## RESEARCH



# The advanced lung cancer inflammation index is associated with mortality in peritoneal dialysis patients

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## Abstract

**Background** There is still a very high morbidity and mortality rate for patients undergoing peritoneal dialysis (PD). The advanced lung cancer inflammation index (ALI) has been demonstrated to be associated with the prognosis in multiple types of cancers. Like in cancer, systemic chronic low-grade inflammation is one of the distinguishing features of PD patients. Therefore, we aimed to investigate the relationships between the ALI and all-cause and cardiovascular disease (CVD) mortality in PD patients.

**Methods** Patients who started PD at Shaoxing People's Hospital between 1 January 2013 and 31 December 2020 (n = 277) were recruited and followed up until 1 July 2023. They were divided into high-ALI group and low-ALI group according to the median of ALI. Kaplan–Meier curves and multivariate Cox regression analyses were used to assess the associations between the ALI and all-cause and CVD mortality. Receiver operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) was calculated to determine the predictive power of the ALI for all-cause and CVD mortality.

**Results** During the median follow-up of 40.50 months (interquartile range, 26.42–59.77 months), a total of 55 patients died, 31 of whom died due to CVD. Kaplan–Meier curves revealed that patients in the low-ALI group had significantly lower cumulative and cardiovascular cumulative survival rates than did those in the high-ALI group (all P < 0.001). After we corrected for confounders, the risk of all-cause and CVD mortality was significantly greater in the low-ALI group [hazard ratio (HR) 1.944, 95% confidence interval (CI) 1.068–3.540, P = 0.030, and HR 2.672, 95% CI 1.188–6.009, P = 0.017, respectively]. The predictive value of ALI (AUC = 0.708, 95% CI 0.630–0.786, P < 0.001) for all-cause mortality was superior to albumin (AUC = 0.644, 95% CI 0.556–0.726, P < 0.001), body mass index (AUC = 0.581, 95% CI 0.496–0.659, P = 0.069) and neutrophil-to-lymphocyte ratio (AUC = 0.675, 95% CI 0.596–0.754, P < 0.001).

**Conclusion** A lower ALI is an independent risk factor for all-cause and cardiovascular mortality in PD patients. The ALI may be an effective indicator for predicting outcomes in PD patients.

**Keywords** Advanced lung cancer inflammation index, Peritoneal dialysis, All-cause mortality, Cardiovascular mortality

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## Background

Peritoneal dialysis (PD) is an effective treatment for patients with end-stage renal disease. Although studies have reported that PD improves the survival and quality of life of patients, the mortality of PD patients remains high. More than half of the deaths of PD patients are related to cardiovascular disease (CVD) [1]. Chronic systemic inflammation is common in PD patients, and approximately 12-65% of PD patients worldwide experience inflammation [2]. There is mounting evidence that chronic inflammation is one of the major risk factors for poor prognosis in PD patients. Chronic inflammation leads to protein-energy wasting (PEW) and is associated with poor cardiovascular outcomes [3-5]. Investigating any treatable cause of inflammation in PD patients with persistently elevated C-reactive protein levels and continuously monitoring nutritional status to identify PD patients with PEW has become one of the key measures for reducing cardiovascular risk [6].

The advanced lung cancer inflammation index (ALI), which is based on albumin (ALB), body mass index (BMI), and the neutrophil-to-lymphocyte ratio (NLR), was first developed by Jafri et al. and has been proven to be a novel inflammatory parameter for predicting the prognosis of patients with metastatic non-small cell lung cancer [7]. It has also been associated with outcomes in chronic inflammatory diseases such as other tumours, heart failure and hypertension [8–11]. However, to our knowledge, no study has evaluated the prognostic value of the ALI in PD patients. In this retrospective study, we aimed to evaluate the associations of the ALI with all-cause and cardiovascular mortality in PD patients.

## Methods

## Study design and participant selection

This study included patients who started PD treatment between 1 January 2013 and 31 December 2020 at Shaoxing People's Hospital. The inclusion criteria were PD patients who have catheters placed at our hospital, underwent regular follow-ups for more than 3 months, and were over 18 years old. The exclusion criteria were as follows: (1) had a malignant tumour, acute infection (pneumonia, bronchiolitis, urinary tract infection, etc.), chronic infection (tuberculosis, active hepatitis, etc.), or other severe underlying disease (chronic obstructive pulmonary disease, cirrhosis, etc.); (2) had a history of previous haemodialysis (HD) or kidney transplantation; (3) were aged <18 years or >80 years; (4) underwent PD for less than 3 months; and (5) lacked baseline data. The enrolled patients received 1.5% or 2.5% lactate-buffered glucose-based PD solutions (Dianeal®, Baxter, China). The dialysis modality was continuous ambulatory peritoneal dialysis (CAPD) with 2-4 exchanges per with 1.5-2 L of dwell volume. During dialysis, the dialysis regimen would be promptly adjusted based on ultrafiltration, blood pressure, edema, and other factors to ensure that patients receive adequate dialysis. Finally, 277 patients were enrolled in this study (Fig. 1). The baseline characteristics were collected in the first 1–3 months after starting PD. This study was conducted in accordance with the ethical standards of the Helsinki Declaration and was approved by the Human Ethics Committees of Shaoxing People's Hospital (2022-K-Y-128-01). All patients signed informed consent forms before study enrolment.

