BMC Nephrology

RESEARCH Open Access

Effect of platelet indices on mortality and comorbidity in peritoneal dialysis: a cohort study

Xiao-Qing Zhang[1], Xin-Kui Tian[1], Ling Wang[2] and Wen Tang[1*]

Abstract

Background There were limited data investigating platelet indices in predicting peritoneal dialysis (PD) outcomes on comorbidities. The aim of this study was to evaluate the association between platelet indices and new-onset comorbidity and all-cause mortality in PD patients.

Methods A single-center, retrospective observational cohort study was conducted in incident PD patients from 28 December 2011 to 24 January 2018, and followed up until 31 December 2022. Time to the first new-onset cardiovascular disease (CVD) and time to the first new-onset infection event after PD were identified as the primary outcomes. All-cause mortality was identified as the secondary endpoint. The correlation between platelet indices and comorbidities and all-cause mortality were assessed by Cox model. Data of liver disease status was not collected and analyzed. Survival curves were performed by Kaplan-Meier method with log-rank tests.

Results A total of 250 incident PD patients with a median follow-up of 6.79 (inter-quarter range 4.05, 8.89) years was included. A total of 81 and 139 patients experienced the first new-onset CVD and infection event respectively during the follow-up period. High mean platelet volume (MPV) was independently associated with high risk of time to the first new-onset CVD (HR 1.895, 95% CI 1.174–3.058, $p=0.009$) and all-cause mortality (HR 1.710, 95% CI 1.155–2.531, $p=0.007$). Patients with low mean platelet volume to platelet count ratio (MPV/PC) were prone to occur the new-onset infection events (log rank 5.693, $p=0.017$). Low MPV/PC (HR 0.652, 95% CI 0.459–0.924, $p=0.016$) was significantly associated with the time to the first new-onset infection event on PD.

Conclusions Platelet indices were associated with the new-onset CVD, infectious comorbidities and all-cause mortality on PD. Low MPV/PC was associated with time to the first new-onset infection event in PD patients. Moreover, high MPV was associated with new-onset CVD and all-cause mortality in the incident PD patients.

Keywords Platelet indices, Mean platelet volume (MPV), Mean platelet volume to platelet count ratio (MPV/PC), Comorbidity, All-cause mortality, Peritoneal dialysis

*Correspondence:
Wen Tang
tanggwen@126.com
[1]Division of Nephrology, Peking University Third Hospital, Beijing 100191, China
[2]Department of Nephrology, Xuzhou First People's Hospital, Xuzhou 221000, Jiangsu, China

Background

Peritoneal dialysis (PD) is one of the renal replacement therapies for patients with end-stage renal disease (ESRD). Cardiovascular diseases (CVD) and infections are recognized as serious complications in patients with PD. More than half of all deaths on PD occur because of cardiovascular or infectious event. As reported by the previous study, cardiovascular disease is the primary cause of death [1, 2].Meanwhile, infectious causes including peritonitis of death account for secondary cause of death on PD (5.9–33%) [1, 3–5]. Identifying patients with high risk of cardiovascular or infectious event on PD could be helpful in clinical practice.

Platelets and their activity have an important role in initiation of atherosclerotic lesions and coronary thrombus formation [6]. Platelet size, measured as mean platelet volume (MPV), has emerged as a reliable marker of thrombopoiesis and platelet function. A systematic review had reported MPV is a potentially useful prognostic biomarker in patients with cardiovascular disease [7]. It had been demonstrated that elevated MPV was an independent predictor of poor outcome in patients with heart failure with preserved ejection fraction [8]. In addition to being important in hemostasis and thrombosis, platelets also involved in modulating inflammation [9–11]. The inverse relationship between MPV and platelet count (PC) was often described in inflammatory disorders [10]. It had been reported that MPV/PC was an independent factor to predict the prognosis of sepsis [12, 13].

Recent researches in peritoneal dialysis had found these platelet indices were associated with adverse clinical outcomes. MPV could be associated with all-cause and cardiovascular mortality in patients with PD [14, 15]. Besides, low mean platelet volume to platelet count ratio (MPV/PC) level was reported to be an independent risk factor for all-cause and cardiovascular mortality in PD patients [11, 15]. However, little is known about the predict value of MPV or MPV/PC to the incidence of new onset of CVD or infectious comorbidities after PD initiation. Therefore, in this study, we aimed to evaluate the association between MPV and MPV/PC and the new-onset CVD and infectious event in PD patients. Meanwhile, investigate the relevance between MPV and all-cause mortality in PD patients. This study may provide insights into the potential utility of MPV and MPV/PC as a prognostic marker in patients with PD. In addition, it may help to identify patients at risk for clinician in PD management.

Methods

Population and data collection

In this retrospective cohort study, all incident patients who started PD therapy from 28 December 2011 to 24 January 2018 from Peking University Third Hospital were included. Patients were excluded if they had received any form of dialysis for more than 1 month, or if they had received previous kidney transplantation. Patients who started PD in other centers were also excluded for we were unable to get their detailed clinical laboratory data information while catheter insertion. A flowchart of patient recruitment for this study is shown in Fig. 1. All patients used a double cuff and straight PD catheter by open surgical insertion and followed by PD clinic of Peking University Third Hospital.

