

The interaction analysis between advanced age and longer dialysis vintage on the survival of patients receiving maintenance hemodialysis

Journal of International Medical Research

50(4) 1–12

© The Author(s) 2022


Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/03000605221088557

journals.sagepub.com/home/imr



Yong Wu^{1,*} , Bihong Huang^{1,*},
Weichen Zhang¹,
Khawlah Ali Ahmed Farhan², Siyao Ge¹,
Mengjing Wang¹, Qian Zhang¹ and
Minmin Zhang¹

Abstract

Objective: To compare the all-cause mortality of aged and younger patients undergoing maintenance hemodialysis (MHD) over the long or short term, and to identify independent risk factors.

Methods: We performed a retrospective cohort study using the medical records of 181 patients undergoing MHD. We compared the clinical characteristics and laboratory data of survivors and participants who died, according to their age and the duration of MHD. Binary stepwise logistic regression was used to identify independent risk factors for all-cause mortality.

Results: Cardiovascular and cerebrovascular diseases were the principal causes of mortality. The number of aged participants with hypertensive nephropathy as their primary kidney disease was significantly higher than the number of younger participants. The proportion with chronic glomerulonephritis was significantly higher for participants undergoing long-term MHD. Logistic regression analysis revealed that low body mass index, single-pool Kt/V, serum albumin, platelet count, and total iron-binding capacity; and high intact parathyroid hormone and N terminal pro B type natriuretic peptide were independent risk factors for all-cause mortality.

Conclusions: Aged patients are more susceptible to hypertensive nephropathy than younger patients. In addition, the survival of patients with chronic glomerulonephritis undergoing MHD is superior to that of those with hypertensive or diabetic nephropathy.

*These authors contributed equally to this work.

Corresponding author:

Minmin Zhang, Department of Nephrology, Huashan Hospital, Fudan University, 12 Middle Wulumuqi Road, Shanghai 200040, China.

Email: zhang_minmin@fudan.edu.cn

¹Department of Nephrology, Huashan Hospital, Fudan University, Shanghai, China

²School of Medicine, Zhejiang University, Hangzhou, China



Keywords

Maintenance hemodialysis, advanced age, duration of dialysis, all-cause mortality, survival, chronic glomerulonephritis, nephropathy

Date received: 1 October 2021; accepted: 2 March 2022

Introduction

Chronic kidney disease (CKD) is a major public health problem worldwide, and is responsible for hospitalization, morbidity, and mortality when it progresses to end-stage renal disease (ESRD), as well as a huge economic burden.^{1,2} Cardiovascular disease (CVD) and infections are the major causes of mortality in patients with CKD, together accounting for up to 70% of all deaths.^{3,4} Specifically, cerebrovascular accidents (CVAs) are associated with a poorer prognosis in patients with CKD. An annual report by the United States Renal Data System (USRDS) showed that the overall prevalence of CVA in patients with CKD was 16.1% and the 2-year survival rate of patients with ESRD and CVA was just 64.1%.⁵

Maintenance hemodialysis (MHD) is a form of renal replacement therapy that improves the prognosis and prolongs the survival of patients with ESRD. However, previous studies have shown a close association between long-term dialysis and mortality in patients undergoing MHD.^{6,7} Furthermore, a large-scale cohort study conducted in Japan showed that the duration of dialysis has differing associations with specific causes of mortality: MHD is associated with a higher risk of infection-related mortality than CVD-related mortality, especially in patients undergoing long-term MHD.⁸ In addition, advanced age is associated with shorter survival in patients undergoing MHD.⁹ Older patients are more likely to die of their primary disease when initiating dialysis and they are

also more likely to experience various complications of dialysis.¹⁰ Previous studies have also shown that advanced age and long-term dialysis are associated with the progression of MHD in patients.^{8–10} However, it has not been determined whether there is a difference in the all-cause mortality of aged and younger patients undergoing MHD or among patients who undergo dialysis for differing durations.