## Data collection

Baseline demographic data, including sex, age, history of diabetes mellitus, CVD, smoking status, and alcohol consumption, were collected. Clinical and biochemical data included BMI, blood pressure, medication use, white blood cell (WBC) count, neutrophil count, lymphocyte count, haemoglobin (Hb) count, platelet count, high sensitivity C-reactive protein (hs-CRP), ALB, serum creatinine (Scr), serum uric acid (SUA), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Indicators of dialysis adequacy were as follows: total urea clearance index (Kt/V), creatinine clearance rate (CCR), and 4-h dialysate-to-plasma ratio of creatinine (4-h D/Pcr). The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.

## Calculation of the ALI

ALI was calculated as the product of BMI  $(kg/m^2)$  and ALB (g/L) divided by the NLR. NLR was calculated as neutrophil counts divided by lymphocyte counts and BMI was calculated as weight (kg) divided by the square of height (m).

## Follow-up and endpoint definitions

All patients were followed up until death, conversion to HD or kidney transplantation, or 1 July 2023. The primary outcome was all-cause mortality. The secondary outcome was cardiovascular mortality, which was defined as death caused by heart failure, acute myocardial infarction, cardiac arrhythmia, coronary arteriosclerotic heart disease, cardiomyopathy, congenital cardiovascular diseases, valvular heart disease, cardiac arrest, ischaemic stroke, or peripheral vascular disease.

## Statistical analyses

Eligible patients were divided into two groups according to the median values of ALI: a low-ALI group (ALI<293.07) and high-ALI group (ALI $\geq$ 293.07). Continuous variables are presented as the mean $\pm$ standard deviation (mean $\pm$ SD) or median (interquartile range), and an independent-samples t test or Mann–Whitney



Fig. 1 Flow chart of patient enrolment and exclusion in this study

U test was used to determine the differences between two groups. Categorical variables are presented as percentages and frequencies, and the x2 test was used to determine the differences between two groups. Kaplan-Meier curves and log-rank tests were used to estimate differences in cumulative survival rates between the two groups. Multivariate Cox regression analyses were performed to evaluate the association between the ALI and mortality. For each outcome of interest, we fitted a series of hierarchically adjusted models: Model 1 was only adjusted for age; Model 2 included Model 1 and further adjusted for demographic data (sex, diabetes mellitus status, CVD status, smoking status, alcohol consumption status, systolic blood pressure, diastolic blood pressure and BMI); Model 3 included Model 2 and further adjusted for medications (angiotensin-converting enzyme inhibitors [ACEIs], angiotensin receptor blockers [ARBs],  $\beta$ -blockers and calcium channel blockers); Model 4 included Model 3 and further adjusted for laboratory markers (Hb, ALB, hs-CRP, SUA, fasting blood glucose, TC, TG, HDL-C, and LDL-C) and 4-h D/Pcr. The dose–response relationship between the ALI and mortality was assessed by restricted cubic splines (RCSs). We used 4 knots located at the 25th, 50th, 75th, and 95th percentiles of the ALI. Receiver operating characteristic (ROC) curve analysis was performed, and the area under the curve (AUC) was calculated to determine the predictive power of the ALI for all- cause and CVD mortality. The statistical analysis was completed with SPSS 26.0 (SPSS, Chicago, IL, USA) and R software (version R-4.3.1, www.project.org). All tests were two-tailed, and P<0.05 was considered to indicate statistical significance.

## Results

## **Baseline characteristics**

A total of 277 PD patients, 147 males (53.1%) and 130 females (46.9%), participated in this study (Table 1). The mean age was  $55.5\pm13.2$  years. The between-group differences in age, diabetes mellitus status, CVD status, BMI, Hb, ALB, hs-CRP, NLR, TG, prealbumin and 4-h D/ Pcr were statistically significant (all P<0.05). The other indicators were not significantly different (all P>0.05).

Table 1 Comparison of baseline data between two groups of patients grouped according to the median ALI