In our center, patients need to be hospitalized to department of nephrology for performing PD catheter implantation. Therefore, patients' clinical history, demographics, clinical lab assay were detailed recorded when admitted. Our data collection did not include the liver disease status of PD patients. All parameters were measured in the clinical laboratory of Peking University Third Hospital. In this study, the complete blood cell counts were performed using the Sysmex automatic blood analyzer XN-10 [B4]. Besides, after PD initiation, all patients were closed followed by dedicated nurse. In our center, patient education and staff education are in line with ISPD recommendations. All the new incident of the complications during the follow-up were recorded in our center. The study protocol was approved by the Peking University Third Hospital Medical Science Research Ethics Committee, IRB00006761-M2023210. Use of data by this study were permitted by Peking University Third Hospital Medical Science Research Ethics Committee.

Patients were followed until death, cessation of PD, failure to follow-up or the end of study as of 31 December 2022. During the follow-up, detailed new onset of cardiovascular disease and infection events were recorded. The primary endpoints were time to the first new onset of cardiovascular disease and the first new onset of infection event after PD. The first new onset of cardiovascular disease was defined as first new onset of coronary arterial events, arrhythmias, congestive heart failure, peripheral vascular disease, or cerebrovascular events including transient ischemic attack, cerebral hemorrhage, or infarction after PD initiation. The first new onset of infection events defined as peritoneal dialysis-associated peritonitis, peritoneal dialysis exit-site or tunnel infection, other bacterial infections, virus infection (e.g. herpes zoster) and other definite infection. Time to the first new onset of event were also recorded. The secondary endpoint was all-cause mortality (censored for permanent HD transfer, renal transplantation, loss to follow-up and end of study).

Statistical analysis

Results were expressed as frequencies and percentages for categorical variables, mean ± standard deviation for continuous normally distributed variables, and median

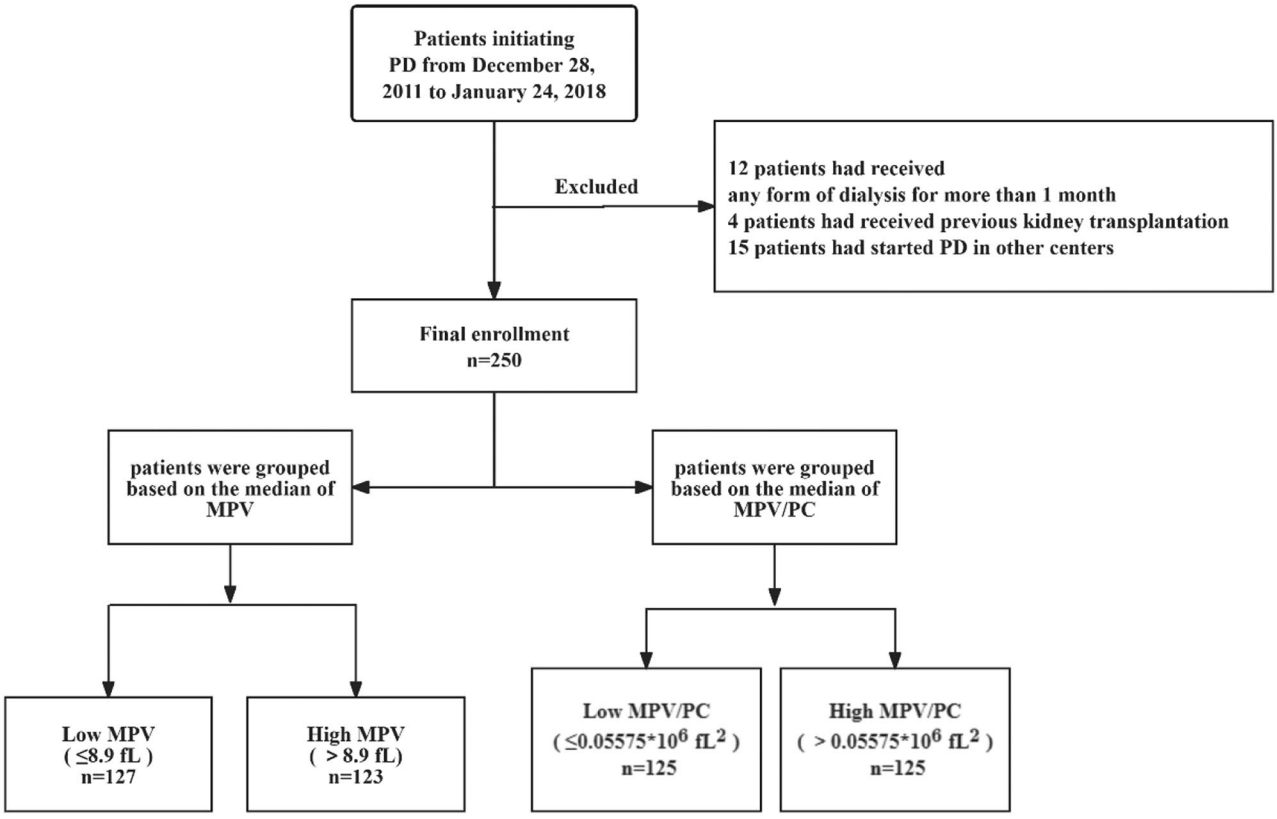


Fig. 1 Flowchart of patient recruitment for this study. Abbreviation: PD: peritoneal dialysis; MPV: mean platelet volume; MPV/PC: mean platelet volume to platelet count ratio

(interquartile range, IQR) for continuous variables that were not normally distributed. Comparison for patients in different groups was performed using chi-square tests, two-tailed unpaired t-tests or Mann–Whitney's tests, depending on data distribution. Mortality risks were analyzed by the Kaplan–Meier and multivariate Cox's proportional hazard model in which all the significant variables ($p<0.1$) from the univariate analysis were included. Forward Stepwise method was adopted when using multivariate Cox's proportional hazard model. Statistical analysis was performed using IBM SPSS software, version 25.0 (Armonk, NY). p Values less than 0.05 were considered statistically significant.

