leukocyte count (10 ⁹ /L)	0.98 (0.75, 1.22)	1.34 (1.18, 1.63)	0.95 (0.85, 1.07)	0.65 (0.52, 0.77)	<0.001
Platelet count (10 ⁹ /L)	142 (103, 180)	156 (123, 194)	132 (99, 162)	129 (92, 170)	0.001
High-sensitivity C-reactive protein (mg/L)	1.60 (0.79, 5.20)	1.50 (0.50, 4.09)	1.40 (0.80, 3.70)	2.90 (1.00, 12.65)	0.091
Serum creatinine (μmol/L)	804.0 (666.3, 1018.3)	760.5 (637.3, 901.3)	851.5 (714.5, 1088.3)	839.0 (656.3, 1076.8)	0.009
Serum urea nitrogen (mmol/L)	29.93 (23.14, 39.55)	26.02 (19.49, 34.66)	31.62 (24.02, 38.30)	36.15 (24.44, 43.84)	<0.001
Serum uric acid (μmol/L)	495.0 (408.8, 596.5)	465.5 (403.5, 569.5)	510.0 (421.3, 632.3)	501.5 (415.8, 591.0)	0.196
Serum corrected calcium (mmol/L)	2.09 (1.84, 2.24)	2.17 (1.95, 2.29)	2.02 (1.82, 2.19)	2.04 (1.73, 2.22)	<0.001
Serum phosphorus (mmol/L)	1.92 (1.56, 2.30)	1.85 (1.51, 2.19)	1.90 (1.62, 2.30)	2.00 (1.57, 2.44)	0.249
Serum albumin (g/L)	33.44 ± 5.62	32.75 ± 6.57	34.56 ± 4.60	33.01 ± 5.38	0.041
Fasting blood glucose (mmol/L)	4.80 (4.37, 5.40)	4.50 (4.11, 4.80)	4.85 (4.46, 5.31)	5.20 (4.73, 6.12)	<0.001
GLR	5.08 (3.79, 6.83)	3.27 (2.90, 3.80)	5.11 (4.60, 5.40)	8.23 (6.84, 10.19)	<0.001
Intact parathyroid hormone (pg/mL)	335 (179, 479)	267 (142, 444)	368 (217, 529)	351 (203, 495)	0.018
Dialysis-related data					
Daily ultrafiltration (mL)	337.52 ± 447.43	293.33 ± 429.67	364.60 ± 510.67	355.75 ± 397.95	0.520
24-hour urine volume (mL)	900 (500, 1300)	825 (500, 1300)	1100 (600, 1500)	800 (500, 1200)	0.045
Total weekly Kt/V	2.11 (1.76, 2.51)	2.13 (1.80, 2.61)	2.00 (1.73, 2.41)	2.18 (1.82, 2.52)	0.543
Glucose exposure (g)	115 (90, 120)	90 (90, 120)	90 (90, 120)	120 (90, 120)	0.125
Peritonitis					
Peritonitis episode n (%)	123 (39.17)	34 (32.08)	39 (37.50)	50 (48.08)	0.054
Follow-up time (months)	27 (13, 50)	35 (15, 55)	27 (15, 52)	24 (10, 41)	0.076

Table 1. Baseline demographic and clinical characteristics of the study population stratified by GLR tertile. GLR: glucose to lymphocyte ratio.

	Total (n=123)	Tertile 1 (n=34)	Tertile 2 (n=39)	Tertile 3 (n=50)	P value
Dialysis effluent WBC count on day 1, cells/mm ³	1483 (545, 3946)	996 (298, 1855)	2090 (974, 4453)	2140 (733, 4636)	0.049
Causative organism					
Culture-negative n (%)	30 (24.39)	9 (26.47)	5 (12.82)	16 (32.00)	
Gram-negative n (%)	28 (22.76)	3 (8.82)	15 (38.46)	10 (20.00)	
Gram-positive n (%)	59 (47.97)	19 (55.88)	18 (46.15)	22 (44.00)	
Fungus n (%)	5 (4.07)	2 (5.88)	1 (2.56)	2 (4.00)	
Polymicrobial n (%)	1 (0.81)	1 (2.94)	0 (0.00)	0 (0.00)	
Peritonitis outcomes					
Complete cure n (%)	109 (88.62)	30 (88.24)	35 (89.74)	44 (88.00)	
Transfer to hemodialysis n (%)	10 (8.13)	3 (8.82)	2 (5.13)	5 (10.00)	
Death n (%)	4 (3.25)	1 (2.94)	2 (5.13)	1 (2.00)	

Table 2. Causative organism and outcomes of 123 episodes of peritonitis stratified by GLR tertile. GLR: glucose to lymphocyte ratio; WBC: white blood cell.