Variables	All	Low ALI	High ALI	P value
	(n=277)	( <i>n</i> = 138)	(n=139)	
Age (year)	55.52±13.20	$58.60 \pm 12.40$	52.47±13.31	< 0.001
Male (n, %)	147 (53.1%)	78 (56.5%)	69 (49.6%)	0.251
Diabetes mellitus (n, %)	83 (30.0%)	50 (36.2%)	33 (23.7%)	0.023
CVD (n, %)	79 (28.5%)	47 (34.1%)	32 (23.0%)	0.042
Smoking (n, %)	68 (24.5%)	32 (23.2%)	36 (25.9%)	0.600
Excessive alcohol consumption (n, %)	39 (14.1%)	19 (13.8%)	20 (14.4%)	0.882
RASIs (n, %)	50 (18.1%)	30 (21.7%)	20 (14.4%)	0.112
CCBs (n, %)	166 (59.9%)	85 (61.6%)	81 (58.3%)	0.573
β-blockers (n, %)	52 (18.8%)	29 (21.0%)	23 (16.5%)	0.341
Body mass index (kg/m <sup>2</sup> )	23.51 ± 3.63	$22.40 \pm 3.26$	24.62 ± 3.65	< 0.001
Systolic blood pressure (mmHg)	134.88±13.58	$135.20 \pm 14.32$	134.57±12.84	0.701
Diastolic blood pressure (mmHg)	81.08±8.88	$80.60 \pm 9.14$	81.56±8.63	0.369
White blood cell count (×10 <sup>9</sup> g/L)	5.86 (4.94, 6.87)	5.79 (4.92, 7.01)	5.87 (4.99, 6.83)	0.851
Haemoglobin (g/L)	102.41±13.63	$100.57 \pm 13.40$	104.22±13.66	0.026
Platelet (×10 <sup>9</sup> g/L)	$202.97 \pm 58.43$	199.31±64.35	$206.61 \pm 51.87$	0.300
Albumin (g/L)	31.47 ± 4.62	$29.23 \pm 4.08$	33.69±4.03	< 0.001
Hs-CRP (mg/L)	2.09 (0.66, 5.99)	3.08 (1.03, 9.12)	1.48 (0.56, 4.02)	< 0.001
NLR	2.63 (2.07, 3.23)	3.19 (2.69, 3.88)	2.12 (1.77, 2.56)	< 0.001
Blood urea nitrogen (mmol/L)	17.95±5.24	17.82±5.40	18.08±5.09	0.680
Serum creatinine (µmol/L)	504.48 (398.50, 652.48)	493.09 (393.50, 653.01)	512.27 (401.70, 655.40)	0.757
Serum uric acid (µmol/L)	393.62±88.33	386.44±86.11	$400.74 \pm 90.22$	0.178
Total cholesterol (mmol/L)	4.85 (3.98, 5.89)	4.86 (4.16, 5.91)	4.82 (3.88, 5.88)	0.374
Triglyceride (mmol/L)	1.50 (1.07, 2.17)	1.39 (1.01, 1.96)	1.61 (1.16, 2.34)	0.021
HDL-C (mmol/L)	1.12 (0.93, 1.40)	1.13 (0.95, 1.40)	1.11 (0.88, 1.37)	0.400
LDL-C (mmol/L)	3.05 (2.40, 3.88)	3.14 (2.42, 3.86)	2.96 (2.37, 3.91)	0.306
Prealbumin (mg/L)	$326.75 \pm 80.05$	$306.68 \pm 85.40$	346.67±69.08	< 0.001
Fasting blood glucose (mmol/L)	4.83 (4.48, 5.49)	4.82 (4.47, 5.87)	4.83 (4.49, 5.34)	0.644
Kt/V (per week)	2.43 (2.10, 2.93)	2.44 (2.04, 2.87)	2.43 (2.11, 2.97)	0.631
CCR (per week)	72.61 (29.52, 100.44)	75.08 (34.75, 102.27)	70.91 (27.73, 97.03)	0.617
4-h D/Pcr	0.69±0.12	0.72±0.12	0.66±0.12	< 0.001

ALI advanced lung cancer inflammation index, CVD cardiovascular disease, RASIs renin-angiotensin system inhibitors, CCBs calcium channel blockers, Hs-CRP high sensitivity C-reactive protein, NLR neutrophil-to-lymphocyte ratio, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, Kt/V total urea clearance index, CCR creatinine clearance rate, 4-h D/Pcr 4-h dialysate-to-plasma ratio of creatinine

The baseline characteristics of all patients are shown in Table 1.

## Relationship between the ALI and mortality

During a median follow-up of 40.5 months, 55 participants died. Of 55 deaths, 31 (56.36%) deaths were due to CVD, 6 (10.91%) deaths due to infection, 9 (16.36%) deaths due to multiple organ failure, 2 (3.63%) deaths due to respiratory failure, and 7 (12.73%) deaths due to other reasons. Kaplan–Meier curves revealed that the cumulative and cardiovascular cumulative survival rates of participants in the low-ALI group decreased significantly (all P < 0.001; Fig. 2). The 1-, 3-, and 5-year estimated cumulative survival rates in the low-ALI group were 95.4%, 77.0% and 67.0%, respectively. The 1-, 3-, and 5-year estimated cumulative survival rates in the high-ALI group were 99.2%, 93.4% and 84.7%, respectively (Fig. 2A). The 1-, 3-, and 5-year estimated cumulative survival rates in the high-ALI group were 99.2%, 93.4% and 84.7%, respectively (Fig. 2A).

survival rates in the low-ALI group were 98.4%, 84.6% and 75.9%, respectively. The 1-, 3-, and 5-year estimated cardiovascular cumulative survival rates in the high-ALI group were 100.0%, 97.1% and 93.4%, respectively (Fig. 2B). After multivariable adjustment in Model 4, patients in the low-ALI group had a 1.944-fold (95% CI 1.068–3.540, P=0.030) greater risk of all-cause mortality and a 2.672-fold (95% CI 1.188-6.009, P=0.017) greater risk of CVD mortality than patients in the high-ALI group did (Table 2). After adjusting for other confounders, we found a linear association between the ALI and the risk of all-cause mortality (P nonlinear=0.1576). The risk of all-cause mortality increased with a decreasing ALI (Fig. 3A). However, there was a nonlinear relationship between the ALI and the risk of CVD mortality (nonlinear *P*=0.0344; Fig. 3B).