We aimed to perform a retrospective cohort study to identify the causes of death and the primary diseases of patients of various ages and durations of dialysis who are undergoing MHD, and to identify independent risk factors for all-cause mortality, with the aim of improving survival and improving the efficacy of hemodialysis.

Methods

Study design and participants

We conducted a retrospective cohort study of patients undergoing MHD three times weekly at the Blood Purification Center of Huashan Hospital, affiliated with Fudan University, between 1 January 2014 and 31 December 2018. The exclusion criteria were: age <18 years, renal transplantation, previous peritoneal dialysis, and previous severe surgical trauma or mental illness. We allocated the eligible participants to two groups: a survival group, comprising patients who were still alive on 31 December 2018, and a mortality group, comprising those who had died for any reason during the study period (Figure 1). All the participants

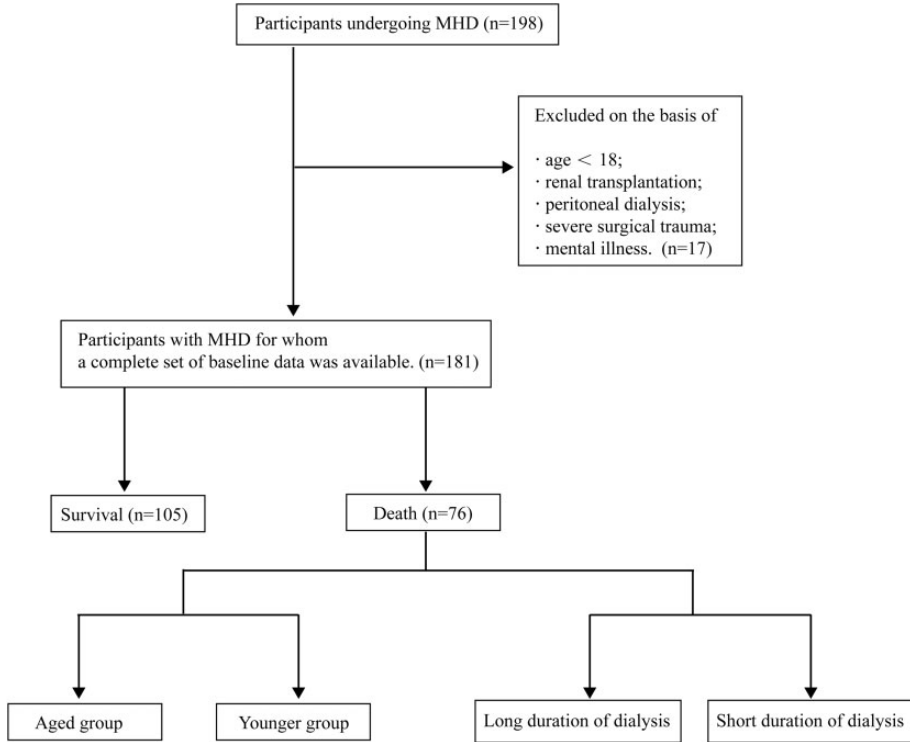


Figure 1. Flowchart of study enrollment. MHD, maintenance hemodialysis.

gave their written informed consent, the study was performed according to the principles of the Declaration of Helsinki, and it was approved by the Ethics Committee for Human Research of Huashan Hospital (No. KY2018-368).

Data collection

The clinical characteristics of the patients, including their age, sex, duration of dialysis, primary kidney disease, pre-dialysis blood pressure, dry body mass, and cause of death, were obtained from the database of the dialysis center. The primary kidney disease was categorized as hypertensive nephropathy (HTN), diabetic nephropathy (DN), chronic glomerulonephritis (CGN), polycystic kidney disease (PKD), or other (such as gout, pyelonephritis, and systemic

lupus erythematosus). The duration of dialysis was defined as the period between the year of initiation of dialysis and the year of the last follow-up examination. Long-term dialysis was defined as a duration of ≥ 10 years. Blood pressure was measured three times, before each hemodialysis session, during the week preceding the end of follow-up. The causes of death were defined as cardiovascular disease (myocardial infarction, aortic dissection, or heart failure), cerebrovascular accident (cerebral hemorrhage or cerebral infarction), severe infection (severe pneumonia, severe acute pancreatitis or septic shock), malignancy, sudden death for unknown reasons, and other diseases.