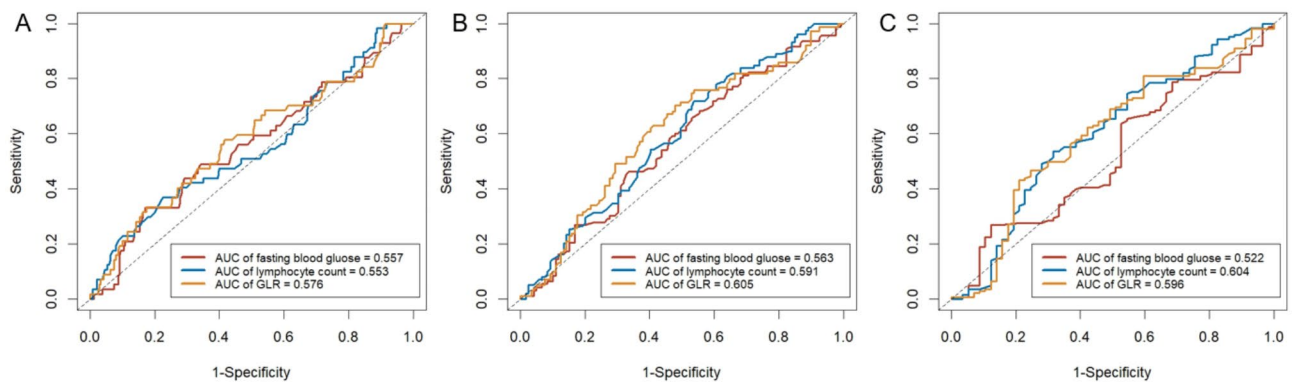


Fig. 2. Receiver operating characteristic curves of fasting blood glucose, lymphocyte count, and GLR for the first peritonitis episode at 1 year (A), 3 years (B), and 5 years (C). AUC: area under the curve; GLR: glucose to lymphocyte ratio.

tertile 3 was significantly higher than in tertile 1. In the unadjusted Cox proportional hazards model, patients in tertile 3, as compared with those in tertile 1, were associated with a higher cumulative risk of the first episode of peritonitis (HR: 1.824, 95% CI: 1.178–2.824, $P=0.007$). After full adjustment for confounding factors, patients in tertile 3 remained at significantly higher risk for the first episode of peritonitis compared to those in tertile 1 (HR: 2.633, 95% CI: 1.223–5.668, $P=0.013$) (Table 3).

Competitive risk analysis

The Fine-Gray competing risk model demonstrated that the cumulative incidence of the first episode of peritonitis was higher in tertile 3 compared to tertile 1 and 2 (Fig. 4). The cumulative incidence of peritonitis increased progressively across tertiles, with tertile 3 showing the highest risk. Gray's test revealed a statistically significant difference among the three groups ($P=0.021$). In the multivariate Fine-Gray analysis, the subdistribution hazard ratio (SHR) across adjusted models consistently showed that patients in tertile 3 were independently associated with a higher risk of developing the first episode of peritonitis compared to those in tertile 1 (Table 3). These findings are consistent with the results observed in the multivariate Cox regression analysis.

Subgroup and sensitivity analyses

The potential association between GLR and the first episode of peritonitis was further evaluated through subgroup analyses stratified by sex, age, DM, and history of CVD. The forest plot revealed no significant interaction effects between GLR and these subgroup variables (Fig. 5).

After performing sensitivity analysis using multiple imputation methods to address missing data, the results of the multivariate Cox regression analysis remained consistent. A statistically significant difference in the incidence of the first peritonitis episode was observed between tertile 3 and tertile 1 (HR: 1.811, 95% CI: 1.117–2.939, $P=0.016$).

