

# ***Mortality Risk Factors in the China Dialysis Outcomes and Practice Patterns Study (DOPPS)***

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## **Research Article**

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# Abstract

## Background

Mortality risk for hemodialysis (HD) patients varies by country and ethnicity. Here, mortality rate and its related risk factors in Chinese HD patients from the Dialysis Outcomes and Practice Patterns Study (DOPPS) were investigated.

## Methods

Data from China DOPPS phase 5 (2012–2015) were used. Patients' demographics, assigned primary causes of end stage kidney disease (ESKD), comorbidities, dialysis prescription, laboratory values, date and cause for death were analyzed. Cox proportional hazards models were used to assess the association of patient characteristics and treatments with mortality.

## Results

1427 HD patients were enrolled. The mean age was  $59.4 \pm 14.9$  years. The median follow-up time was 1.9 (1.1–2.1) years. There was total 205 deaths with at least 103 from cardiovascular disease (50.2%). The overall mortality rate was 8.8 per 100 patient-years. In the multivariate Cox model, older, serum albumin (Alb < 4g/dl, blood platelets <  $100 \times 10^9/L$ , pulse pressure (PP) > 63mmHg, and congestive heart failure history were independent risk factors for all-cause mortality.

## Conclusions

Attention should be paid to patients who were older, with lower Alb and blood platelets level, higher PP and congestive heart failure history. Our results highlighted that there might be some modifiable risk factors for patients' survival, such as Hgb, Alb, blood platelets, and blood pressure management.

## Introduction

Hemodialysis (HD) therapy is a life-saving and life-sustaining procedure that improves the life expectancy of patients with end stage kidney disease (ESKD). However, the adjusted all-cause mortality rate was 6.5–7.9 times greater for dialysis patients than for individuals in the general population[1, 2].

Understanding the mortality risk and its influencing factors in HD patients are of great interest and value, especially those modifiable risk factors. We previously reported that the crude mortality rate for maintenance HD patients in Beijing was much lower than that in the United State[3]. However, our previous analysis only included patients from one major city in China, and lacked information about risk factors for mortality, and was limited in sample size.

Previous studies have shown that mortality rates varied remarkably among different countries and ethnic groups. The United States Renal Data Services (USRDS) 2018 annual report showed that all-cause mortality was 16.6 per 100 patient-years for American maintenance HD patients[4]. In 2017, the Annual Report of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry covered a general population of 694 million people. For patients commencing renal replacement therapy (RRT) during 2008–2012, the unadjusted 5-year patient survival probability for all RRT modalities combined was 50.8%. According to the annual survey of the Japanese Society for Dialysis Therapy Renal Data Registry, the total number of patients undergoing dialysis treatment was 339,841 at the end of 2018, and the crude annual death rate was 10.0%[5]. These countries were all developed countries, and Japan was the only country from Asia. China is a large developing Asian country and has an increasing HD population. However, the related information we hold about Chinese HD population was lacking. It is necessary to investigate the mortality rate and risk factors for Chinese HD patients and to optimize the treatment practices for its ESKD patients. Therefore, we analyzed the data of China DOPPS phase 5 (2012–2015) to describe the overall death rate and explore modifiable risk factors for patient mortality.

## Materials And Methods

### Study design and subjects

The DOPPS is an international prospective cohort study of in-center HD patients  $\geq 18$  years of age [6, 7]. Our previous works also described the methodology for the China DOPPS[8]. The current study includes patients selected for China DOPPS phase 5 (2012 to 2015).

Demographic and clinical characteristics were abstracted from medical records using a web-based data collection tool. Death events and reasons were recorded during follow-up period. The study was approved by the Ethics Committee of Peking University People's Hospital (ethical approval number: 2018PHB028-01). All patients signed the written informed consent. The authors confirm that all the methods used in this study comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration.