## Number at risk

Mouths	0	12	24	36	48	60	72	84	96	108	120	
High ALI	139	126	111	89	58	35	24	13	8	4	0	
Low ALI	138	120	105	75	53	32	11	7	3	1	0	

Fig. 2 Comparison of the event-free survival rates for all-cause mortality (A) and CVD mortality (B) between the low-ALI group and the high-ALI group. ALI advanced lung cancer inflammation index, CVD cardiovascular disease

Tab	le 2	Association o	<sup>-</sup> th	e ALI	with	al	l-cause and	(	CVD	mortal	ity in	PD	patients
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Characteristic	Low ALI		High ALI	
	HR (95% CI)	P value	HR (95% CI)	P value
All-cause mortality				
Unadjusted	2.834 (1.581, 5.078)	< 0.001	1.000 (reference)	/
Model 1 <sup>a</sup>	2.093 (1.153, 3.800)	0.015	1.000 (reference)	/
Model 2 <sup>b</sup>	1.977 (1.092, 3.579)	0.024	1.000 (reference)	/
Model 3 <sup>c</sup>	1.927 (1.060, 3.503)	0.031	1.000 (reference)	/
Model 4 <sup>d</sup>	1.944 (1.068, 3.540)	0.030	1.000 (reference)	/
CVD mortality				
Unadjusted	3.378 (1.508, 7.568)	0.003	1.000 (reference)	/
Model 1 <sup>a</sup>	2.776 (1.217, 6.333)	0.015	1.000 (reference)	/
Model 2 <sup>b</sup>	2.667 (1.182, 6.018)	0.018	1.000 (reference)	/
Model 3 <sup>c</sup>	3.203 (1.400, 7.331)	0.006	1.000 (reference)	/
Model 4 <sup>d</sup>	2.672 (1.188, 6.009)	0.017	1.000 (reference)	/
and the second s				

Model 1 was only adjusted for age

<sup>b</sup>Model 2 was further adjusted for sex, diabetes mellitus status, CVD status, smoking status, alcohol consumption status, systolic blood pressure, diastolic blood pressure and BMI

<sup>c</sup>Model 3 was further adjusted for medications (ACEIs or ARBs,  $\beta$ -blockers and calcium channel blockers)

<sup>d</sup>Model 4 was further adjusted for laboratory markers (Hb, ALB, hs-CRP, SUA, fasting blood glucose, TC, TG, HDL-C, and LDL-C) and 4-h D/Pcr (low transport: <0.50; low-average transport: 0.50–0.64; high-average transport: 0.65–0.81; high transport: >0.81)

ALI advanced lung cancer inflammation index, CVD cardiovascular disease, PD peritoneal dialysis, CI confidence interval, HR hazard ratio; BMI body mass index; ACEIs angiotensin-converting enzyme inhibitors; ARBs angiotensin receptor blockers; Hb hemoglobin; ALB albumin; hs-CRP high sensitivity C-reactive protein; SUA serum uric acid; TC total cholesterol; TG triglyceride; HDL-C high-density lipoprotein cholesterol; LDL-C low-density lipoprotein cholesterol; 4-h D/Pcr 4-h dialysate-to-plasma ratio of creatinine

## Prognostic value of the ALI for all-cause and CVD mortality outcomes

The ROC curves showed that the AUCs for the baseline ALI, ALB, NLR and BMI for the prediction of all-cause mortality were 0.708 (95% CI 0.630–0.786, P<0.001), 0.644 (95% CI 0.556–0.726, P<0.001), 0.675 (95% CI

0.596–0.754, P<0.001) and 0.581 (95% CI 0.469–0.659, P=0.069), respectively. When cardiovascular mortality was used as an endpoint, the AUC for the ALI was 0.683 (95% CI 0.573–0.783, P=0.001), the AUC for the ALB was 0.558 (95% CI 0.445–0.651, P=0.302), the AUC for the NLR was 0.687 (95% CI 0.576–0.784, P<0.001) and



Fig. 3 Multivariable-adjusted restricted cubic spline plots of HRs for all-cause mortality (A) and CVD mortality (B) according to the ALI (as a continuous measure). The solid line represents the HR, and the shaded area indicates the 95% confidence intervals. The horizontal dotted line corresponds to the normal reference HR of 1.0. The overall median value of ALI (ALI = 293.07) was chosen as the reference. The multivariable-adjusted model was adjusted for Model 4 (see Table 2). HR hazard ratio, CVD cardiovascular disease, ALI advanced lung cancer inflammation index



Fig. 4 ROC curves for the associations of the ALI, ALB, NLR, and BMI with all-cause mortality (A) and CVD mortality (B). ROC receiver operating characteristic, ALI advanced lung cancer inflammation index, ALB albumin, NLR neutrophil-to-lymphocyte ratio, BMI body mass index, CVD cardiovascular disease

the AUC for the BMI was 0.563 (95% CI 0.464–0.660, P=0.257). The ALI was superior to the ALB, NLR, and BMI in predicting all-cause mortality. However, the NLR had a better ability to predict cardiovascular mortality (Fig. 4; Table 3).