The following laboratory data were collected: serum creatinine, blood urea

nitrogen (BUN), serum albumin, alkaline phosphatase (ALP), intact parathyroid hormone (iPTH), calcium, phosphorus, potassium, C-reactive protein (CRP), carbon dioxide combining power (CO₂-CP), N terminal pro B type natriuretic peptide (NT-proBNP), platelet count, iron, unsaturated transferrin, total iron-binding capacity (TIBC), ferritin, and β_2 -microglobulin (β_2 -MG), and the hematocrit (HTC). These data were obtained from the hemodialysis records immediately prior to the primary study endpoint of death or the end of the study.

Statistical analysis

Continuous data are summarized using mean \pm SD or median (interquartile range, IQR), and categorical data are expressed as frequency and percentage. Comparisons between continuous datasets were performed using unpaired Student's *t*-test for parametric data or the Mann–Whitney Rank Sum test for non-parametric data. The chi-square test was used to compare categorical datasets. $P < 0.05$ was considered to represent statistical significance. Binary stepwise logistic regression was used to identify independent risk factors for all-cause mortality. Analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA) or GraphPad Prism software version 8.0 (GraphPad Software, Inc., La Jolla, CA, USA).

Results

Comparison of the mortality associated with cardiovascular and cerebrovascular events during each year

During the years 2014 to 2018, the annual mortality rates for the participants were 7.9%, 6.4%, 7.3%, 8.7%, and 6.6%, respectively, with a mean annual mortality rate of 7.4%. Seventy-six participants died

during the study, of whom 39.5% were women. Regarding the causes of mortality, 21.1% deaths were caused by cardiovascular disease, 25.0% by cerebrovascular disease, 29.0% by severe infection, and 7.9% by malignancy; 5.3% of the deaths were sudden, with no cause identified; and 11.8% of deaths were caused by other diseases. The proportions of the annual total mortality accounted for by cardiovascular events were 23.5%, 42.9%, 20.0%, 17.7%, and 0, respectively; and those accounted for by cerebrovascular events were 29.4%, 21.4%, 13.3%, 29.4%, and 30.8%, respectively (Figure 2).

Comparison of the causes of death in and the primary kidney diseases of aged and younger participants

Fifty-nine of the participants were ≥ 65 years old, and they accounted for 77.6% of the total number of deaths. The mean ages of the aged and younger participants were 77 ± 7 years and 56 ± 8 years, respectively. Cardiovascular or cerebrovascular diseases were the cause of death in 47.5% and 41.2% of the aged and younger participants, respectively. The number of patients with HTN as the primary kidney disease in the aged group was significantly higher than that in the younger group (37.3% vs. 11.8%, respectively, $P = 0.046$), whereas the prevalences of DN (29.4% vs. 23.7%, respectively) and CGN (47.1% vs. 23.7%, respectively) tended to be higher in the younger group, although these differences did not achieve statistical significance (Table 1).

Comparison of the causes of death in and the primary kidney disease of participants who had undergone dialysis over the long or short term