Results

Baseline patient characteristics

A total of 250 incident PD patients with a median follow-up of 6.79 (inter-quarter range 4.05, 8.89) years were included in the analysis. They hospitalized at Peking University Third Hospital to receive PD treatment from 28 December 2011 to 24 January 2018, and continued to be followed up until 31 December 2022. Of these, 244 (97.6%) patients underwent continuous ambulatory peritoneal dialysis (CAPD) therapy and 6 (2.4%) patients performed APD treatment. And the connection method is all by manual connection. 57(22.8%) patients were survival; 114(45.6%) patients were death; 24(9.6%) patients transferred to hemodialysis; 14(5.6%) patients transferred to other centers; 18(7.2%) patients underwent renal transplantation; 23(9.2%) patients were loss of follow. Clinical and laboratory characteristics at the initiation of PD are depicted in Table 1.

The correlation of MPV and time to the first new-onset cardiovascular disease on PD

A total of 81 the first new onset of cardiovascular events during the follow-up period was occurred and recorded during the study. The types of cardiovascular event included sudden death (13.2% vs. 11.6%, respectively), cardiovascular or cerebrovascular death (18.4% vs. 11.6%), myocardial infarction (10.5% vs. 14.0%), angina (0.0% vs. 2.3%), cerebral hemorrhage (7.9% vs. 14.0%), cerebral infarction (15.8% vs. 18.6%), congestive heart failure (7.9% vs. 20.9%), atrial fibrillation (10.5% vs. 4.7%), low blood pressure due to cardiovascular disease (10.5% vs. 0.0%), and other (5.3% vs. 2.3%). Time to the first onset of cardiovascular event is 1.91 (inter-quarter range 0.82, 4.52) years. Patients who have occurred new-onset cardiovascular event have higher level of MPV than patients who haven't [9.2 (inter-quarter range 8.4, 10.3)

Table 1 Clinical and laboratory characteristics at the initiation of PD by MPV group