## Discussion

This retrospective study revealed that a lower ALI was independently associated with all-cause (linear association) and CVD (nonlinear association) mortality. In addition, the ALI was shown to be superior to individual parameters for predicting all-cause mortality.

ALB is a highly water-soluble protein synthesized by the liver, and its synthesis as a negative acute-phase protein is influenced by inflammation and blood volume status [12, 13]. Therefore, the ALB is not a sensitive indicator for assessing malnutrition in chronic kidney disease (CKD) patients [14]. The BMI is an objective index that can be easily obtained in the clinic to evaluate systemic nutrition, but it is also affected by fat mass and hydration status [15, 16]. A special state of chronic inflammatory

Table 3 /	AUCs of the ALI, ALB,	NLR, and BMI for	r all-cause and CVE	) mortality
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	AUC (95% CI)	P Value	Cut-off value	Youden Index	Sensitivity (%)	Specificity (%)
All-cause mortality						
ALI	0.708 (0.630, 0.786)	< 0.001	≤224.4993	0.361	56.4	79.7
ALB	0.644 (0.556, 0.726)	< 0.001	≤28.815	0.288	49.1	79.7
NLR	0.675 (0.596, 0.754)	< 0.001	> 3.0842	0.297	54.5	75.2
BMI	0.581 (0.496, 0.659)	0.069	≤24.025	0.173	72.7	44.6
CVD mortality						
ALI	0.683 (0.573, 0.783)	0.001	≤222.1859	0.393	61.3	78.0
ALB	0.558 (0.445, 0.651)	0.302	≤29.125	0.192	45.2	74.0
NLR	0.687 (0.576, 0.784)	< 0.001	> 3.0886	0.349	61.3	73.6
BMI	0.563 (0.464, 0.660)	0.257	≤25.085	0.180	83.9	34.1

ALI advanced lung cancer inflammation index, ALB albumin, NLR neutrophil-to-lymphocyte ratio, BMI body mass index, CVD cardiovascular disease, AUC area under the curve, CI confidence interval

immunosuppression exists in CKD patients, and some scholars have named this a CKD-associated immune dysfunction that is manifested by abnormal activation of the innate immune system (neutrophil involvement) and dysfunction of the adaptive immune system (lymphocyte involvement) [17]. The NLR was calculated as the peripheral blood neutrophil count divided by the lymphocyte count. A higher NLR may reflect an imbalance between the two immune responses in CKD patients [18]. The ALI is a combination of the ALB, BMI and NLR and has been proven to be related to the prognosis of non-small cell lung cancer, gastrointestinal tumours, diffuse large B-cell lymphoma, head and neck tumours, etc [7, 19–21]. A recent study showed that the ALI was associated with long-term all-cause mortality in hypertensive patients and was used as a comprehensive indicator of nutrition status and inflammation [22]. Another study revealed that the ALI was a valid predictor of all-cause and cardiovascular mortality in elderly patients with heart failure. When comparing the value of the geriatric nutritional risk index (GNRI) and the ALI in evaluating long-term mortality, the results indicated that both indices have comparable predictive value for all-cause and cardiovascular mortality at 2 years [10]. A large cohort study enrolling 9727 cancer patients compared the associations of different inflammatory markers with sarcopenia in cancer patients. The results showed that the ALI was superior to the NLR, prognostic nutritional index (PNI), systemic immunoinflammatory index (SII) and plateletto-lymphocyte ratio (PLR) for predicting and differentiating sarcopenia. Patients with a low ALI and severe malnutrition had a 2.262-fold increased risk of mortality [23]. Like many chronic diseases, CKD patients exhibit a prolonged state of low-grade inflammation. Persistent inflammation accelerates PEW by promoting systemic protein catabolism, inducing anorexia, reducing voluntary activity and promoting insulin resistance [24, 25]. Our study also confirmed the close relationship between a low ALI and adverse outcomes in PD patients. Multivariate Cox regression analyses revealed that a lower ALI is an independent risk factor for all-cause mortality and cardiovascular mortality in PD patients. Survival curves showed that the risk of all-cause and cardiovascular mortality was significantly greater in the low-ALI group than in the high-ALI group. In this study, we further compared the ability of the ALI, the ALB, the NLR, and the BMI to predict mortality in PD patients. The ROC curve showed that the ALI had the highest efficiency in predicting allcause mortality, indicating that the ALI might be a more comprehensive index for predicting all-cause mortality in PD patients than a single indicator.