Twenty-nine participants had undergone long-term MHD (≥ 10 years), and this

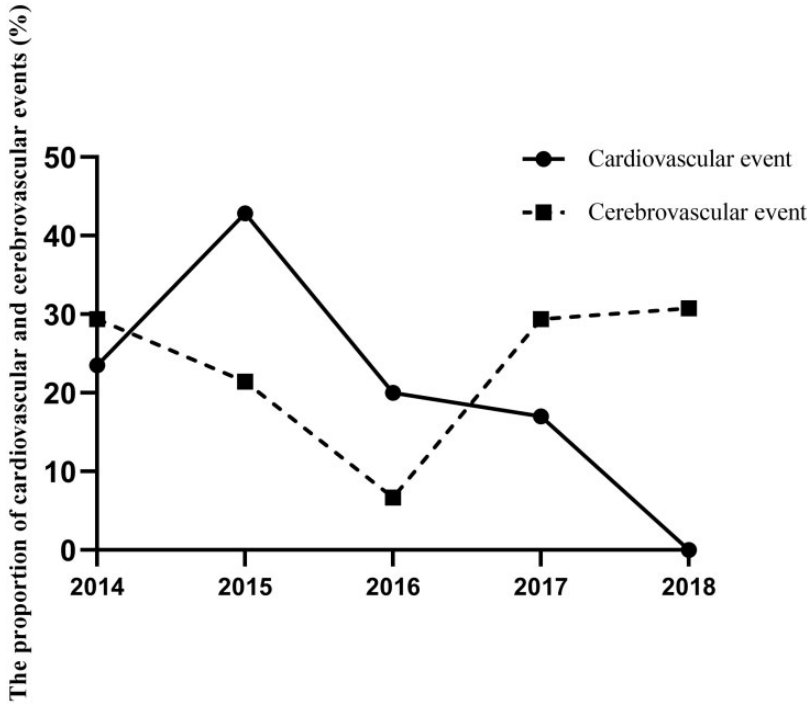


Figure 2. Trends in the prevalences of death secondary to cardiovascular and cerebrovascular events during the years of the study.

group accounted for 38.2% of the total number of deaths. In comparison, 47 had undergone short-term dialysis (<10 years), and this group accounted for 61.8% of the total number of deaths. The mean durations of dialysis were 15.9 ± 3.2 years and 5.4 ± 2.8 years in the long- and short-term groups, respectively. The proportions of deaths caused by cardiovascular or cerebrovascular events were 44.8% and 46.8% in the long- and short-term groups, respectively. The proportions of deaths caused by other diseases were 24.1% and 4.3% in the long- and short-term groups, respectively ($P=0.025$) (Table 2). The proportion of the participants with DN as their primary kidney disease was significantly higher in the short-term dialysis group than in the long-term dialysis group (36.2% vs. 6.9%, respectively; $P=0.04$), whereas the proportion of the participants who had CGN was

significantly higher in the long-term dialysis group (48.3% vs. 17.0%, respectively; $P=0.04$) (Table 2).

Comparison and binary stepwise logistic regression analysis of the clinical characteristics of participants who survived or died

Of the 181 participants, 105 survived and 76 died during the study period. At baseline, the mean ages of the two groups were 63 ± 12 and 72 ± 11 years, and their mean durations of MHD were 8.9 ± 6.7 and 9.4 ± 5.9 years, respectively. There were significant differences in the following parameters between the groups: age; proportion who were ≥ 65 years old; body mass index (BMI); pre-dialysis systolic blood pressure; pre-dialysis diastolic blood pressure; single-pool (sp)Kt/V; normalized

Table 1. Comparison of the causes of death and the primary kidney disease in participants who were aged or younger.

Characteristic	Aged group (n = 59)	Younger group (n = 17)	P-value
Age (years)	77 ± 7	56 ± 8	<0.01
Male (n, %)	9 (52.9)	37 (62.7)	0.468
Duration of dialysis (year)	8.7 ± 5.9	11.8 ± 5.6	0.057
BMI (kg/m ²)	20.5 ± 3.9	20.6 ± 4.7	0.790
SBP (mmHg)	124.8 ± 24.7	112.5 ± 27.7	0.084
DBP (mmHg)	67.9 ± 13.0	63.4 ± 16.8	0.247
spKt/V	1.34 ± 0.24	1.29 ± 0.37	0.661
nPCR (g/kg/day)	1.09 ± 0.57	1.14 ± 0.23	0.077
Causes of death (n, %)			
CVD	10 (17.0)	6 (35.3)	0.195
Cerebrovascular accident	18 (30.5)	1 (5.9)	0.080
Severe infection	15 (25.4)	7 (41.2)	0.338
Malignancy	5 (8.5)	1 (5.9)	0.900
Sudden death	4 (6.8)	0	0.569
Other	7 (11.9)	2 (11.8)	0.900
Primary kidney disease (n, %)			
HTN	22 (37.3)	2 (11.8)	0.046
DN	14 (23.7)	5 (29.4)	0.874
CGN	14 (23.7)	8 (47.1)	0.118
PKD	3 (5.1)	1 (5.9)	0.900
Other	6 (10.2)	1 (5.9)	0.950