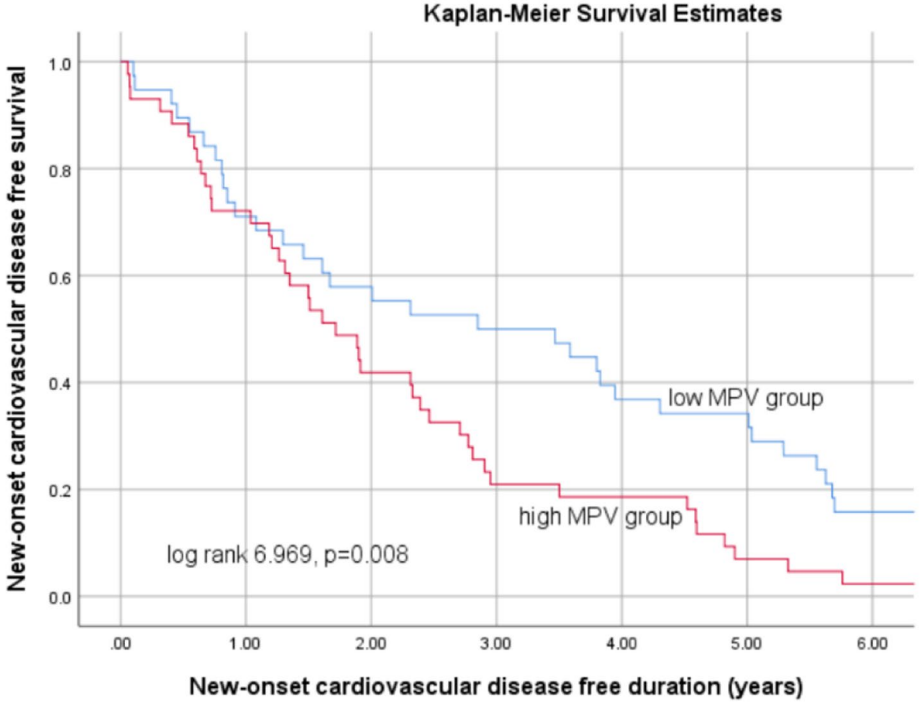
	MPV			
Variables	**Total (*n* = 250)**	**≤ 8.9 (*n* = 127)**	**>8.9 (*n* = 123)**	**P value**
MPV	9.10 ± 1.69	7.83 ± 1.19	10.42 ± 0.98	
Patients' characteristics				
Age (years)	60.96 (49.24,72.74)	58.98 (47.76,71.69)	60.63 (49.24,72.74)	0.329
Male Gender (%)	139 (55.6%)	76 (59.8%)	63 (51.2%)	0.170
BMI (kg/m^2)	23.39 ± 3.91	23.49 ± 3.36	23.29 ± 4.43	0.688
Height (cm)	163.85 ± 8.76	164.22 ± 8.94	163.46 ± 8.58	0.496
Weight (kg)	61.00 (54.00,71.00)	62.00 (54.00,72.00)	62.58 (53.00,71.00)	0.352
Laboratory parameters				
WBC (*10^9/L)	5.72 (4.59,7.30)	5.90 (4.58,7.10)	5.58 (4.59,7.72)	0.665
HGB (g/L)	87.15 ± 18.17	87.57 ± 19.55	86.72 ± 16.70	0.709
MCV (fL)	90.20 (87.05,94.70)	95.20 (84.95,101.10)	90.15 (87.03,94.08)	0.056
PLT (*10^9/L)	166.00 (131.00,271.00)	174.00 (45.00,199.00)	165.50 (134.00,224.50)	0.406
PDW (fL)	11.50 (10.45,13.35)	8.60 (4.25,14.10)	11.65 (10.63,13.38)	<0.001
PCT (%)	0.15 (0.11,0.18)	0.13 (0.10,0.15)	0.16 (0.13,0.22)	<0.001
hs-CRP(mg/L)	3.47 (1.14,11.26)	3.65 (0.99,10.67)	3.61 (1.32,17.62)	0.508
Ferritin(ng/mL)	204.50 (106.70,438.10)	188.10 (98.48,386.25)	221.00 (107.40,452.00)	0.253
Creatinine (mmol/L)	710.50 (549.00,869.50)	758.00 (565.00,889.00)	666.00 (565.00,868.00)	0.169
Urea (mmol/L)	28.20 (21.90,34.10)	29.60 (23.50,35.10)	26.50 (20.80,32.90)	0.047
Albumin (g/L)	36.59 ± 5.76	36.47 ± 6.25	36.72 ± 5.23	0.775
Potassium(mmol/L)	4.56 (4.08,5.19)	4.54 (4.07,5.15)	4.48 (3.94,4.98)	0.136
Sodium(mmol/L)	139.70 (137.00,141.10)	139.60 (137.20,142.00)	139.00 (137.00,142.00)	0.409
Calcium (mmol/L)	1.96 (1.77,2.12)	1.91 (1.71,2.09)	1.99 (1.83,2.14)	0.676
Phosphorus (mmol/L)	1.92 (1.56,2.31)	1.93 (1.61,2.35)	1.81 (1.463,2.25)	0.144
Parathyroid hormone (pg/ml)	307.2 (170.30,456.25)	298.80 (160.85,451.05)	318.90 (178.38,459.53)	0.588
Systolic blood pressure (mmHg)	148.22 ± 23.033	147.29 ± 23.41	149.19 ± 22.69	0.517
Diastolic blood pressure (mmHg)	82.00 (74.25,93.00)	81.50 (73.75,95.00)	82.00 (76.75,92.00)	0.806
Pulse pressure (mmHg)	60.00 (50.00,77.00)	56.50 (48.00,74.50)	63.50 (50.00,78.00)	0.240
Urine volume (per 100-ml increase)	11.78 ± 6.21	11.91 ± 5.63	11.65 ± 6.77	0.743
eGFR (per 1-ml/min.1.73m^2 increase, CKD-EPI)	6.46 ± 2.96	6.32 ± 2.54	6.62 ± 3.33	0.424
Comorbidities				
Diabetes mellitus	105(42.0%)	44(34.6%)	61(49.6%)	0.017
Coronary heart disease	52 (20.8%)	23 (18.1%)	29 (23.6%)	0.287
Cerebral infarction	33 (13.2%)	10 (7.9%)	23 (18.7%)	0.011
Cerebral hemorrhage	3 (1.2%)	2 (1.6%)	1 (0.8%)	1.000

Abbreviation: CI: confidence interval; BMI: body mass index; WBC: white blood cell; HGB: hemoglobin; MPV: mean platelet volume; PLT: platelet count; PDW: platelet distribution width; PCT: plateletcrit; eGFR: estimated glomerular filtration rate

fL vs. 8.8 (inter-quarter range 8.0, 10.2) fL, p=0.249]. The patients were grouped based on the median of MPV: low MPV (≤8.9 fL) and high MPV (>8.9 fL). Of them, 38 patients (47%) with low MPV and 43 patients (53%) with high MPV. Univariate Cox regression analysis showed that the parameters associated with the first new-onset cardiovascular event on PD were MPV (HR 1.866, 95% CI 1.167–2.985, p=0.009), PDW (HR 0.939, 95% CI 0.872–1.010, p=0.091) and age (HR 1.022, 95% CI 1.004–1.040, p=0.016). Patients with high MPV were prone to occur new-onset cardiovascular disease than patients with low MPV (log rank 6.969, p=0.008) (Fig. 2). Multivariate Cox regression analysis showed higher MPV (HR 1.895, 95% CI 1.174–3.058, p=0.009) was independently associated with high risk of time to the first new-onset cardiovascular disease on PD after adjusting for age (Table 2).

