# **BMJ Open** Mortality and associated risk factors between young and elderly maintenance haemodialysis patients: a multicentre retrospective cohort study in China

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#### ABSTRACT

**Objectives** Mortality and associated risk factors in young and elderly haemodialysis patients with end-stage kidney disease (ESKD) have not been well examined in China. Therefore, we aimed to assess the all-cause mortality and risk factors associated with all-cause mortality between young and elderly haemodialysis patients in China.

**Design** A population-based multicentre retrospective cohort study.

**Setting** Using the Dialysis Initiation based on Fuzzy mathematics Equation study data, patients with ESKD undergoing maintenance haemodialysis from 24 centres in China from 1 January 2008 to 30 September 2015.

**Participants** 1601 enrolled patients with ESKD were categorised into young group (18–44 years old) and elderly (≥60 years old) group.

**Outcome measures** The primary outcome was all-cause mortality. We estimated overall survival using a log-rank test. Cox proportional hazard regression analysis was implemented to identify risk factors and HR associated all-cause mortality.

**Results** During a mean follow-up of  $48.17\pm25.59$  months, of the 1601 subjects, 319 (19.92%) patients death, including 64 (9.97%) in young group and 255 (26.59%) in elderly group, respectively. The cumulative survival in elderly group was lower than young group (Log Rank tests=63.31, p<0.001). Multivariate Cox proportional hazards analysis showed the cardiovascular disease (HR, 2.393; 95% Cl 1.532 to 3.735; p<0.001), cerebrovascular disease (HR, 2.542; 95% Cl 1.364 to 4.739; p=0.003) and serum albumin<3.5 g/dL (HR, 1.725; 95% Cl 1.091 to 2.726; p=0.020) at the haemodialysis initiation were associated with increased risk of all-cause mortality in elderly groups; however, the cardiovascular disease only was associated with increased risk of all-cause mortality in young groups.

**Conclusions** The all-cause mortality of elderly haemodialysis patients were higher than young haemodialysis patients in China. Identified risk factors associated all-cause mortality may inform development of age-appropriate treatment, intervention strategies and improve survival prognosis of this unique population.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ A population-based multicentre retrospective cohort study for assessing the all-cause mortality and associated risk factors between young and elderly haemodialysis patients.
- $\Rightarrow$  Has a relatively long follow-up period.
- ⇒ Using the Dialysis Initiation based on Fuzzy mathematics Equation study data in China.
- ⇒ Limitations including some important variables were missing from patient's baseline data, many variables assessed as risk factors were not updated regularly and the selection bias of the included patients were from high-quality haemodialysis units in developed areas mainland China.

## **INTRODUCTION**

Haemodialysis is the major modality of renal replacement therapy for patients with endstage kidney disease (ESKD) worldwide,<sup>1</sup> approximately 553 000, accounting for 91.0% of all dialysis patients in China.<sup>2</sup> The incidence of patients with ESKD undergoing maintenance haemodialysis with an annual increasing rate of 52.9% in China.<sup>3</sup> The numbers of elderly haemodialysis patients has been increasing in recent years; meanwhile, young patients also account for significant proportion in haemodialysis patients.<sup>4–8</sup>

The 2021 United States Renal Data System (USRDS) Annual Data Report indicated that adjusted incidence of ESKD among individuals aged 65–74 years was 1307 pmp and among individuals aged more than 75 years was 1587 pmp.<sup>9</sup> The 2016 annual data report from China Kidney Disease Network (CK-NET) showed that among individuals aged 18–44 years, the incidence of dialysis patients was 66.94 pmp, among individuals aged more than 65 years, the incidence of dialysis patients was 286.31 pmp.<sup>8</sup> As expected, elderly haemo-dialysis patients were associated with higher mortality risk than the young haemodialysis

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patients,<sup>10</sup> The Dialysis Outcomes and Practice Patterns Study showed that elderly haemodialysis patients aged more than 75 years had a threefold to sixfold higher mortality risk than younger patients aged less than 45 years, adjusted for demographics and comorbidities.<sup>11</sup> The 2021 USRDS Annual Data Report showed that elderly dialysis patients with more than 65 years old had significant higher mortality rate than younger patients with less than 44 years of age.<sup>9</sup> The reason for the difference in mortality of haemodialysis patients may be due to the most elderly haemodialysis patients suffered from more common cardiovascular disease, malignancies, frailty, malnutrition, diabetes and poorer quality of life versus younger haemodialysis patients.<sup>10–13</sup> To improve the outcomes of haemodialysis patients, it is critical to identify the contributions of potentially risk factors. However, the mortality rate and associated risk factors between young and elderly undergoing haemodialysis patients have not been well assessed in China. Therefore, the objective of this retrospective cohort study was to evaluate the clinical characteristics, all-cause mortality and associated risk factors between young and elderly patients with ESKD undergoing maintenance haemodialysis in China.