Values are expressed as mean ± SD, or number (percentage), as appropriate. Data were analyzed using the unpaired Student's *t*-test, the Mann-Whitney Rank Sum test, or the chi-square test, as appropriate. Aged group: ≥65 years of age; Younger group: <65 years of age.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; spKt/V, single-pool Kt/V; nPCR, normalized protein catabolic rate; CVD, cardiovascular disease; HTN, hypertensive nephropathy; DN, diabetic nephropathy; CGN, chronic glomerulonephritis; PKD, polycystic kidney disease.

protein catabolic rate (nPCR); the proportion with diabetes; and pre-dialysis blood creatinine, urea nitrogen, albumin, ALP, iPTH, serum potassium, CRP, NT-proBNP, platelet count, hemoglobin, serum iron, HCT, TIBC, and β_2 -MG (all $P < 0.05$) (Table 3). Binary stepwise logistic regression analysis showed that low BMI (odds ratio [OR] 5.878, $P = 0.015$), spKt/V (OR 7.224, $P = 0.007$), albumin (OR 9.741, $P = 0.002$), platelet count (OR 7.630, $P = 0.006$), and TIBC (OR 6.080, $P = 0.014$); and high iPTH (OR 4.355, $P = 0.037$) and NT-proBNP (OR 6.499, $P = 0.011$) were independent risk factors for all-cause mortality (Table 4).

Discussion

According to an annual report by the USRDS, cardiovascular events and infection are the most common causes of death among patients undergoing MHD.¹¹ In addition, Ali and colleagues showed that cardiovascular events, infection, and malignancy are the leading causes of the mortality in patients commencing MHD.¹² However, a recent multi-center study conducted in China showed that the most common cause of death is a cardiovascular event (37.9%), followed by a cerebrovascular event (20.3%).¹³ Consistent with this, we found that cardiovascular and

Table 2. Comparison of the cause of death and primary kidney disease in participants who had undergone long- or short-term dialysis.

Duration of dialysis	≥10 years (n = 29)	<10 years (n = 47)	P-value
Age (year)	71 ± 13	73 ± 11	0.363
Male (n, %)	14 (48.3)	32 (68.1)	0.086
Duration of dialysis (year)	15.9 ± 3.2	5.4 ± 2.8	<0.01
BMI (kg/m ²)	20.0 ± 3.5	20.9 ± 4.3	0.324
SBP (mmHg)	117.9 ± 26.3	124.6 ± 25.3	0.27
DBP (mmHg)	65.2 ± 16.4	67.9 ± 12.2	0.416
spKt/V	1.34 ± 0.31	1.32 ± 0.24	0.772
nPCR (g/kg/day)	1.08 ± 0.22	1.12 ± 0.63	0.719
Cause of death (n, %)			
CVD	5 (17.2)	11 (23.4)	0.522
Cerebrovascular accident	8 (27.6)	11 (23.4)	0.683
Severe infection	7 (24.1)	15 (31.9)	0.468
Malignancy	1 (3.5)	5 (10.6)	0.489
Sudden death	1 (3.5)	3 (6.4)	0.978
Other	7 (24.1)	2 (4.3)	0.025
Primary kidney disease (n, %)			
HTN	7 (24.1)	17 (36.2)	0.273
DN	2 (6.9)	17 (36.2)	0.004
CGN	14 (48.3)	8 (17.0)	0.004
PKD	3 (10.3)	1 (2.1)	0.303
Other	3 (10.3)	4 (8.5)	0.999

Values are expressed as mean ± SD, or number (percentage), as appropriate. Data were analyzed using the unpaired Student's *t*-test, the Mann-Whitney Rank Sum test, or the chi-square test, as appropriate.