## Statistical analysis

Baseline characteristics were reported as continuous or categorical variables. Normally distributed continuous variables were presented as mean and standard deviation (SD), otherwise, expressed as median (25th, 75th ). Crude mortality rates were estimated as the number of deaths per 100 patient-years. Patients were divided into 2 groups, survived or died. Differences in baseline data between survived and died groups were evaluated by using independent sample t-test or Wilcoxon rank-sum test respectively. Differences in categorical variables between 2 groups were estimated by using chi-square test.

We examined proposed clinically relevant variables by univariate Cox regression models, and relatively significant variables ( $P < 0.15$ ) were added into multivariate Cox regression analysis. The variables included in the multivariate Cox regression were age, vascular access, pulse pressure (PP), serum

albumin (Alb), hemoglobin (Hgb), platelet counts, spKt/V, serum corrected calcium, phosphate, comorbidities (congestive heart failure (CHF), cancer, other cardiovascular disease, cerebrovascular disease, fracture, history cirrhosis of the liver, diabetes, hypertension, hepatitis, lung disease, peripheral vascular disease). PP was defined as the difference value of the mean pre-dialysis systolic blood pressure and the mean diastolic blood pressure. The PHREG procedure based on the Cox proportional hazards model were used to analysis association of patient characteristics with death. Patients from the same facility tend to have similar practice patterns, so we accounted for facility clustering using a robust sandwich estimator of the covariance. After adjustment, age, serum Alb level, platelet counts, comorbidities (CHF) and PP were significant and included in the final Cox model.

We converted continuous variables considered as risk factors of all-cause mortality in final Cox model into categorical variables to investigate the differences in death risk among subgroups of each variable. Alb was divided into 3 groups by  $< 3.5\text{g/l}$ ,  $3.5\text{-}3.9\text{g/l}$ , and  $\geq 4.0\text{g/l}$ ; platelets counts were divided into 3 groups by  $< 100 \times 10^9/\text{l}$ ,  $101\text{-}299 \times 10^9/\text{l}$ ,  $\geq 300 \times 10^9/\text{l}$ ; and PP were divided into 2 groups by  $< 63\text{mmHg}$  and  $\geq 63\text{mmHg}$ .

We performed MI procedure to impute the missing data, and continuous and categorical variables were imputed by fully conditional specification (FCS) regression and logistic regression, respectively. After 25 steps of imputation, 25 data sets were combined for the final analysis of Cox regression model. Percentages of missing for most variables were  $< 10\%$ , except for Kt/V (37.8%) and transferrin saturation (40.6%). P value  $< 0.05$  was seen as statistically significant. Statistical analysis was performed with SAS, version 9.4 (SAS institute, Cary, NC; USA), and the forest plot of subgroup analysis were performed by R software, version 3.2.3.

## Results

1427 HD patients were enrolled in this study. The mean age was  $59.4 \pm 14.9$  years. The median follow-up time was 1.9 (interquartile range = 1.1, 2.1) years. According to the outcome status, we divided patients into survived and died groups, and characteristics between groups were compared (Table 1). Patients in died group differed from survived patients in many ways: for instance, they were older, with a higher proportion of catheter use, had lower Hgb and Alb. Meanwhile, died patients had higher pre-dialysis and post-dialysis diastolic blood pressure (DBP) than survived patients. Compared with survived patients, patients who died had a higher proportion of diabetes, CHF and other cardiovascular disease, cerebrovascular disease, fracture, hypertension, osteoporosis, lung disease and peripheral vascular disease (Table 1).