#### MATERIAL AND METHODS Data sources

We conducted this population-based multicentre retrospective cohort study from the database of Dialysis Initiation based on Fuzzy mathematics Equation study (DIFE),<sup>14</sup> which focuses on adults patients with ESKD undergoing maintenance haemodialysis in China and aims to establish a novel equation of timing of haemodialysis initiation based on a fuzzy mathematical method.<sup>15 16</sup>

#### **Study participants**

The enrolled patients with ESKD undergoing maintenance haemodialysis from 24 haemodialysis centres in China from 1 January 2008 to 30 September 2015. Patients who met the inclusion criteria and did not meet the exclusion criteria were included in our study. The inclusion criteria were the following: (1) 18–44 or more than 60 years old, (2) undergoing haemodialysis treatment for more than 3 months and (3) haemodialysis treatment for more than 3 months and (3) haemodialysis treatment with three times a week. The exclusion criteria were the following: (1) patients undergone peritoneal dialysis or kidney transplantation before or after haemodialysis, (2) patients with the presence of chronic infection defined as lasted more than 3 months, including bacterial, viral, fungal infection and so on, (3) liver cirrhosis and (4) cancer diseases.

The enrolled patients were categorised into young group (18–44 years old) and elderly group ( $\geq 60$  years old) according to their age on the initiation of the haemodialysis. Patients were followed up to 30 September 2016, and the primary outcome was all-cause mortality of haemodialysis patients.

All started haemodialysis and survival prognostic data of patients were obtained and reviewed from electronic medical records of outpatient and inpatient of 24 haemodialysis centres. The demographics data included age, gender, height, weight, body mass index (BMI). Clinical data included date of haemodialysis initiation, type of haemodialysis associated vascular access, causes of ESKD. Nutritional status were assessed using serum albumin and Geriatric Nutritional Risk Index (GNRI).<sup>17</sup> Comorbid conditions were assessed using the Charlson comorbidity index (CCI).<sup>18</sup> Heart failure defined according to the New York Heart Association functional class. The laboratory tests were performed within 1 month before haemodialysis initiation, and the tested items included haemoglobin, blood urea nitrogen, creatinine, uric acid, serum sodium, serum potassium, serum calcium, serum phosphorus, carbon dioxide combining power, serum albumin, cholesterol, parathyroid hormone. The estimated glomerular filtration rate (eGFR) was calculated based on serum creatinine at the time of haemodialysis initiation using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.<sup>19</sup> The survival time of the patients was measured in months and was calculated from the date of haemodialysis initiation to the date of death or to the final follow-up date.

#### Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

#### **Statistical analysis**

Continuous variables with normal distribution were expressed as means and SD, whereas variables with nonnormal distribution were expressed as medians and IQRs, and categorical variables were presented as frequencies with percentages. A student independent t-test or a Mann-Whitney U test was used for analysis in the case of normally or non-normally distributed continuous variables. Categorical variables data were compared using  $\chi^2$  tests or Fisher's exact test. A multiple imputation approach was applied to process missing data. Patients were censored because of loss to follow-up, withdraw or survival to end of the study. The survival prognosis was compared using the Kaplan-Meier survival curves and log-rank test. The HR of mortality of elderly patients relative to young patients was assessed using univariate and multivariate Cox proportional hazards regression analysis. The risk factors associated all-cause mortality were assessed using univariate and multivariable Cox proportional hazards regression analysis, adjusting for sex, hypertension, diabetes, heart failure, cardiovascular disease, cerebrovascular disease, eGFR, serum albumin, GNRI and CCI scores. All hypothesis tests were evaluated using two-sided with 95% CIs and p<0.05 indicated statistical significance. All analyses were performed with SPSS software (V.19.0, IBM, Armonk, New York, USA) .