The correlation of MPV/PC and time to the first new-onset infection events on PD

A total of 139 the first new onset of infection events during the follow-up period was recorded. The types of infection events included peritoneal dialysis-associated peritonitis (28.2% vs. 37.7%, respectively), respiratory infection (44.9% vs. 34.4%), peritoneal dialysis exit or tunnel infection (9.0% vs. 9.8%), Herpes Zoster virus infection (3.8% vs. 8.2%), urinary tract infection (6.4% vs. 4.9%), intestinal infection (1.3% vs. 1.6%), cholecystitis (1.3% vs. 1.6%), and other (5.1% vs. 1.6%). Time to the first onset of infection event is 0.82 (inter-quarter range 0.25, 1.82) years. Patients who have occurred new-onset infection event have lower level of MPV/PC than patients who haven't [0.0527 (inter-quarter range 0.0427, 0.0689) $*10^6$ fL^2 vs. 0.0606 (inter-quarter range 0.0453, 0.0770) $*10^6$ fL^2, p=0.166]. The patients were grouped based on the median of MPV/PC: low MPV/PC (≤0.05575$*10^6$ fL^2) and high MPV/PC (>0.05575$*10^6$ fL^2). Of them, 78 patients (56.1%) with low MPV/PC and 61 patients (43.9%) with high MPV/PC. Univariate Cox regression analysis showed that factors associated with new-onset infection events on PD were WBC (HR 1.053, 95% CI 0.997–1.113, p=0.066), PLT (HR 1.002, 95% CI 1.000-1.005, p=0.083), MPV/PC median group (HR 0.661, 95% CI 0.469–0.931, p=0.018), phosphorus (HR 1.406, 95% CI 1.059–1.866, p=0.018), previous coronary heart disease history (HR 0.672, 95% CI 0.443–1.021, p=0.062). Patients with low MPV/PC were prone to occur the



At risk

low MPV group	127	116	111	108	103	102	95
high MPV group	123	111	98	89	88	83	81

Fig. 2 Probability of PD patients with low or high MPV and time to the first new-onset CVD. Abbreviation: PD: peritoneal dialysis; MPV: mean platelet volume; CVD: cardiovascular disease

Table 2 Cox regression analysis of predictors of time to the first new-onset cardiovascular disease on PD

	Univariable Cox regression		Multivariable Cox regression	
Variable	**HR[95% CI]**	**p**	**HR [95% CI]**	**P**
Patients' characteristics				
Age (years)	1.022[1.004–1.040]	0.016	1.022[1.004–1.039]	0.015
Male Gender	0.858[0.544–1.351]	0.508		
BMI (kg/m2)	0.977[0.924–1.034]	0.423		
Height (cm)	1.000[0.976–1.026]	0.974		
Weight (kg)	0.994[0.978–1.011]	0.485		
Laboratory parameters				
WBC (*10^9/L)	1.022[0.933–1.119]	0.641		
HGB (g/L)	0.994[0.981–1.007]	0.358		
MCV (fL)	0.994[0.960–1.029]	0.720		
PLT (*10^9/L)	1.000[0.996–1.004]	0.918		
MPV (fL) median GROUP (low MPV median group as reference)	1.866[1.167–2.985]	0.009	1.895[1.174–3.058]	0.009
PDW (fL)	0.939[0.872–1.010]	0.091		
PCT (%)	1.953[0.045–85.180]	0.728		
MPV/PC median GROUP	1.107[0.710–1.727]	0.653		
hs-CRP(mg/L)	1.002[0.990–1.014]	0.729		
Ferritin(ng/mL)	1.001[1.000-1.002]	0.171		
Creatinine (mmol/L)	1.000[0.999–1.001]	0.643		
Urea (mmol/L)	1.013[0.990–1.037]	0.270		
Albumin (g/L)	1.007[0.971–1.045]	0.699		
Potassium(mmol/L)	1.065[0.813–1.395]	0.646		
Sodium(mmol/L)	0.971[0.921–1.024]	0.278		
Calcium (mmol/L)	1.086[0.576–2.050]	0.799		
Phosphorus (mmol/L)	1.172[0.791–1.735]	0.429		
Parathyroid hormone (pg/ml)	0.999[0.998–1.001]	0.421		
Systolic blood pressure (mmHg)	0.999[0.991–1.007]	0.829		
Diastolic blood pressure (mmHg)	1.002[0.988–1.016]	0.765		
Pulse pressure (mmHg)	0.997[0.987–1.008]	0.610		
Urine volume (per 100-ml increase)	0.985[0.951–1.020]	0.387		
eGFR (per 1-ml/min.1.73m^2 increase, CKD-EPI)	0.955[0.884–1.033]	0.248		
Comorbidities				
Diabetes mellitus	1.319[0.839–2.075]	0.230		
Coronary heart disease	0.988[0.607–1.608]	0.960		
Cerebral infarction	1.468[0.866–2.489]	0.154		
Cerebral hemorrhage	1.738[0.238–12.696]	0.586		

Abbreviation: CI: confidence interval; BMI: body mass index; WBC: white blood cell; HGB: hemoglobin; MPV: mean platelet volume; PLT: platelet count; MPV/PC: mean platelet volume to platelet count ratio; PDW: platelet distribution width; PCT: plateletcrit; eGFR: estimated glomerular filtration rate

Multivariate Cox's proportional hazard model included all the significant variables ($p<0.1$) from the univariate analysis and Forward Stepwise method was adopted when using multivariate Cox's proportional hazard model

new-onset infection events than patients with high MPV/PC (log rank 5.693, $p=0.017$) (Fig. 3). Multivariate Cox regression analysis showed lower MPV/PC (HR 0.652, 95% CI 0.459–0.924, $p=0.016$) was significantly associated with the time to the first new-onset infection events on PD (Table 3).