Discussion

In this study, we observed a consistent increase in the cumulative incidence of peritonitis across GLR tertiles, with tertile 3 showing the highest risk. Elevated GLR in tertile 3, as compared to tertile 1, was independently associated with an increased risk of the first peritonitis episode in patients treated with PD. This association remained significant even after fully adjusting for potential confounding factors. The robustness of this finding was further confirmed by the competitive risk analysis, subgroup and sensitivity analyses.

GLR is calculated based on fasting blood glucose and lymphocyte count, which reflect glucose metabolism and systemic immune status¹¹, and is a novel biomarker associated with chronic inflammation⁸. Previous research has primarily focused on its association with the prognosis of various diseases. Several studies have indicated that GLR serves as a predictive factor for the prognosis of patients with malignant tumors, including hepatocellular carcinoma¹², breast cancer¹³, metastatic gastric cancer¹⁴, colorectal cancer¹⁵, renal cell carcinoma¹⁶, and pancreatic cancer¹¹. Additionally, GLR has been identified as a clinical biomarker for in-hospital mortality in intensive care unit (ICU) patients with acute myocardial infarction⁷, acute respiratory distress syndrome¹⁷, sepsis¹⁸, and acute exacerbation chronic obstructive pulmonary disease¹⁹. Li et al. found that GLR was an independent predictor for the development of acute kidney injury after cardiac surgery in ICU patients⁶. Furthermore, a recent cohort study conducted among PD patients in China indicated that GLR was an independent prognostic factor for all-cause and CVD mortality⁸.

Our research indicated that GLR was associated with the first peritonitis episode in patients treated with PD. The underlying mechanisms between them remain unclear. We speculate that it may be related to chronic inflammation, glucose metabolism disorder, and impaired immune function. Inflammation is common in patients treated with PD, and its reasons are multifactorial, interacting synergistically. These include the accumulation of uremic toxins, elevated endotoxin levels, decreased clearance of proinflammatory cytokines, oxidative stress, the presence of the PD catheter as a foreign body, and continuous exposure of the peritoneum to biologically incompatible glucose-based dialysis solution, among others^{3,20}. GLR is a biomarker of chronic