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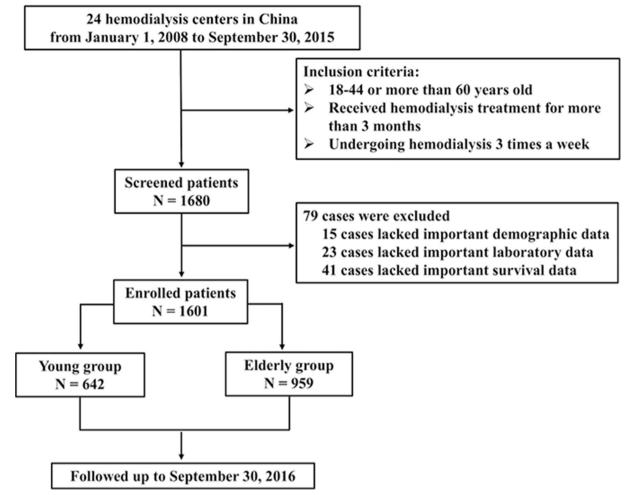


Figure 1 Flowchart of the study.

## RESULTS

#### **Participants**

A total of 1680 young and elderly patients with ESKD were screened. A total of 79 patients were excluded as lacking of important demographic, laboratory and survival data. Finally, a total of 1601 patients were subsequently enrolled in our study. The research flowchart is shown in figure 1.

#### **Baseline patient characteristics**

The baseline demographics and clinical characteristics of the young and elderly undergoing haemodialysis patients are described in table 1. A total of 642 young patients and 959 elderly patients were enrolled in this study. The young and elderly patients had different sex and BMI distribution, 417 males (64.95%) in young group compared with 535 males (55.79%) in elderly group, respectively ( $X^2$ =13.404, p<0.001). The young patients had a higher average BMI than the elderly patients (p=0.014). There were also obviously differences of causes of ESKD, lower prevalence of diabetes (7.32%), higher glomerulonephritis (44.39%) in young group compared with the higher prevalence of diabetes (29.82%), lower glomerulonephritis (15.53%) in the elderly group ( $X^2=233.6$ , p<0.001). At the haemodialysis initiation, the elderly patients showed a higher mean

eGFR levels than the young patients  $(6.37\pm3.30 \text{ mL/min}/1.73 \text{ m}^2 \text{ vs } 5.25\pm3.02 \text{ mL/min}/1.73 \text{ m}^2, \text{ p}<0.001)$ . The young patients showed significantly higher levels of diastolic pressure, serum creatinine, serum phosphorus, serum albumin and parathyroid hormone. However, the elderly patients showed higher levels of CCI scores, serum calcium, haemoglobin and serum sodium.

## Mortality

Of the 1601 subjects, the mean follow-up duration was  $48.17\pm25.59$  months, 319 (19.92%) patients death, including 64 (9.97%) in young group and 255 (26.59%) in elderly group, the HR of mortality of elderly patients relative to young patients were assessed using Cox proportional hazards regression analysis. Multivariate Cox proportional hazards analysis showed that the HR of overall all-cause mortality of elderly patients relative to young patients, 7.129 (95% CI 3.827 to 13.279, p<0.001), the HR of 1-year mortality of elderly patients relative to young patients, 3.922 (95% CI 1.367 to 11.249, p<0.001), the HR of 3-year mortality of elderly patients relative to young patients, 6.543 (95% CI 3.002 to 14.260, p<0.001). The comparison of mortality between young and elderly haemodialysis patients is summarised in table 2.