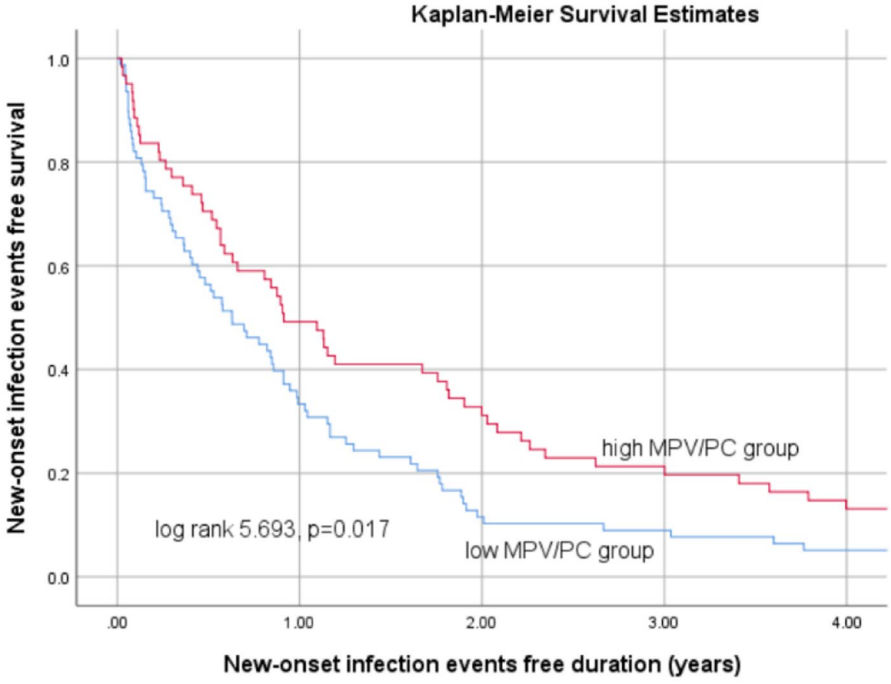
The relationship of MPV and all-cause mortality

A total of 114 (45.6%) patients died during the follow-up period. Patients with low MPV showed a higher survival rate than patients with high MPV (log rank 8.243, $p=0.004$) (Fig. 4). Multivariate Cox regression analysis showed that higher MPV (HR 1.710, 95% CI 1.155–2.531, $p=0.007$) was independently associated with increased all-cause mortality after adjusting for age (HR 1.052, 95% CI 1.036–1.069, $p<0.001$), albumin (HR 0.562, 95% CI 0.378–0.835, $p=0.004$), urine volume (HR 0.966, 95% CI 0.934–0.998, $p=0.036$) and other confounding factors.

Discussion

In this study, we found that MPV/PC was correlated with time to the first new-onset infection event on PD. We confirmed that MPV was associated with time to the first cardiovascular disease and all-cause mortality in incident PD patients. To our knowledge, this was the first study examining the relationship between platelet indices and the first infectious comorbidities or new-onset CVD on PD.

Low MPV/PC had been reported to be an independent risk factor for all-cause and cardiovascular mortality in PD patients [11, 15]. Hitherto, no studies explored the association with time to the first new-onset infection event in PD patients. Our study found that lower MPV/PC was associated with time to the first new-onset infection event. Roles of platelets were not only hemostasis and thrombosis, but also inflammation [16]. It seemed that the size of circulating platelets is dependent on the intensity of systemic inflammation [10]. Thrombocytosis with an increase in the quantity of low-sized platelets was a frequent feature in inflammatory bowel disease [17, 18], suggesting an intense consumption of large platelets



At risk

low MPV/PC group	125	73	56	54	51
high MPV/PC group	125	94	83	77	72

Fig. 3 Probability of PD patients with low or high MPV/PC and time to the first new-onset infection events. Abbreviation: PD: peritoneal dialysis; MPV/PC: mean platelet volume to platelet count ratio

[10]. Wu et al. found that the MPV/PC was inversely associated with the patient's survival, who with sepsis in the intensive care unit [13]. Our study confirmed that patients with lower MPV/PC were prone to be infectious in PD population. The relationship between MPV/PC and infection in patients treated with PD can be accounted for this way. Uremic involved persistent low-grade inflammation, which infection event could aggravate. Inflammatory response induced the release and activation of Interleukin 6 (IL-6), leading to the enhanced megakaryopoiesis and increased PC [19]. Additionally, the consumption of large platelets was enhanced in high-grade inflammatory states, thus reducing MPV [10]. In turn, the low MPV/PC would appear in the infectious status of PD patients.

MPV was a biomarker of platelet activity. High MPV had a higher thrombotic potential [20]. Many researchers had shown their interest in MPV and its relationship with cardiovascular disease. Evidence derived from both retrospective and prospective studies suggested that high MPV was a predictor of cardiovascular and cerebrovascular disease [10]. However, it was a vacancy in ESRD patients underwent PD. Interestingly, we found that high MPV was independently associated with new-onset cardiovascular event in PD patients. It represented that MPV may be a promising, widely applicable marker candidate among PD patients. According to previous literature, the possible mechanism that an increase in MPV correlated with new-onset cardiovascular event in patients treated with PD may be explained that the increase in platelet volume was accompanied by an increase in density [21] and these platelets contained more secretory granules which may trigger cytokines release and pro-inflammatory effect predisposing the occurrence of cardiovascular disease [20, 22, 23].