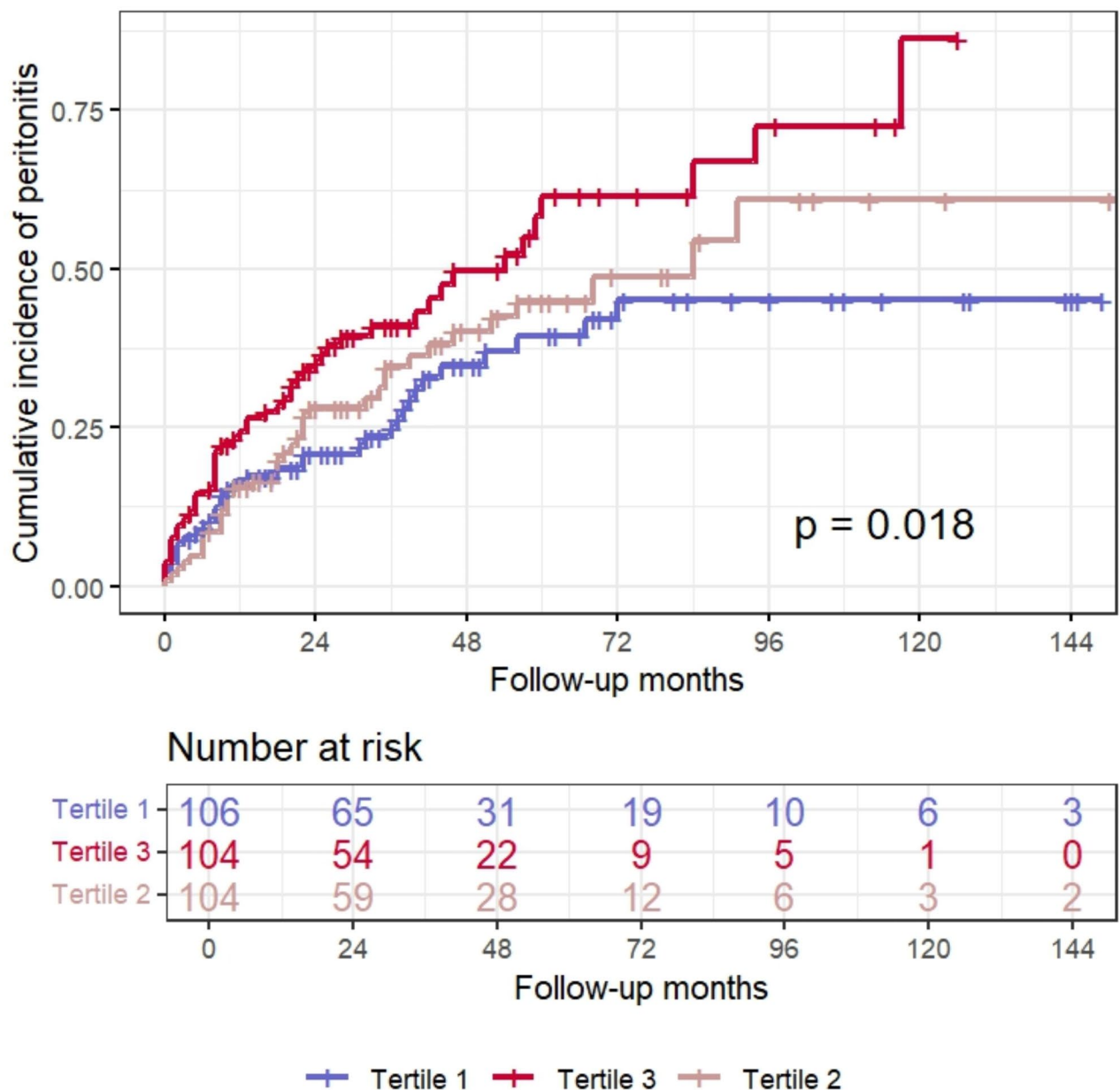


Fig. 3. Kaplan-Meier curves for GLR tertiles illustrating the cumulative incidence of the first peritonitis episode. GLR: glucose to lymphocyte ratio.

inflammation. In this study, patients in GLR tertile 3 had higher levels of hs-CRP compared to those in tertile 1, and elevated hs-CRP levels have been shown to predict the risk of peritonitis in patients treated with PD²¹.

Elevated GLR indicates an increase in glucose levels and/or a decrease in lymphocyte counts. Patients with CKD often experience disorders in glucose and insulin homeostasis, which may be further aggravated in patients treated with PD through exposure to glucose from dialysis solution⁴. A meta-analysis revealed an elevated risk of glucose metabolism disorders among patients treated with PD in China²². Elevated fasting blood glucose levels were associated with an increased risk of all-cause mortality in PD patients with diabetes²³. A study involving 3075 older black and white participants showed that dysglycemia was related to inflammation, and this relationship was consistent in both diabetic individuals and those with impaired fasting glucose and impaired glucose tolerance²⁴. Hyperglycemia can maintain a chronic inflammation status by upregulating the expression of proinflammatory cytokines and synergizing with hypoxia²⁵, while chronic inflammation is a risk factor for peritonitis episodes. Moreover, patients treated with PD generally use glucose-based dialysis solutions. The high glucose environment brought about by the glucose-based dialysis solution can induce microenvironmental hypoxia, drive increased levels of proinflammatory cytokine in the abdominal cavity, activate chronic inflammatory and oxidative stress, result in changes in the structure and function of the peritoneum, impair host defenses, and ultimately increase susceptibility to peritonitis^{26,27}. Additionally, high glucose exposure can also cause intestinal barrier dysfunction by altering its morphological, structural, and functional properties, increasing intestinal wall permeability, and

	Cox regression model			Fine-Gray competing risk model	
	HR (95% CI)	P-value	Concordance index	SHR (95% CI)	P-value
Unadjusted			0.563		
Tertile 1	Reference			Reference	
Tertile 2	1.240 (0.782–1.965)	0.361		1.220 (0.774–1.920)	0.390
Tertile 3	1.824 (1.178–2.824)	0.007		1.780 (1.151–2.740)	0.009
Model 1			0.588		
Tertile 1	Reference			Reference	
Tertile 2	1.243 (0.783–1.972)	0.357		1.252 (0.797–1.970)	0.330
Tertile 3	1.727 (1.111–2.684)	0.015		1.671 (1.080–2.590)	0.021
Model 2			0.599		
Tertile 1	Reference			Reference	
Tertile 2	1.221 (0.769–1.941)	0.397		1.230 (0.782–1.934)	0.370
Tertile 3	1.738 (1.116–2.708)	0.015		1.680 (1.082–2.610)	0.021
Model 3			0.656		
Tertile 1	Reference			Reference	
Tertile 2	1.475 (0.770–2.822)	0.241		1.607 (0.850–3.041)	0.140
Tertile 3	2.152 (1.139–4.066)	0.018		2.287 (1.215–4.305)	0.010
Model 4			0.712		
Tertile 1	Reference			Reference	
Tertile 2	1.891 (0.864–4.140)	0.111		1.976 (0.907–4.305)	0.087
Tertile 3	2.633 (1.223–5.668)	0.013		2.765 (1.205–6.345)	0.016