Variables	Young group (n=642)	Elderly group (n=959)	P value
Age (year)	34.31±6.80	68.55±6.53	< 0.001
Male (%)	417 (64.95%)	535 (55.79%)	< 0.001
Body mass index (kg/m <sup>2</sup> )	25.34±3.32	24.45±3.82	0.014
Systolic pressure (mm Hg)	152.61±24.66	153.38±23.05	0.093
Diastolic pressure (mm Hg)	92.94±16.28	81.64±13.15	<0.001
Cause of ESKD (%)			
Diabetic nephropathy	47 (7.32%)	286 (29.82%)	< 0.001
Hypertensive nephropathy	56 (8.72%)	168 (17.51%)	
Glomerulonephritis	285 (44.39%)	149 (15.53%)	
Others	254 (39.56%)	356 (37.12%)	
Comorbidity (%)			
Diabetes	84 (13.08%)	446 (46.51%)	<0.001
Hypertension	255 (39.72%)	688 (71.74%)	<0.001
Coronary artery disease	66 (10.28%)	303 (31.59%)	< 0.001
Heart failure	183 (28.50%)	378 (39.42%)	< 0.001
Cerebrovascular disease	15 (2.33%)	68 (7.09%)	< 0.001
CCI Scores	2.36±0.57	5.57±0.75	< 0.001
Types of vascular accesses			
AVF	136 (21.18%)	244 (25.44%)	0.055
TCC	59 (9.19%)	103 (10.74%)	
NTC	447 (69.63%)	612 (63.82%)	
Laboratory tests			
Haemoglobin (g/L)	81.60±22.50	85.20±19.50	0.001
Blood urea nitrogen (mg/dL)	98.30±40.97	81.44±32.66	< 0.001
Serum creatinine (mg/dL)	12.44±5.39	8.33±3.24	<0.001
eGFR (mL/min/1.73 m <sup>2</sup> )	5.25±3.02	6.37±3.30	<0.001
Serum albumin (g/dL)	3.51±0.65	3.43±0.61	0.014
Serum sodium (mmol/L)	138.65±4.01	139.07±4.71	0.007
Serum potassium (mmol/L)	4.79±0.92	4.77±0.96	0.336
Serum phosphorus (mmol/L)	2.23±0.79	1.84±0.59	< 0.001
Serum calcium (mmol/L)	1.99±0.40	2.01±0.36	0.001
Parathyroid hormone (pg/mL)	352.86±324.60	281.88±263.90	0.002

AVF, arteriovenous fistula; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; NTC, non-tunnelled catheter; TCC, tunnelled cuffed catheter.

## **Survival prognosis**

The Kaplan-Meier survival curve of all-cause mortality between young and elderly displayed the overall cumulative survival was lower in elderly group than young group (Log Rank tests=63.31, p<0.001), which are shown in figure 2. The median survival time of young and old patients was 93.59 and 78.63 months, respectively. The HR of mortality of elderly patients relative to young patients, 2.884 (95% CI 2.309 to 3.602, p<0.001). To assess the effects of the timing of haemodialysis initiation on survival of young and elderly patients, patients were divided into the early dialysis starting subgroup (eGFR>5 mL/min.1.73 m<sup>2</sup>) and the late dialysis starting subgroup (eGFR $\leq$ 5 mL/ min.1.73 m<sup>2</sup>) according to eGFR at the initiation of haemodialysis. The Kaplan-Meier survival curve showed that overall cumulative survival was lower in the elderly group than the young group no matter whether in the early dialysis starting subgroup (Log Rank tests=36.06, p<0.001) or in the late dialysis starting subgroup (Log Rank tests=23.16, p<0.001), which are shown in figure 3A and figure 3B, respectively. In the early dialysis starting subgroup, the HR of mortality of elderly patients relative to young patients, 3.428, (95% CI 2.525 to 4.653, p<0.001). In the late dialysis starting subgroup, the HR of mortality of elderly patients relative to young patients, 2.399, (95% CI 1.714 to 3.358, p<0.001).

Table 2 The c	comparison of mo	ortality betwe	Table 2         The comparison of mortality between young and elderly haemodialysis patients	erly haemodi	ialysis patient	S				
	Young group		Elderly group		Univariate	Univariate analysis		Multivari	Multivariate analysis	
Variables	Event (%)	Total	Event (%)	Total	HR	95% <b>CI</b>	P value	НВ	95% <b>CI</b>	P value
Overall mortality	64 (9.97)	642	255 (26.59)	959	2.888	2.195 to 3.798	<0.001	7.129	3.827 to 13.279	<0.001
1-year mortality 17 (2.65)	v 17 (2.65)	642	53 (5.53)	959	2.115	1.225 to 3.652	0.007	3.922	1.367 to 11.249	<0.001
3-year mortality 48 (10.50)	y 48 (10.50)	457	149 (20.84)	715	2.09	1.510 to 2.894	<0.001	6.543	3.002 to 14.260	<0.001
Cox regression v eGFR, estimated	Cox regression was used to calculate HR, eGFR, estimated glomerular filtration rate.	te HR, adjustn n rate.	nent for sex, hyperter	nsion, diabete	ss, heart failure,	, cardiovascular diseas	e, cerebrovascu	lar disease, eG	Cox regression was used to calculate HR, adjustment for sex, hypertension, diabetes, heart failure, cardiovascular disease, cerebrovascular disease, eGFR and serum albumin. eGFR, estimated glomerular filtration rate.	