MPV was proved to be associated with mortality risk in various previous studies [24, 25]. Higher MPV was indicative of increased platelet turnover by the bone marrow in response to stress [24]. Younger, larger platelets were also functionally more active, which with augmented thrombotic potential, showing spontaneous aggregation in the circulation [24, 26]. On the other hand, high MPV was an indicator of an active and invasive systemic infection [24, 27]. In the field of hemodialysis, Li et al. showed MPV in non-survivors was higher, and proved MPV was a predict marker of in-hospital mortality of acute cardiorenal syndrome patients receiving continuous renal replacement therapy [28]. Moreover, in a 5-year

Table 3 Cox regression analysis of predictors of time to the first new-onset infection events on PD

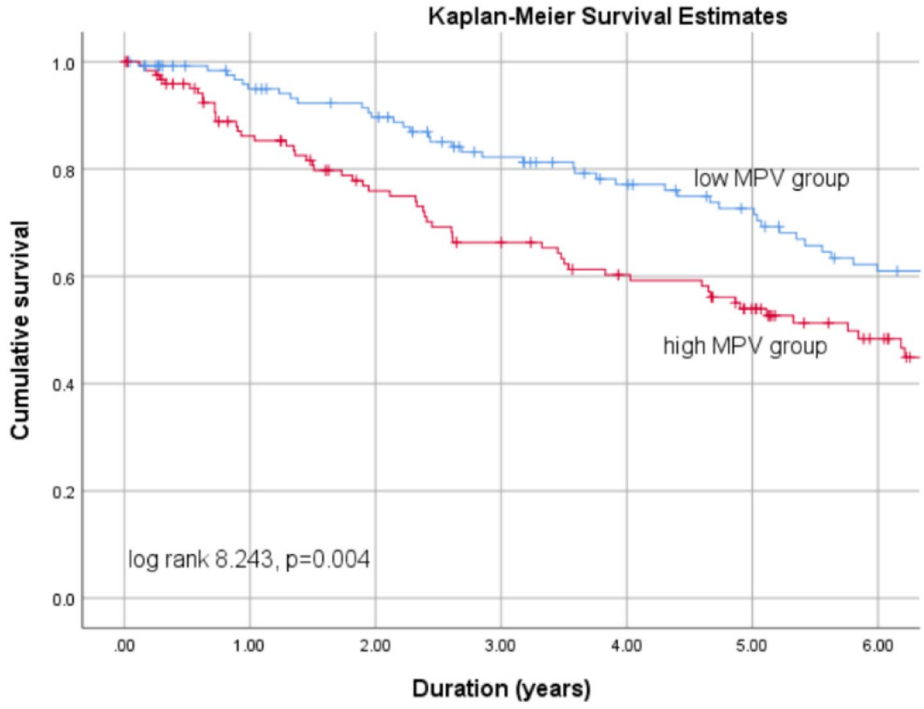
	Univariable Cox regression		Multivariable Cox regression	
Variable	**HR [95% CI]**	**p**	**HR [95% CI]**	**P**
Patients' characteristics				
Age(years)	1.000 [0.989–1.011]	0.981		
Male Gender	1.180[0.842–1.652]	0.337		
BMI(kg/m^2)	0.991[0.955–1.029]	0.642		
Height(cm)	0.985[0.966–1.003]	0.107		
Weight(kg)	0.993[0.983–1.004]	0.220		
Laboratory parameters				
WBC(*10^9/L)	1.053[0.997–1.113]	0.066		
HGB(g/L)	0.996[0.987–1.006]	0.450		
MCV(fL)	0.994[0.965–1.024]	0.676		
PLT(*10^9/L)	1.002[1.000-1.005]	0.083		
MPV(fL)median GROUP	0.855[0.606–1.204]	0.370		
PDW(fL)	1.006[0.952–1.064]	0.819		
PCT(%)	5.210[0.436–62.267]	0.192		
High MPV/PC median GROUP (low MPV/PC median group as reference)	0.661[0.469–0.931]	0.018	0.652[0.459–0.924]	0.016
hs-CRP(mg/L)	1.005[0.997–1.014]	0.188		
Ferritin(ng/mL)	1.000[0.999–1.001]	0.958		
Creatinine(mmol/L)	1.000[0.999–1.001]	0.897		
Urea(mmol/L)	1.013[0.995–1.030]	0.153		
Albumin(g/L)	1.004[0.973–1.037]	0.793		
Potassium(mmol/L)	1.105[0.890–1.372]	0.367		
Sodium(mmol/L)	1.007[0.972–1.044]	0.702		
Calcium(mmol/L)	1.030[0.567–1.870]	0.924		
Phosphorus(mmol/L)	1.406[1.059–1.866]	0.018		
Parathyroid hormone(pg/ml)	1.000[0.999-1.000]	0.214		
Systolic blood pressure(mmHg)	0.998[0.991–1.005]	0.612		
Diastolic blood pressure(mmHg)	0.995[0.984–1.006]	0.385		
Pulse pressure (mmHg)	1.000[0.992–1.009]	0.958		
Urine volume(per 100-ml increase)	0.977[0.948–1.007]	0.136		
eGFR(per 1-ml/min.1.73m^2 increase, CKD-EPI)	0.984[0.924–1.047]	0.601		
Comorbidities				
Diabetes mellitus	1.000[0.708–1.413]	0.999		
Coronary heart disease	0.672[0.443–1.021]	0.062		
Cerebral infarction	1.346 [0.796–2.276]	0.268		
Cerebral hemorrhage	1.539[0.213–11.092]	0.669		