Table 3. Associations of GLR with the first episode of peritonitis. Model 1: age, sex, and body mass index. Model 2: Model 1 covariates plus diabetes mellitus and history of cardiovascular disease. Model 3: Model 2 covariates plus hemoglobin, platelet count, serum creatinine, serum uric acid, serum corrected calcium, serum phosphorus, serum albumin, intact parathyroid hormone, and high-sensitivity C-reactive protein. Model 4: Model 3 covariates plus daily ultrafiltration, 24-hour urine volume, total weekly Kt/V, and glucose exposure. HR: hazard ratio; SHR: subdistribution hazard ratio; CI: confidence interval; GLR: glucose to lymphocyte ratio.

making it easier for bacteria to invade the abdominal cavity, which may be a partial reason for the increased risk of peritonitis episode²⁸.

Lymphocytes serve as integral constituents of the human immune system and can reflect the systemic immune status. Previous studies have indicated that a decreased lymphocyte count could be used to predict poor treatment response in peritonitis²⁹ and was a predictive factor for mortality and technique failure in patients treated with PD³⁰. Patients with CKD commonly exhibit impaired immune function³¹. This impairment can be attributed to reasons such as impaired kidney function, the accumulation of uremic toxins³², elevated fibroblast growth factor 23, which suppresses vitamin D and proinflammatory responses³³, and more. For CKD patients undergoing PD, prolonged exposure of the peritoneum to dialysis solution containing supraphysiologic concentrations of glucose can exacerbate inflammation³⁴ and impair immune defense in the peritoneal cavity⁵. Decreased lymphocyte counts indicate abnormal immune function³⁵, making patients more susceptible to bacterial infections and unable to clear bacteria in a timely and effective manner, leading to an increased risk of peritonitis. Additionally, Hu et al. pointed out that T lymphocyte cells could improve intestinal barrier dysfunction in heatstroke, implying that decreased lymphocyte counts may exacerbate intestinal barrier dysfunction and increase the incidence of peritonitis³⁶.

The culture-negative peritonitis rate in this study was 24.39%, exceeding the 15% recommended by the ISPD peritonitis guideline¹⁰. This disparity may be attributed to differences in the definition and technique of microbiological isolation. Additionally, some patients had already received antibiotic therapy before dialysis effluent specimens were collected.

Dai et al. confirmed that DM was an independent predictor for peritonitis episodes⁹. However, in our study, we did not observe a similar association between DM and peritonitis episodes, which may be due to regional and demographic differences. Moreover, no statistically significant difference in the proportion of DM was observed in this study, and subgroup analyses indicated no interaction between DM and GLR. GLR was identified as a risk factor for peritonitis episodes in the non-diabetes group, but this relationship was not observed in the diabetes group. Nevertheless, the sample size of our study was relatively small, and caution is required in interpreting the results of subgroup analysis.

To the best of our knowledge, this study is the first to explore the potential relationship between GLR and the first peritonitis episode in patients treated with PD. As a cost-effective and readily available biomarker, GLR simultaneously reflects both glucose metabolism and systemic immune status, offering a more comprehensive predictive marker for the risk of the first peritonitis episode in patients treated with PD. This may contribute to developing personalized medical decision-making and improving patient prognosis. Moreover, since patients treated with PD are prone to disorders in glucose metabolism and immune function, GLR holds greater