Table 1  
Patient Baseline Characteristics of survived and died groups

Variables	Survived (n = 1222)	Died (n = 205)	All (n = 1427)	P-value
Age (years)	58.5 (49.0, 69.0)	70.0 (59.0, 79.0)	60 (49, 71)	< 0.001*
Female (%)	45.2	43.9	45	0.800
BMI	21.9 ± 3.7	21.8 ± 4.0	21.9 ± 3.7	0.799
Vintage (years)	2.6 (0.8–5.5)	2.5 (1.0–5.0)	2.6 (0.9–5.4)	0.390
Diabetes	25.8	36.1	27.3	0.008*
Blood access types				0.047*
Fistula	85.7	80.0	84.9	
Catheter and others	13.3	19.5	14.2	
spKt/V	1.4 ± 0.3	1.3 ± 0.3	1.4 ± 0.3	0.611
spKt/V < 1.2 (%)	18	18.4	18.4	0.500
stdKt/V	2.1 (1.8–2.2)	2.1 (1.9–2.3)	2.1 (1.8–2.3)	0.815
Albumin (g/dl)	3.9 ± 0.5	3.7 ± 0.5	3.9 ± 0.5	< 0.001*
WBC (per 10 <sup>9</sup> /L)	6.0 (4.9–7.3)	5.8 (4.6–7.5)	6.0 (4.9–7.3)	0.280
Hgb (g/dl)	10.5 ± 1.9	10.1 ± 2.0	10.4 ± 1.9	0.021*
Hgb < 9 g/dl (%)	18.3	27.3	19.6	0.031*
Calcium (mg/dl)	9.1 ± 1.0	9.0 ± 1.0	9.1 ± 1.0	0.7269
Phosphate (mg/dl)	5.7 (4.6–7.2)	5.2 (4.2–6.7)	5.6 (4.6–7.2)	0.001*
iPTH (pg/dl)	264.2 (134.0-517.6)	233.3 (125.5-444.7)	259.0 (131.0-509.0)	0.180
< 3-times weekly HD (%)	21.4	20.0	21.23	0.379

Values are expressed as mean ± SD or median (interquartile range). BMI, body mass index; spKt/V, single-pooled Kt/V; stdKt/V, standard Kt/V; WBC, white blood cells; Hgb, hemoglobin; HD, hemodialysis; HDF, hemodiafiltration; HF, hemofiltration; BUN, blood urea nitrogen; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHF, congestive heart failure; GI, gastrointestinal.

Variables	Survived (n = 1222)	Died (n = 205)	All (n = 1427)	P-value
HD sub-modality				0.134
HD	90.9	94.6	91.5	
HDF	7.4	4.4	7.0	
HF	0.1	0.5	0.1	
Mixed	1.1	0	1.0	
Urine output $\geq$ 200 ml/day (%)	32.7	27.3	31.9	0.100
pre-BUN (mg/dl)	40.3 (32.8–52.7)	37.2 (30.6–52.6)	39.9 (32.5– 52.6)	0.030*
post-BUN (mg/dl)	13.5 (10.1–18.2)	13.2 (9.3–18.8)	13.5 (10.0-18.4)	0.380
Sodium (mEq/l)	139.1 $\pm$ 3.9	138.7 $\pm$ 3.6	139.0 $\pm$ 3.5	0.512
Potassium (mEq/l)	5.0 $\pm$ 0.8	4.9 $\pm$ 0.9	5.0 $\pm$ 0.8	0.089
pre-Weight (kg)	62.0 $\pm$ 11.9	61.0 $\pm$ 11.5	61.9 $\pm$ 11.8	0.269
post-Weight (kg)	59.7 $\pm$ 11.7	58.7 $\pm$ 11.2	59.6 $\pm$ 11.6	0.245
Interdialytic weight loss	3.9 (2.8, 5.0)	3.8 (2.6, 5.1)	3.9 (2.8-5.0)	0.324
pre-SBP (mmHg)	147.9 $\pm$ 20.3	150.3 $\pm$ 20.7	148.2 $\pm$ 20.4	0.149
pre-DBP (mmHg)	79.7 $\pm$ 12.4	77.2 $\pm$ 12.6	79.4 $\pm$ 12.5	0.009*
post-SBP (mmHg)	140.7 $\pm$ 22.7	141.8 $\pm$ 21.5	140.9 $\pm$ 22.6	0.544
post-DBP (mmHg)	78.7 $\pm$ 12.5	75.6 $\pm$ 13.0	78.3 $\pm$ 12.6	0.002*
pre-Pulse	76.4 $\pm$ 9.3	75.2 $\pm$ 10.6	76.2 $\pm$ 9.5	0.126
post-Pulse	77.2 $\pm$ 10.2	75.8 $\pm$ 10.7	77.0 $\pm$ 10.2	0.113
Comorbidities (%)				
CHF	21.8	36.1	23.8	< 0.001*
Calciphylaxis	7.7	9.8	8.0	0.222
Cancer	3.4	6.3	3.9	0.102