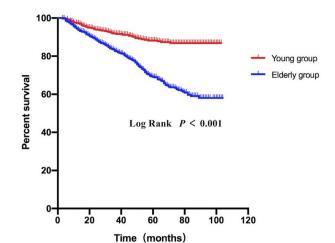


Figure 2 Kaplan-Meier survival curve between the young and elderly groups. The elderly group survival was significantly lower than young group (Log Rank tests=63.31, p<0.001).

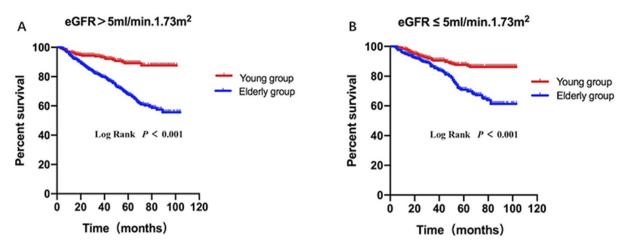
#### **Risk factors of all-cause mortality**

The risk factors associated all-cause mortality of young haemodialysis patients were assessed using Cox proportional hazards regression analysis. Univariate Cox proportional hazards analysis showed that cardiovascular disease (HR, 3.046; 95% CI 1.178 to 7.875; p=0.022) was the risk factor associated all-cause mortality in young haemodialysis patients. Multivariate Cox proportional hazards analysis with a forward stepwise regression method (Forward LR) showed that only cardiovascular disease (HR, 3.349; 95% CI 1.059 to 10.587; p=0.040) was the risk factor associated all-cause mortality in young haemodialysis patients, which are shown in table 3.

The risk factors associated all-cause mortality of elderly haemodialysis patients were assessed using Cox proportional hazards regression analysis. Univariate Cox proportional hazards analysis showed that cardiovascular disease, cerebrovascular disease, serum albumin<3.5 g/ dL, 82≤GNRI<92, GNRI<82 and CCI≥6 were the risk factors associated all-cause mortality in elderly haemodialysis patients. However, multivariate Cox proportional hazards analysis with a forward stepwise method (Forward LR) showed that cardiovascular disease (HR, 2.393; 95% CI 1.532 to 3.735; p<0.001), cerebrovascular disease (HR, 2.542; 95% CI 1.364 to 4.739; p=0.003) and serum albumin<3.5 g/dL (HR, 1.725; 95% CI 1.091 to 2.726; p=0.020) were the risk factors associated all-cause mortality in elderly haemodialysis patients, which are shown in table 4.

#### DISCUSSION

The longitudinal nationwide cohort study was the first to assess that the clinical characteristics, mortality rate and risk factors associated all-cause mortality between young and elderly patients undergoing maintenance haemodialysis in China. Our study demonstrated that the overall mortality rate of elderly haemodialysis patients was higher



**Figure 3** Kaplan-Meier survival curve between young and elderly patients groups in the early and late dialysis starting subgroups. (A) The elderly patients survival was significantly lower than young patients in early dialysis starting subgroup with eGFR>5.0 mL/min 1.73 m<sup>2</sup> (Log Rank tests=36.06, p<0.001). (B) The elderly group survival was significantly lower than young group in late dialysis starting subgroup with eGFR $\leq$ 5.0 mL/min 1.73 m<sup>2</sup> (Log Rank tests=23.16, p<0.001). eGFR, estimated glomerular filtration rate.

than that of young haemodialysis patients (26.59% vs 9.97%), the 1-year mortality rate of young and elderly patients was 2.65% and 5.53%, and the 3-year mortality rates of young and elderly patients were 10.50% and 20.84%, respectively. Our findings were consistent with

previous studies that the elderly patients undergoing haemodialysis had a higher mortality risk.<sup>20 21</sup> Based on the USRDS registry, the 1-year mortality rate after dialysis initiation for older adults patients was currently approximately 30%.<sup>22</sup> A recent study showed that the mortality