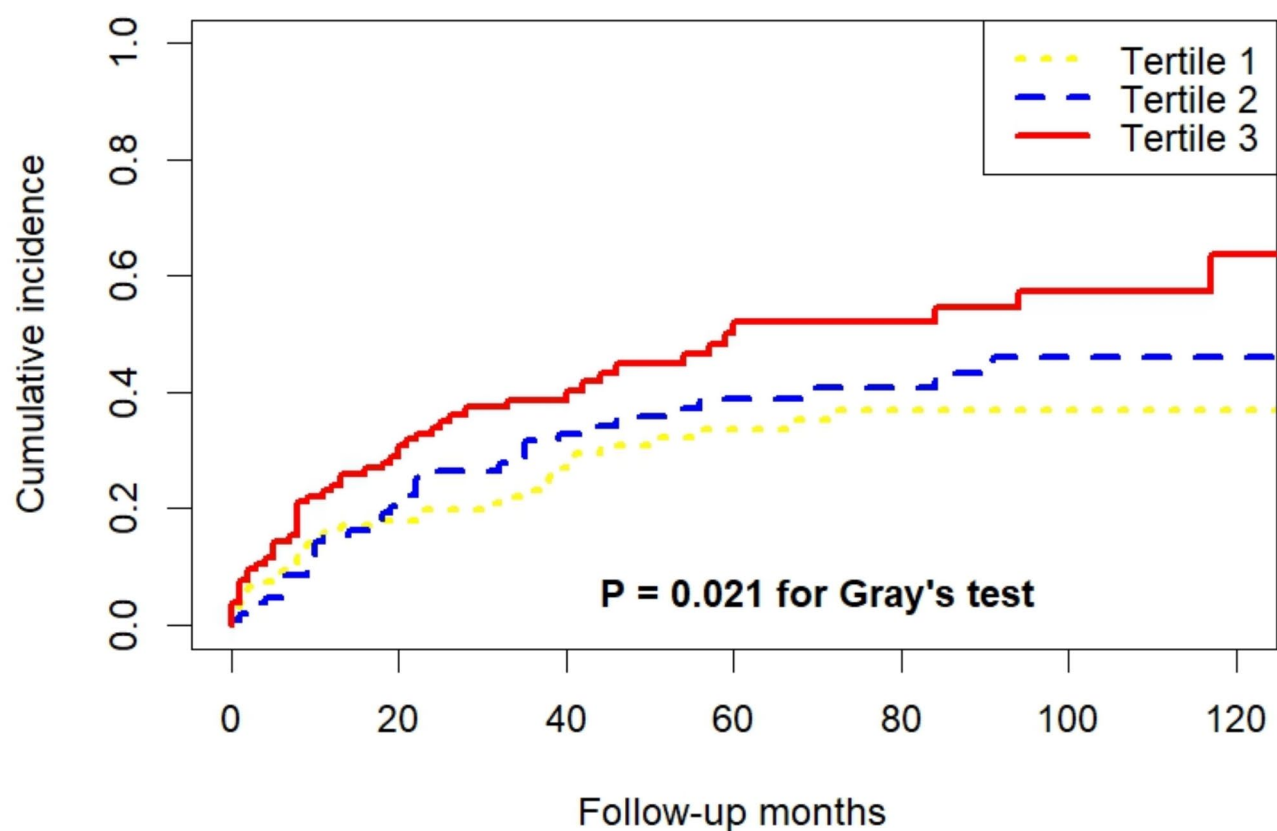


Fig. 4. Cumulative incidence of the first peritonitis episode considering competing risks using the Fine-Gray model. GLR: glucose to lymphocyte ratio.

clinical significance in this special population. However, several limitations must be acknowledged. First, as a retrospective study, it can only establish an association between GLR and the first peritonitis episode in patients treated with PD, without clarifying any causal relationship. Second, the AUC for GLR in predicting the first peritonitis episode was relatively low, and the small sample size limits the generalizability of our findings, which requires further validation in larger, multi-center cohorts. Third, we only considered baseline GLR levels and did not account for potential changes in GLR over the follow-up period. Fourth, due to significant collinearity between DM and the use of antidiabetic drugs, the latter was not included in the multivariate Cox regression models to avoid model instability. Finally, we cannot eliminate all potential confounding factors that may affect the peritonitis episode, such as living environment, education levels, and economic conditions.

Conclusion

In conclusion, our study suggests that elevated GLR is associated with an increased risk of the first peritonitis episode in patients with PD. Further large-scale prospective studies and exploration of underlying mechanisms are needed to confirm this association.