SBP, systolic blood pressure; DBP, diastolic blood pressure; spKt/V, single-pool Kt/V; nPCR, normalized protein catabolic rate; CVD, cardiovascular disease; HTN, hypertensive nephropathy; DN, diabetic nephropathy; CGN, chronic glomerulonephritis; PKD, polycystic kidney disease.

cerebrovascular diseases were the commonest causes of death in participants undergoing hemodialysis. A prospective cohort study comprising phases 4 and 5 of the Dialysis Outcomes and Practice Patterns Study (DOPPS) found that although cardiovascular events were common among patients undergoing hemodialysis, their incidence varied geographically.¹⁴ During recent years, with advances in the prevention of cardiovascular events, including the regular use of echocardiography and coronary computed tomography to assess calcification, the incidence of cardiovascular events at our center has decreased substantially, whereas that of CVA has increased.

A previous cohort study conducted in the UK showed that the incidence of cerebrovascular events in patients undergoing MHD was more than 10 times higher than in the general population, and the mortality rate was approximately three times higher.¹⁵ Thus, CVA poses a significant threat to the survival of patients undergoing MHD. Given that the institution of preventive measures and timely medical interventions should reduce these risks, regular screening for cerebrovascular events and close monitoring should be instituted, especially for patients with a previous history of stroke.

It was previously shown that long-term dialysis was associated with high all-cause

Table 3. Comparison of the clinical characteristics of participants who survived or died during the study period.

Characteristic	Survival group (n = 105)	Mortality group (n = 76)	Z/ χ^2 /t value	P-value
Age (years)	63 ± 12	72 ± 11	-5.251	<0.001
Male (n, %)	55 (52.4)	46 (60.5)	1.186	0.276
Duration of dialysis (year)	8.9 ± 6.7	9.4 ± 5.9	-0.890	0.373
Age ≥65 years (n, %)	45 (42.9)	59 (77.6)	21.811	<0.001
Duration of dialysis ≥10 years (n, %)	45 (42.9)	29 (38.2)	0.403	0.526
BMI (kg/m ²)	21.4 ± 3.1	20.5 ± 4.0	-1.792	0.073
Dialysis-related indicators				
SBP (mmHg)	133.0 ± 24.8	122.0 ± 25.7	2.890	0.004
DBP (mmHg)	75.0 ± 13.1	66.9 ± 13.9	3.988	<0.001
spKt/V	1.52 ± 0.34	1.26 ± 0.40	-4.755	<0.001
nPCR (g/kg/day)	1.28 ± 0.28	1.08 ± 0.53	-5.257	<0.001
Previous history (n, %)				
Diabetes mellitus	23 (22.1)	30 (39.5)	6.369	0.012
CVD	33 (31.7)	26 (34.2)	0.123	0.726
Cancer	12 (11.5)	8 (10.5)	0.046	0.831
Residual renal function	14 (13.5)	11 (14.5)	0.038	0.846
Laboratory parameters				
Serum creatinine (μmol/L)	872 ± 284	773 ± 232	-3.101	0.002
BUN (mmol/L)	26.2 ± 7.6	24.0 ± 6.2	-2.325	0.020
Serum albumin (mmol/L)	0.632 ± 0.045	0.542 ± 0.090	-7.819	<0.001
ALP (mmol/L)	75 (64, 96)	92 (66, 111)	-2.204	0.028
iPTH (pmol/L)	18.9 (9.3, 37.5)	30.3 (13.0, 54.3)	-2.232	0.026
Serum calcium (mmol/L)	2.42 ± 0.25	2.37 ± 0.29	1.088	0.279
Serum phosphorus (mmol/L)	1.67 ± 0.48	1.54 ± 0.68	1.437	0.153
Serum potassium (mmol/L)	4.8 ± 0.7	4.5 ± 0.8	-3.401	0.001
CRP (nmol/L)	22.0 (8.7, 60.5)	53.9 (21.9, 99.5)	-4.301	<0.001
CO ₂ -CP (mmol/L)	23.2 ± 9.9	22.2 ± 4.0	-0.093	0.926
NT-proBNP (pmol/L)	435 (211, 969)	1786 (515, 4139)	-5.459	<0.001
Platelet count (×10 ⁹ /L)	184 ± 60	169 ± 76	-2.355	0.019
Hemoglobin (g/L)	111 ± 14	101 ± 20	-3.071	0.002
Serum iron (μmol/L)	13.6 ± 4.8	10.2 ± 5.0	-4.998	<0.001
HCT (%)	34.6 ± 3.9	32.4 ± 6.3	-2.108	0.035
Unsaturated transferrin (μmol/L)	0.358 ± 0.111	0.338 ± 0.106	-1.575	0.115
TIBC (μmol/L)	42.6 ± 7.8	37.2 ± 8.1	-4.531	<0.001
Ferritin (nmol/L)	0.321 (0.124, 0.866)	0.528 (0.279, 0.777)	-1.267	0.205
β ₂ -MG (nmol/L)	3562 ± 1154	2417 ± 297	-3.648	<0.001