Values are expressed as mean  $\pm$  SD or median (interquartile range). BMI, body mass index; spKt/V, single-pooled Kt/V; stdKt/V, standard Kt/V; WBC, white blood cells; Hgb, hemoglobin; HD, hemodialysis; HDF, hemodiafiltration; HF, hemofiltration; BUN, blood urea nitrogen; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHF, congestive heart failure; GI, gastrointestinal.

Variables	Survived (n = 1222)	Died (n = 205)	All (n = 1427)	P-value
Other cardiovascular disease	19.5	29.8	21.0	0.003*
Carpal tunnel syndrome	1.1	2.4	1.2	0.203
Cerebrovascular disease	12.7	24.4	14.4	< 0.001*
Cirrhosis of the liver	1.1	2.4	1.3	0.174
Diabetes	25.9	36.1	27.3	0.009*
Fracture	1.9	5.4	2.4	0.008*
GI Bleeding	2.5	2.0	2.4	0.895
Hepatitis	12.3	16.1	12.8	0.313
Hypertension	85.9	80.5	85.1	0.048*
Hyperlipidemia	33.6	36.6	34.0	0.569
Lung disease	4.0	10.2	4.9	< 0.001*
Neurologic disease	2.2	3.4	2.4	0.573
Osteoporosis	27.0	39.0	28.7	0.002*
Peripheral vascular disease	7.9	15.1	9.0	0.003*
Parathyroid Surgery	2.4	0	2.0	0.068
Peripheral Neuropathy	9.5	10.2	9.6	0.846
Psychiatric Disorder	2.0	2.4	2.0	0.900
Recurrent Cellulitis	1.5	3.4	1.8	0.134
Values are expressed as mean $\pm$ SD or median (interquartile range). BMI, body mass index; spKt/V, single-pooled Kt/V; stdKt/V, standard Kt/V; WBC, white blood cells; Hgb, hemoglobin; HD, hemodialysis; HDF, hemodiafiltration; HF, hemofiltration; BUN, blood urea nitrogen; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHF, congestive heart failure; GI, gastrointestinal.				

During the follow-up period, 205 patients died. The overall mortality rate was 8.8 per 100 patient-years. Main causes of death including: cardiovascular disease (105, 51.2%), infection (33, 16.1%, Table 2). Other causes included malignant disease (19, 9.3%), gastrointestinal (8, 3.9%), metabolic (6, 2.9%), liver disease (2, 1.0%) and unknown (32, 15.6%).

Table 2  
The distribution of primary causes of death

Causes of deaths	Numbers (%)
Cardiac/Vascular	105 (51.2)
Liver Disease	2 (1.0)
Infection	33 (16.1)
Gastrointestinal	8 (3.9)
Metabolic	6 (2.9)
Other	19 (9.3)
Unknown	32 (15.6)