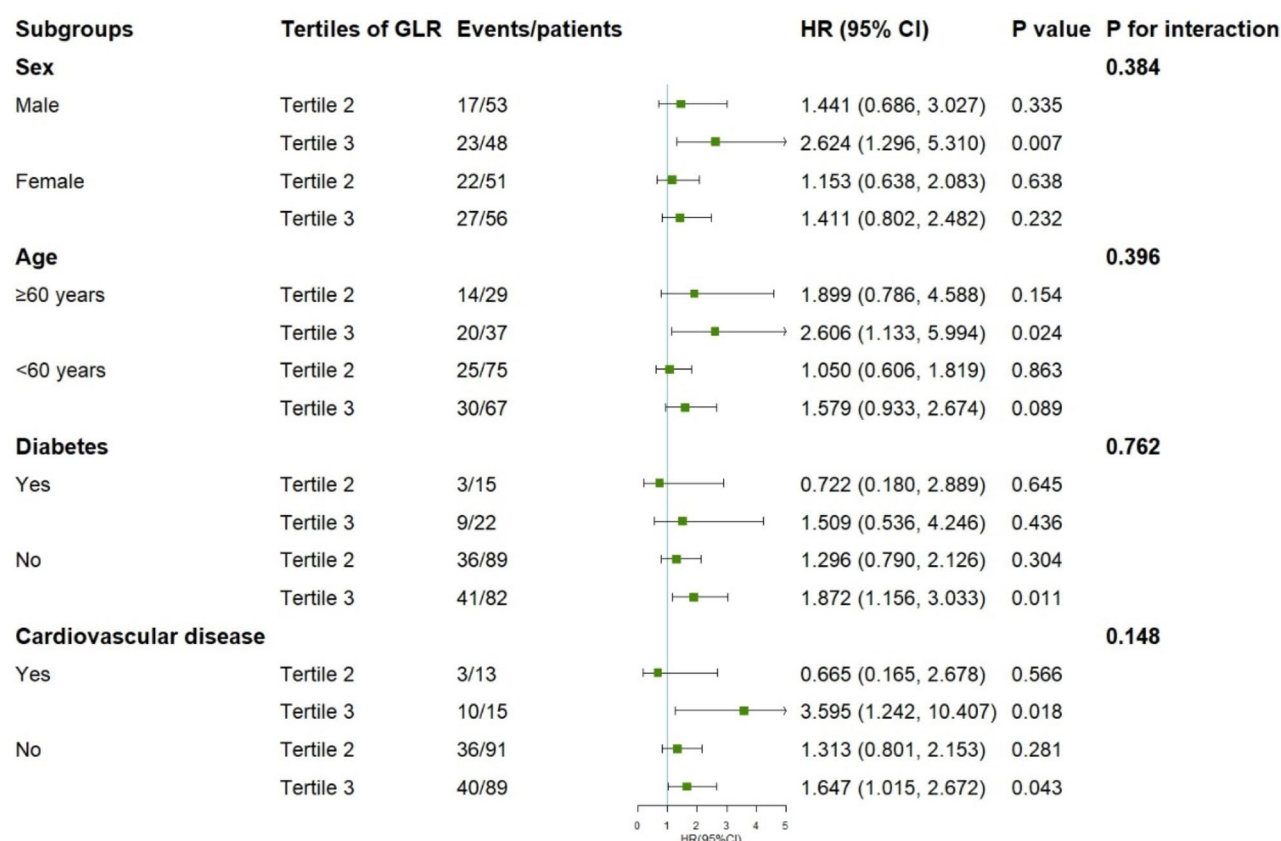


Fig. 5. Forest plot of relationship between GLR and the first peritonitis episode in different subgroups. Tertile 1 of GLR was taken as the reference group. HR: hazard ratio; CI: confidence interval; GLR: glucose to lymphocyte ratio.

Data availability

The data used during this study are available from the corresponding author on reasonable request.

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Author contributions

Q.Y. designed study, performed analysis, and drafted the manuscript. D.W. designed and directed the study. G.L., R.W., D.L., X.C. and J.C. collected data. All authors reviewed the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Ethnic approval

This study was approved by the ethics committee of the Second Affiliated Hospital of Anhui Medical University (authorization number: KY201302).

Additional information

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