Table 3 Univariate and multivariate Cox proportional hazards regression analysis of risk factors associated with all-o	ause
mortality of young patients	

	Univariate a	nalysis		Multivaria	ate analysis	
Variables	HR	95% <b>CI</b>	P value	HR	95% <b>CI</b>	P value
Sex						
Female	Reference					
Male	1.58	0.907 to 2.752	0.106			
Hypertension	1.558	0.502 to 4.836	0.443			
Diabetes	0.772	0.333 to 1.791	0.547			
Heart failure	0.574	0.306 to 1.074	0.083			
Cardiovascular disease	3.046	1.178 to 7.875	0.022	3.349	1.059 to 10.587	0.040
Cerebrovascular disease	3.024	0.397 to 23.052	0.286			
eGFR level						
eGFR>5mL/min 1.73 m <sup>2</sup>	Reference					
eGFR≤5 mL/min 1.73 m²	1.178	0.710 to 1.955	0.525			
Serum albumin						
≥3.5 g/dL		Reference				
<3.5g/dL	1.07	0.654 to 1.751	0.788			
CCI scores						
CCI (1 to 3)		Reference				
CCI (4 to 5)	0.7	0.171 to 2.865	0.62			

Cox regression was used to calculate HR, adjustment for sex, hypertension, diabetes, heart failure, cardiovascular disease, cerebrovascular disease, eGFR, serum albumin and CCI scores.

CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate.

 Table 4
 Univariate and multivariate Cox proportional hazards analysis of risk factors associated with all-cause mortality of elderly patients

Variables	Univariate analysis			Multivariate analysis		
	HR	95% <b>CI</b>	P value	HR	95% <b>CI</b>	P value
Sex						
Female	Referenc	e				
Male	1.15	0.089 to 1.476	0.273			
Comorbidity						
Hypertension	0.981	0.672 to 1.432	0.922			
Diabetes	1.104	0.863 to 1.432	0.43			
Heart failure	1.245	0.969 to 1.600	0.086			
Cardiovascular disease	1.479	1.069 to 2.046	0.018	2.392	1.532 to 3.735	<0.001
Cerebrovascular disease	2.901	1.896 to 4.438	<0.001	2.542	1.364 to 4.739	0.003
eGFR level						
eGFR>5mL/min 1.73 m <sup>2</sup>	Referenc	e				
eGFR≤5 mL/min.1.73 m <sup>2</sup>	0.812	0.630 to 1.046	0.107			
Serum albumin						
≥3.5g/dL		Reference			Reference	
< 3.5 g/dL	1.584	1.235 to 2.031	<0.001	1.725	1.091 to 2.726	0.020
GNRI						
GNRI>98		Reference				
92≤GNRI ≤ 98	1.232	0.800 to 1.898	0.343			
82≤GNRI < 92	1.625	1.094 to 2.414	0.016			
GNRI<82	2.063	1.316 to 3.234	0.002			
CCI scores						
CCI (1 to 3)		Reference				
CCI (4 to 5)	1.339	0.646 to 2.775	0.432			
CCI (≥6)	3.038	1.494 to 6.177	0.002			

Cox regression was used to calculate HR, adjustment for sex, hypertension, diabetes, heart failure, cardiovascular disease, cerebrovascular disease, eGFR, serum albumin, GNRI and CCI scores.

CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index.

rate among patients more than 65 years old was 54.5% at the first year.<sup>23</sup> The 1-year mortality rate of the elderly aged 65–74 years old was 28%, more than 75 years old was 41%.<sup>24</sup> Obviously, the 1-year mortality of haemodialysis patients in our study was significantly lower than that in USA, it may be associated with the majority of enrolled patients were from higher quality haemodialysis centres with higher survival quality.