We use univariate Cox regression analysis to select variables related to all-cause mortality from proposed clinically relevant ones (Table 3). Variables with  $P < 0.15$  were entered as possible factors in the multivariate Cox regression model. We found that age, Alb, blood platelets, history of CHF and PP were related to all-cause mortality in the final model (Table 4). For each 10-years increasing of age, the risk of all-cause mortality rose by 52% (HR = 1.52, 95%CI: 1.35–1.71). Compared with Alb  $\geq 4.0$  g/dl, patients with Alb in 3.5–3.9 and  $< 3.5$  g/dl had an increased risk of death after adjustment (HR = 1.50, 95%CI: 1.10–2.11 and HR = 2.45, 95%CI: 1.65–3.63, respectively). Meanwhile, low blood platelets ( $< 100 \times 10^9/L$ ) were related to a higher death rate (HR = 1.97, 95%CI: 1.42–2.72) than normal blood platelets ( $100–299 \times 10^9/L$ ). Patients who had a history of CHF (HR = 1.57, 95%CI: 1.16–2.11) tend to have a higher mortality risk than patients without this comorbidity. Patients with higher PP ( $\geq 63$ mmHg) had a 1.41-fold higher risk for all-cause mortality (95% CI, 1.01–1.96;  $P = 0.042$ ).

Table 3  
Univariate Cox regression model of All-Cause Mortality in China DOPPS5 patients

Variables	Hazard ratios	95% CI	P value
Age	1.053	1.041–1.065	< 0.001
ESKD causes (CGN as reference)			
Diabetic nephropathy	2.211	1.546–3.164	< 0.001
Hypertension	1.822	1.205–2.755	0.005
Others	1.465	0.99–2.167	0.056
Albumin	0.453	0.363–0.567	< 0.001
Blood calcium	0.842	0.724–0.979	0.026
Blood glucose	1.001	1.000–1.003	0.053
Hemoglobin	0.902	0.841–0.967	0.004
Phosphorus	0.907	0.841–0.977	0.010
Potassium	0.844	0.713–0.998	0.047
Creatinine	0.854	0.816–0.894	< 0.001
Platelet	0.996	0.993–0.998	< 0.001
Kt/V < 1.2 ( $\geq 1.2$ as reference)	1.443	0.967–2.153	0.073
Systolic blood pressure-pre-dialysis	1.005	0.998–1.012	0.149
Diastolic blood pressure- pre-dialysis	0.985	0.974–0.997	0.014
Diastolic blood pressure-post-dialysis	0.983	0.972–0.995	0.004
Pulse pressure	1.013	1.005–1.021	0.001
Pulse- pre-dialysis	0.987	0.972–1.003	0.104
Pulse- post-dialysis	0.989	0.974–1.003	0.127
Blood access type (fistula as reference)	1.812	1.282–2.562	< 0.001
Comorbidities (yes vs. no)			
Diabetes	1.647	1.234–2.196	< 0.001
Coronary arterial disease	2.009	1.517–2.661	< 0.001
Congestive heart failure	1.965	1.476–2.616	< 0.001

Values are expressed as mean  $\pm$  SD or median (interquartile range). ESKD, end stage kidney disease; Kt/V, Kt/Vurea;

Variables	Hazard ratios	95% CI	P value
Cancer	1.766	1.007–3.099	0.047
Other cardiovascular disease	1.596	1.182–2.154	0.002
Carpal tunnel syndrome	1.979	0.815–4.808	0.132
Cerebrovascular disease	2.035	1.479–2.802	< 0.001
Cirrhosis of the liver	2.044	0.841–4.964	0.114
Fracture	2.371	1.291–4.354	0.005
Hepatitis	1.335	0.919–1.938	0.129
Lung disease	2.464	1.568–3.873	< 0.001
Osteoporosis	1.525	1.150–2.022	0.003
Peripheral vascular disease	1.945	1.326–2.852	< 0.001
Recurrent Cellulitis	2.404	1.131–5.111	0.023

Values are expressed as mean  $\pm$  SD or median (interquartile range). ESKD, end stage kidney disease; Kt/V, Kt/Vurea;

Table 4  
Multivariate Cox regression model of All-Cause Mortality in China DOPPS5 patients