Hs-CRP is a recognized biomarker of inflammation and plays an important role in the occurrence and development of atherosclerosis. Many studies have proven that an increase in hs-CRP at a single time point is an independent predictor of all-cause and cardiovascular mortality in dialysis patients [26-28]. However, Li et al. reached a different conclusion. They found that higher longitudinal hs-CRP levels over time rather than higher baseline levels were predictive of both all-cause and CVD mortality [29]. Consistent with the results of Li et al., we found that baseline hs-CRP was not associated with allcause mortality or CVD mortality, even after adjustment for other parameters (Supplementary Table 1). There are many possible reasons for this result. One explanation may be that hs-CRP fluctuated significantly during the follow-up period in this study. Studies have shown that the correlation between higher CRP levels and poor prognosis in patients who have been followed up for a long time (2-3 years of follow-up) is not as good as that in patients who have been followed up for a short time (1) year of follow-up) [30]. Another possible reason could be related to our small sample size, which may have biased the results. We further plotted an ROC curve to evaluate the predictive value of baseline hs-CRP for all-cause mortality and cardiovascular mortality in PD patients. Our results suggested that baseline hs-CRP levels have limited value in predicting the adverse outcomes in PD patients (Supplementary Fig. 1). The baseline ALI was better at predicting all-cause and CVD mortality than was the

hs-CRP, which implied that the ALI might be a potential marker for evaluating the prognosis of PD patients.

In this study, the proportion of patients with diabetes mellitus and CVD was greater in the low-ALI group. A previous prospective study demonstrated that dialysis patients with comorbidities were more likely to be malnourished, and the relative risk of malnutrition in patients with comorbidities was 3.9 times greater than that in patients without comorbidities [31]. In another study of 683 CKD patients in China, Dai et al. reported that the incidence of malnutrition was significantly greater in CKD patients with diabetes mellitus than in CKD patients without diabetes mellitus [32]. We also found that PD patients with a lower ALI had greater peritoneal transport. Previous studies have suggested that the incidence of malnutrition may be significantly greater in patients with high peritoneal transport. Liu et al. followed 283 continuous ambulatory peritoneal dialysis (CAPD) patients for 1 year and reported that higher peritoneal transport status at baseline was strongly associated with poor short-term nutritional status in CAPD patients [33]. The mechanism may include a high level of inflammation as well as increased glucose absorption from the dialysate in high peritoneal transport states, leading to a loss of appetite. A recent study demonstrated that a low PNI was independently associated with high peritoneal transit status after adjusting for relevant influencing factors (OR=3.42, 95% CI 1.43 to 8.15) [34]. In addition, our results also showed that patients in the low-ALI group had lower Hb levels. One study divided HD patients into the PEW group and the non-PEW groups according to the malnutrition inflammation score (MIS); patients in the PEW group responded poorly to treatment with erythropoietin and tended to be more anaemic in combination with malnutrition [35, 36].

This study has several limitations. First, this was a single-centre, retrospective study with a small sample size, which might have resulted in selection bias and the follow-up time was insufficient. Second, we collected data only for the initial period of dialysis and did not dynamically monitor the data during the follow-up period. Third, although we included common risk factors such as age, sex and comorbidities in our multivariate model, there may have been other unmeasured confounders that affected the results. Finally, our study lacked the comparison between ALI and common clinical prediction tools. Therefore, we plan to continue expanding the sample size and include other tools for assessing PEW, such as subjective global assessment (SGA) and MIS, in the future. We will compare these indicators with the ALI in predicting the prognosis of PD patients.

In summary, the ALI is an inexpensive and easily accessible marker that can be used to assess the prognosis of PD patients. Prospective studies with large sample sizes and multiple centres are needed to further validate our results.

## Abbreviations

ALI	Advanced lung cancer inflammation index
PD	Peritoneal dialysis
PEW	Protein-energy wasting
HD	Haemodialysis
CVD	Cardiovascular disease
BMI	Body mass index
WBC	White blood cell
Hb	Hemoglobin
hs-CRP	High sensitivity C-reactive protein
ALB	Albumin
Scr	Serum creatinine
SUA	Serum uric acid
TC	Total cholesterol
TG	Triglyceride
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
Kt/V	Total urea clearance index
CCR	Creatinine clearance rate
4-h D/Pcr	4-h dialysate-to-plasma ratio of creatinine
eGFR	Estimated glomerular filtration rate
NLR	Neutrophil-to-lymphocyte ratio
ACEIs	Angiotensin-converting enzyme inhibitors
ARBs	Angiotensin receptor blockers
ROC	Receiver operating characteristic
AUC	Area under the curve
RASIs	Renin-angiotensin system inhibitors
HR	Hazard ratio
CI	Confidence interval
CKD	Chronic kidney disease
GNRI	Geriatric nutritional risk index
PNI	Prognostic nutritional index
SII	Systemic immunoinflammatory index
PLR	Platelet-to-lymphocyte ratio
CAPD	Continuous ambulatory peritoneal dialysis
SGA	Subjective Global Assessment
MIS	Malnutrition inflammation score

## **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12882-024-03645-4.

Supplementary Material 1

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#### Author contributions

Study design, ZHR and SJS; acquisition, analysis, and interpretation of data, JYW and ZHR; manuscript writing, ZHR and JYW; review manuscript, SJS and JYW; revise and refine manuscript, SRW and MWZ. All authors have read and agreed to the published version of the manuscript.