Our study showed the eGFR of initiation of haemodialysis was  $5.25\pm3.02 \,\text{mL/min}/1.73 \,\text{m}^2$  in the young group compared with  $6.37\pm3.30 \,\text{mL/min}/1.73 \,\text{m}^2$  in the elderly group, which indicated that the timing of haemodialysis initiation of elderly patients was earlier than young patients. Our findings were consistent with previous studies which timing of haemodialysis initiation of elderly patients was earlier than young patients.<sup>25</sup> The possible reasons may be associated with the elderly patients with ESKD may be more likely to start earlier haemodialysis due to more ESKD complications, comorbidity, poor nutritional status and worsen tolerance to uraemia symptoms than young patients with ESKD.<sup>4 26–28</sup> Although our study demonstrated that the timing of haemodialysis initiation of elderly patients was earlier than young patients; however, the overall mortality was higher in elderly patients compared with young patients, and the findings were similar to previous studies that early initiation of haemodialysis was not associated with an improvement in survival or clinical outcomes.<sup>20 29–31</sup>

The timing of haemodialysis initiation is one of the important factors influencing survival prognosis of patients with ESKD.<sup>32 33</sup> Previous studies did not assess the impaction of timing of dialysis on survival prognosis in different age patients especially between young and elderly patients together. The Kaplan-Meier survival curve showed that overall survival was lower in elderly than young patients no matter whether in the early dialysis

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starting subgroup or in the late dialysis starting subgroup. Multivariate Cox regression indicated that the eGFR was not the risk factor associated all-cause mortality in young or elderly haemodialysis patients. Therefore, the timing of dialysis initiation based on eGFR did not affect survival outcomes in elderly and young haemodialysis patients.

A multivariate Cox regression model of 2920 patients with uraemia demonstrated that the risk of death increased 1.25 times for each additional 10 years of age of dialysis patients.<sup>34</sup> The poor prognosis of elderly patients may be associated with primary diseases, higher prevalence of cardiovascular disease, diabetes, frailty, cognition disorder, higher levels of CCI scores, lower levels of serum albumin, serious dialysis complications and reduced life expectancy together, which may lead to increased mortality risk compared with younger dialysis patients.<sup>10-13</sup> To assess the risk factors associated all-cause mortality between young and elderly undergoing haemodialysis patients in China, we calculated HR using univariate and multivariable Cox proportional hazards regression analysis, adjusting of the demographics and clinical characteristics of the patients, including sex, hypertension, diabetes, heart failure, cardiovascular disease, cerebrovascular disease, eGFR, serum albumin, GNRI and CCI scores. Our study indicated young and elderly haemodialysis patients with cardiovascular disease on the haemodialysis initiation had a significantly increased risk of all-cause mortality than those without such disease. As we know, cardiovascular disease was a leading cause of death among patients with ESKD, accounting for nearly 50% of deaths in haemodialysis population,<sup>35 36</sup> and accounted for nearly 40% of deaths in young adults with incident ESKD based on from USRDS data.<sup>37</sup> The 2021 USRDS Annual Data Report showed that arrhythmia or cardiac arrest accounted for 34.7% of deaths, and cardiovascular disease, collectively, was the cause of death in 42.5%.<sup>9</sup>

A systematic review and meta-analysis showed that lower serum albumin was the risk of mortality and cardiac death in patients undergoing haemodialysis.<sup>38</sup> Our study also demonstrated that the significantly increased risk of all-cause mortality in elderly haemodialysis patients with serum albumin less than 3.5 g/dL than those with serum albumin  $\geq 3.5 \text{ g/dL}$  using multivariable Cox proportional hazards regression analysis. However, serum albumin was not associated with increased risk of all-cause mortality in young haemodialysis patients.

The present study has the following several aspects limitation. First, some important variables were missing from patient's baseline data, such as left ventricular ejection fraction, left ventricular mass index, brain natriuretic peptide and many variables assessed as risk factors were not updated regularly, and the data were collected only at the baseline and at the end of the study. Additionally, the selection bias of the included patients mainly were from high-quality haemodialysis units in developed areas, no coverage of community haemodialysis units with poor medical and economic conditions. Moreover, not all potential risk factors were available for analysis, including residual renal function, haemodialysis prescription, medications. Therefore, in the future, we will conduct a multicentre, large-sample prospective randomised controlled study including comprehensive and detailed variables, haemodialysis centres covering different regions, medical and economic levels in mainland China,

#### CONCLUSION

The all-cause mortality of elderly haemodialysis patients were higher than young haemodialysis patients in China. Cardiovascular disease was the risk factors associated all-cause mortality of young and elderly haemodialysis patients, cerebrovascular disease and lower serum albumin were the risk factor associated all-cause mortality of elderly haemodialysis patients. Identified risk factors associated all-cause mortality could be helpful to inform development of age-appropriate treatment and intervention strategies for undergoing haemodialysis patient to improve survival prognosis of this unique population.

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