Variables	Hazard ratios	95% CI	P value
Age (per 10 years)	1.52	1.35–1.71	< 0.001*
Albumin (g/dl)			
≥ 4.0	Ref.	Ref.	
3.5–3.9	1.50	1.10–2.11	0.019*
< 3.5	2.45	1.65–3.63	< 0.001*
Blood platelets (10 <sup>9</sup> /L)			
100–299	Ref.	Ref.	
< 100	1.97	1.42–2.72	< 0.001*
≥ 300	0.61	0.18–2.13	0.441
Congestive heart failure (yes vs. no)	1.57	1.16–2.11	0.004*
Pulse pressure (mmHg)			
≤ 63	Ref.	Ref.	
> 63	1.41	1.01–1.96	0.042*

## Discussion

In this large prospective study of 1,427 Chinese HD patients, we reported the all-cause mortality rate and explored related risk factors. The overall mortality rate was 8.8 per 100 patient-years in our patients. Cardiovascular death was the leading cause of death, which account for more than half of all deaths. Patients that were older, with lower Alb, blood platelets, higher PP and had a history of CHF had a higher risk of all-cause mortality.

We reported a lower overall mortality rate compared with other western DOPPS countries, such as North America (14.3 per 100 patient-years) and Europe countries (13.1 per 100 patient-years)[9]. But it was a little higher than that in Japan (7.87 per 100 patient-years)[10]. Prior DOPPS analyses noted that many beneficial dialysis practices (such as high use of arteriovenous fistula, longer or more frequent dialysis sessions, more effective volume management, good patient compliance, mineral and bone disorder control) were more common in Japan than in other countries[11]. However, in European and North American countries, kidney transplantation was more common among ESKD patients than Asian countries, such as China and Japan. In other words, many healthier and younger patients have opted for kidney transplantation instead of maintenance dialysis treatment in those countries. Therefore, transplantation may deplete the dialysis pool of healthier patients in North America and Europe, but not in China and Japan[11]. Although this may have impact on mortality rate among countries, mortality rate differences among countries may still exist after this factor adjusted.

Some widely recognized risk factors found in our results were consistent with previous researches, such as aging, low Alb, comorbidities. Not surprisingly, aging was known to be a significant risk factor for death. And the guideline of Kidney Disease Outcomes Quality Initiative (K/DOQI) suggested that the optimal serum Alb level of chronic kidney disease (CKD) patients was equal to or greater than the lower limit of the normal range (approximately 4.0 g/dL)[12]. We had 42.0% of our patients with serum Alb  $\geq$  4g/l, and 83.6% patients  $\geq$  3.5g/l. Patients with Alb  $\geq$  4g/l also have survival benefits, compared with patients with Alb in 3.5–3.9 g/l. Serum Alb was regarded as the reflection of visceral protein stores, so it can act as a marker of protein malnutrition. Malnutrition was a strong contributor for increasing mortality in HD patients[13, 14]. Deaths due to cardiovascular and infectious causes were increased with malnutrition and hypoalbuminemia[15, 16]. Therefore, for most patients, they should try to make serum Alb meet the target of 4 g/l, and for patients with Alb < 3.5g/l, special attention should be paid to improving their nutritional status. Comparing the clinical data of the 2 groups of patients, we found that patients who died combined with more comorbidities than those who survived. In the Cox model, patients with a history of CHF had higher mortality risk. As more than half of our patients died from cardiovascular causes, patients with a history of cardiovascular disease have a higher risk of death than other patients.

In our results, patients with low platelet counts ( $< 100 \times 10^9/L$ ) had a higher risk of all-cause mortality. Thrombocytopenia may have serious consequences, such as increasing the risk of internal and external bleeding, delaying in wound healing and coagulation defects. Previous studies have reported that

thrombocytopenia was associated with an increased risk of all-cause death and cardiovascular death in general populations and patients with lung disease[17–19]. In one study about the association about mean platelet volume (MPV) and mortality in incident HD patients, the author also showed that lower baseline platelet counts were associated with higher mortality risk across all multivariable models, which was in line with our findings[20]. Furthermore, there was a prothrombotic adverse drug reaction called Heparin-induced thrombocytopenia (HIT)[21]. Heparin is a common anticoagulant used during HD period to prevent clotting. Some patients may produce platelet-activating antibodies when they received heparin[22], and show unusual clinical features, such as thrombocytopenia, sometimes accompanied by disseminated intravascular coagulation and microvascular thrombosis. Several studies showed that HD patients with HIT were at a higher risk of cardiovascular mortality and arteriovenous fistula thrombosis than patients without HIT[23, 24].