Abbreviation: CI: confidence interval; BMI: body mass index; WBC: white blood cell; HGB: hemoglobin; MPV: mean platelet volume; PLT: platelet count; MPV/PC: mean platelet volume to platelet count ratio; PDW: platelet distribution width; PCT: plateletcrit; eGFR: estimated glomerular filtration rate

Multivariate Cox's proportional hazard model included all the significant variables ($p<0.1$) from the univariate analysis and Forward Stepwise method was adopted when using multivariate Cox's proportional hazard model

cohort study of 149,118 patients observed that hemodialysis patients with higher MPV had heightened all-cause mortality risk [29]. Those were compatible with our work, that was PD patients with high MPV had a higher all-cause mortality. However, Conflicting result existed regarding MPV and all-cause mortality in PD population. Jiang et al [14]. and Zhu et al [15]. showed that low MPV was related to all-cause mortality in patients with PD, which our result was opposite with. The generation of these conflict results may due to the different laboratory data and the heterogeneity of cohort population. Notably, they [14, 15] included patients accepting at least 90 days of PD therapy and collected baseline data regarding blood sample results 1–3 months after PD happened. While we included incident patients on PD and collected baseline data at the initiation of PD. Therefore, further researches are needed to investigate whether MPV at onset of PD or MPV at PD stabilization is more valuable in predicting the adverse outcome of PD patients. Besides, there was a difference in the proportion of patients with diabetes mellitus, which was correlated with increased MPV [10, 30]. Additionally, our study population was elder. Previous study showed that MPV increased with age [31]. Presumably, the different age may be also a reason for the different results. In conclusion, more researches with more samples are needed to investigate whether increased MPV is associated with increased all-cause mortality in patients with PD.

There are certain limitations to our study. First, this is a retrospective study. Prospective studies needed to be conducted to further validate the feasibility of this result; Second, though our center is a relatively large PD center (with average managed patients per year are more than 200 patients), this is a single-center design study. Therefore, interpreting this result and generalization to other centers should be cautious. Third, the relative low sample size would limit the interpretation ability from the result of this study. Fourth, we have made effort to control for known confounding factors. However, we acknowledge that there may be confounding factors that are not identified or controlled for, such as liver disease, malignancy



At risk

low MPV group	127	121	115	107	102	98	88
high MPV group	123	107	96	86	80	74	70

Fig. 4 Kaplan–Meier's survival curve for peritoneal dialysis patients with low or high MPV. Abbreviation: MPV: mean platelet volume

and so on, which may have affected the findings. Fifth, although we have discussed the possible underlying mechanisms, we cannot provide direct mechanisms. Finally, how changes in these indices can improve outcomes for PD patients needs to be explored by future studies.

Conclusion

At present, there are no reports that explore the relationship between MPV or MPV/ PC and time to the first new-onset CVD or infectious comorbidities on PD. Our study demonstrated that platelet indices were associated with the new-onset CVD, infectious comorbidities and all-cause mortality on PD. Low MPV/PC was associated with time to the first new-onset infection event in PD patients. Moreover, high MPV was associated with new-onset cardiovascular event and all-cause mortality in the incident PD patients. MPV and PC are generally assessed in most clinical laboratories and easy to get, the link between these indicators to new-onset CVD and infection event could give clinician a new angle for PD patients' management. Our findings may help the risk stratification of patients by using these inexpensive and simple laboratory indicators.

Abbreviations

PD	Peritoneal dialysis
CVD	Cardiovascular disease
MPV	Mean platelet volume
MPV/PC	Mean platelet volume to platelet count ratio
ESRD	End-stage renal disease
PC	Platelet count
IQR	Interquartile range
CI	Confidence interval
BMI	Body mass index
WBC	White blood cell
HGB	Hemoglobin
PLT	Platelet count
PDW	Platelet distribution width
PCT	Plateletcrit
eGFR	Estimated glomerular filtration rate

Acknowledgements

Not applicable.

Author contributions

W.T. and L.W. conceived, designed the study. X.Q.Z. and W.T. performed the data acquisition and the data analysis. X.Q.Z. wrote the initial manuscript. W.T. and K.X.T. read and revised the manuscript. All authors contributed to editorial changes in the manuscript. All authors have read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China (U23A20468), Clinical Cohort Construction Program of Peking University Third

Hospital (grand number BYSYDL2023004) and the Xuzhou Scientific and Technological Projects (grand number KC23143).

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the Peking University Third Hospital Medical Science Research Ethics Committee, IRB00006761-M2023210. Use of data and waiver of informed consent by this study were permitted by Peking University Third Hospital Medical Science Research Ethics Committee.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 26 April 2024 / Accepted: 7 August 2024
Published online: 28 August 2024

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