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#### Data availability

The datasets used and analyzed during the current study available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

This study was conducted in accordance with the ethical standards of the Helsinki Declaration and was approved by the Human Ethics Committees of Shaoxing People's Hospital. All patients signed written informed consent before study enrollment.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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#### References

- Bello AK, Okpechi IG, Osman MA, Cho Y, Cullis B, Htay H, Jha V, Makusidi MA, McCulloch M, Shah N, et al. Epidemiology of peritoneal dialysis outcomes. Nat Rev Nephrol. 2022;18(12):779–93.
- Li PK, Ng JK, McIntyre CW. Inflammation and peritoneal Dialysis. Semin Nephrol. 2017;37(1):54–65.
- Graterol Torres F, Molina M, Soler-Majoral J, Romero-Gonzalez G, Rodriguez Chitiva N, Troya-Saborido M, Socias Rullan G, Burgos E, Paul Martinez J, Urrutia Jou M et al. Evolving Concepts on Inflammatory Biomarkers and Malnutrition in Chronic Kidney Disease. Nutrients: 2022:14(20).
- 4. Cobo G, Lindholm B, Stenvinkel P. Chronic inflammation in end-stage renal disease and dialysis. Nephrol Dial Transpl. 2018;33(suppl\_3):iii35–40.
- Cozzolino M, Mangano M, Stucchi A, Ciceri P, Conte F, Galassi A. Cardiovascular disease in dialysis patients. Nephrol Dial Transpl. 2018;33(suppl\_3):iii28–34.
- Wang AY, Brimble KS, Brunier G, Holt SG, Jha V, Johnson DW, Kang SW, Kooman JP, Lambie M, McIntyre C, et al. ISPD Cardiovascular and Metabolic guidelines in Adult Peritoneal Dialysis patients Part I - Assessment and Management of various Cardiovascular Risk factors. Perit Dial Int. 2015;35(4):379–87.
- Jafri SH, Shi R, Mills G. Advance lung cancer inflammation index (ALI) at diagnosis is a prognostic marker in patients with metastatic non-small cell lung cancer (NSCLC): a retrospective review. BMC Cancer. 2013;13:158.
- Zhang X, Wang D, Sun T, Li W, Dang C. Advanced lung cancer inflammation index (ALI) predicts prognosis of patients with gastric cancer after surgical resection. BMC Cancer. 2022;22(1):684.
- Kusunoki K, Toiyama Y, Okugawa Y, Yamamoto A, Omura Y, Ohi M, Araki T, Kusunoki M. Advanced lung Cancer inflammation index predicts outcomes of patients with Colorectal Cancer after Surgical Resection. Dis Colon Rectum. 2020;63(9):1242–50.
- 10. Yuan X, Huang B, Wang R, Tie H, Luo S. The prognostic value of advanced lung cancer inflammation index (ALI) in elderly patients with heart failure. Front Cardiovasc Med. 2022;9:934551.
- Tu J, Wu B, Xiu J, Deng J, Lin S, Lu J, Yan Y, Yu P, Zhu J, Chen K, et al. Advanced lung cancer inflammation index is associated with long-term cardiovascular death in hypertensive patients: national health and nutrition examination study, 1999–2018. Front Physiol. 2023;14:1074672.
- 12. Kaysen GA. Inflammation: cause of vascular disease and malnutrition in dialysis patients. Semin Nephrol. 2004;24(5):431–6.
- Mukai H, Villafuerte H, Qureshi AR, Lindholm B, Stenvinkel P. Serum albumin, inflammation, and nutrition in end-stage renal disease: C-reactive protein is needed for optimal assessment. Semin Dial. 2018;31(5):435–9.
- 14. Friedman AN, Fadem SZ. Reassessment of albumin as a nutritional marker in kidney disease. J Am Soc Nephrol. 2010;21(2):223–30.
- 15. Carrero JJ, Avesani CM. Pros and cons of body mass index as a nutritional and risk assessment tool in dialysis patients. Semin Dial. 2015;28(1):48–58.
- Ikizler TA, Burrowes JD, Byham-Gray LD, Campbell KL, Carrero JJ, Chan W, Fouque D, Friedman AN, Ghaddar S, Goldstein-Fuchs DJ, et al. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 update. Am J Kidney Dis. 2020;76(3 Suppl 1):S1–107.
- Espi M, Koppe L, Fouque D, Thaunat O. Chronic kidney Disease-Associated Immune dysfunctions: impact of protein-bound Uremic Retention Solutes on Immune cells. Toxins (Basel) 2020;12(5).

- Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to lymphocyte ratio: an emerging marker of the relationships between the Immune System and diseases. Int J Mol Sci 2022;23(7).
- Feng JF, Huang Y, Chen QX. A new inflammation index is useful for patients with esophageal squamous cell carcinoma. Onco Targets Ther. 2014;7:1811–5.
- Park YH, Yi HG, Lee MH, Kim CS, Lim JH. Prognostic value of the pretreatment advanced lung Cancer inflammation index (ALI) in diffuse large B cell lymphoma patients treated with R-CHOP chemotherapy. Acta Haematol. 2017;137(2):76–85.
- Tsai YT, Hsu CM, Chang GH, Tsai MS, Lee YC, Huang El, Lai CH, Fang KH. Advanced lung Cancer inflammation index predicts survival outcomes of patients with oral Cavity Cancer following curative surgery. Front Oncol. 2021;11:609314.
- 22. Zhang Y, Pan Y, Tu J, Liao L, Lin S, Chen K, Ding S, Xiao G. The advanced lung cancer inflammation index predicts long-term outcomes in patients with hypertension: National health and nutrition examination study, 1999–2014. Front Nutr. 2022;9:989914.
- Ruan GT, Ge YZ, Xie HL, Hu CL, Zhang Q, Zhang X, Tang M, Song MM, Zhang XW, Liu T, et al. Association between Systemic Inflammation and malnutrition with survival in patients with Cancer Sarcopenia-A prospective Multicenter Study. Front Nutr. 2021;8:811288.
- 24. Han SH, Han DS. Nutrition in patients on peritoneal dialysis. Nat Rev Nephrol. 2012;8(3):163–75.
- 25. Ikizler TA. Nutrition, inflammation and chronic kidney disease. Curr Opin Nephrol Hypertens. 2008;17(2):162–7.
- Wang AY, Woo J, Lam CW, Wang M, Sea MM, Lui SF, Li PK, Sanderson J. Is a single time point C-reactive protein predictive of outcome in peritoneal dialysis patients? J Am Soc Nephrol. 2003;14(7):1871–9.
- den Elzen WP, van Manen JG, Boeschoten EW, Krediet RT, Dekker FW. The effect of single and repeatedly high concentrations of C-reactive protein on cardiovascular and non-cardiovascular mortality in patients starting with dialysis. Nephrol Dial Transpl. 2006;21(6):1588–95.
- Liu SH, Li YJ, Wu HH, Lee CC, Lin CY, Weng CH, Chen YC, Chang MY, Hsu HH, Fang JT, et al. High-sensitivity C-reactive protein predicts mortality and technique failure in peritoneal dialysis patients. PLoS ONE. 2014;9(3):e93063.
- Li W, Xiong L, Fan L, Wang Y, Peng X, Rong R, Qiu Y, Shen J, Lin J, Yu X, et al. Association of baseline, longitudinal serum high-sensitive C-reactive protein and its change with mortality in peritoneal dialysis patients. BMC Nephrol. 2017;18(1):211.
- Meuwese CL, Stenvinkel P, Dekker FW, Carrero JJ. Monitoring of inflammation in patients on dialysis: forewarned is forearmed. Nat Rev Nephrol. 2011;7(3):166–76.
- Prasad N, Gupta A, Sinha A, Sharma RK, Saxena A, Kaul A, Bhaduria D, Gupta A. Confounding effect of comorbidities and malnutrition on survival of peritoneal dialysis patients. J Ren Nutr. 2010;20(6):384–91.
- Dai LL, Li WL, Zheng DF, Wang WH, Xie HF, Ma JW. Prevalence and Management Recommendations for Disease-Related Malnutrition in Chronic Kidney Disease Patients with and without Diabetes. Int J Endocrinol 2022;2022:4419486.
- 33. Liu Y, Huang R, Guo Q, Yang Q, Yi C, Lin J, Yu X, Yang X. Baseline higher peritoneal transport had been associated with worse nutritional status of incident continuous ambulatory peritoneal dialysis patients in Southern China: a 1-year prospective study. Br J Nutr. 2015;114(3):398–405.
- Huang Y, Zhang X, Tang X, Tang L, Shang S, Wang X, Wen Y, Feng X, Zhou Q, Su N, et al. A low Prognostic Nutritional Index is a risk factor for high peritoneal transport status in patients undergoing peritoneal Dialysis. J Ren Nutr. 2023;33(1):201–7.
- Gonzalez-Ortiz A, Correa-Rotter R, Vazquez-Rangel A, Vega-Vega O, Espinosa-Cuevas A. Relationship between protein-energy wasting in adults with chronic hemodialysis and the response to treatment with erythropoietin. BMC Nephrol. 2019;20(1):316.
- Chavez-Mendoza CA, Martinez-Rueda AJ, Ortega-Vargas JL, Becerra-Laparra IK, Ardavin-Ituarte JM, Correa-Rotter R, Ramirez-Sandoval JC, Vega-Vega O. Anemia, overhydration, and lower muscle strength in hemodialysis patients with protein-energy wasting. Hemodial Int. 2022;26(3):415–23.

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