And high PP was an independent predictor of all-cause mortality. Compared with  $PP < 63\text{mmHg}$ ,  $PP \geq 63\text{mmHg}$  was associated with a 64.8% increase in hazard ratio for death. Regarding blood pressure control, PP was not widely considered as a risk factor in ESKD patients. But several studies reported that PP was associated with all-cause mortality and/or cardiovascular mortality in HD patients[25, 26]. Meanwhile, cardiac dysfunction was a widespread problem in ESKD patients, and cardiovascular death was the major cause in those patients. Elevated PP was usually due to increased central aortic stiffness and accompanied by increased pulse-wave velocity. Said et al found that PP was associated with an increased risk of developing cardiovascular disease and cardiovascular mortality in a large community-based population[27]. Elevated pressure during systole induce left ventricular hypertrophy, then lead to left ventricular failure, whereas lower pressure throughout diastole had the possibility to limit coronary perfusion and lead to ischemia[25]. This may contribute to the high prevalence of cardiovascular disease in ESKD patients[28].

Overall, the mortality rate of our HD patients was comparatively low compared with other countries. Among China and other countries, especially developed countries, there were obvious differences in race, lifestyle, economic status, medical insurance policies and so on. Whether the risk of mortality is affected by these factors and how they affect need further investigation. Therefore, it was important to explore the risk factors related to death in Chinese HD patients and the modifiable dialysis patterns.

However, our study had several limitations. Firstly, this is an observational study which might have inherent shortcomings such as selection bias and confounding factors. Secondly, the limited number of deaths in our study makes it impossible for us to perform some more detailed subgroup analysis. Thirdly, the China DOPPS study only included patients from three major cities. We didn't include patients receiving HD treatment in smaller cities or rural areas, and their conditions may be worse than what we reported. Therefore, the results can not represent for the whole country. Even though, the results of this study have irreplaceable significance for us to understand the current situation of Chinese HD patients and to explore modifiable practice patterns to improve patients' survival.

In conclusion, results in this study were important and complement to previous findings and added new knowledge to the understanding of mortality risks for prevalent HD patients globally. Our analysis highlighted that there were some modifiable risk factors for Chinese patients' survival. Attention should also be paid to patients who were older, with lower Alb, low platelet counts, higher PP, and had a history of CHF.

## Abbreviations

DOPPS, China Dialysis Outcomes and Practice Patterns Study; HD, hemodialysis; ESKD, end stage kidney disease; PP, pulse pressure; Alb, albumin; USRDS, United States Renal Data Services; ERA-EDTA, European Renal Association-European Dialysis and Transplant Association; RRT renal replacement therapy; SD, standard deviation; Hgb, hemoglobin; CHF, congestive heart failure; FCS, fully conditional specification; DBP, diastolic blood pressure; K/DOQI, Kidney Disease Outcomes Quality Initiative; CKD, chronic kidney disease; MPV, mean platelet volume; HIT, Heparin-induced thrombocytopenia;

## Declarations

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Peking University People's Hospital (ethical approval number: 2018PHB028-01). All patients signed the written informed consent.

### Consent for publication

Not Applicable.

### Availability of data and material

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

### Competing interests

The authors declare that they have no competing interests.

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### Authors' Contributions

XZ, LZ contributed to conception and design of the research; XZ, QN analyzed the data; XZ, QN, LG, LZ interpreted the results of experiments; XZ, QN, LG wrote the drafted manuscript; ZN, XC, YC, FFH, XL, LZ,

JZ, BB, BR edited and revised the manuscript; LG, LZ have primary responsibility for the final content. All authors have read and approved the manuscript.

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