Values are expressed as mean ± SD, median (IQR), or number (percentage), as appropriate. Data were analyzed using the unpaired Student's *t*-test, the Mann-Whitney Rank Sum test, or the chi-square test, as appropriate.

BMI, body mass index; spKt/V, single-pool Kt/V; nPCR, normalized protein catabolic rate; CVD, cardiovascular disease; BUN, blood urea nitrogen; ALP, alkaline phosphatase; iPTH, intact parathyroid hormone; CRP, C-reactive protein; CO₂-CP, carbon dioxide combining power; NT-proBNP, N terminal pro B type natriuretic peptide; HCT, hematocrit; TIBC, total iron-binding capacity; β₂-MG, β₂-microglobulin.

Table 4. Independent risk factors for all-cause mortality in the participants, assessed using binary stepwise logistic regression analysis.

Parameter	β	Standard error	Odds ratio	P	95% CI
BMI (kg/m ²)	-0.767	0.316	5.878	0.015	0.250–0.863
spKt/V	-12.183	4.533	7.224	0.007	0.000–0.037
NT-proBNP (ng/L)	0.000	0.000	6.499	0.011	1.000–1.000
Albumin (g/L)	-0.835	0.268	9.741	0.002	0.257–0.733
iPTH (pg/mL)	0.005	0.002	4.355	0.037	1.000–1.009
Platelet count ($\times 10^9/L$)	-0.027	0.010	7.630	0.006	0.954–0.992
TIBC ($\mu\text{mol/L}$)	-0.192	0.078	6.080	0.014	0.708–0.961

BMI, body mass index; spKt/V, single-pool Kt/V; NT-proBNP, N terminal pro B type natriuretic peptide; iPTH, intact parathyroid hormone; TIBC, total iron-binding capacity; CI, confidence interval.

mortality in a large cohort of patients undergoing hemodialysis in Japan.⁸ A recent cohort study also showed that physical quality of life deteriorates as the duration of dialysis increases in older patients undergoing MHD.¹⁶ To our knowledge, few studies have investigated the relationships of the duration of dialysis and the survival or prognosis of patients with specific primary kidney diseases. Notably, we found that the duration of dialysis was associated with the identity of the primary kidney disease, and specifically that the survival and prognosis of participants with CGN were significantly better than those of participants with HTN or DN. CGN was the most common cause of glomerulosclerosis and ESRD, and involved proteinuria and hematuria,¹⁷ CGN exists in a variety of complex pathological types, including IgA nephropathy, membranoproliferative glomerulonephritis (MPGN), focal segmental glomerulosclerosis (FSGS), and idiopathic membranous nephropathy (IMN); and therefore the therapy and prognosis of CGN varies from person to person. Furthermore, Litovkina *et al.* found that genes involved in the regulation of vascular homeostasis have a significant effect on the renal survival rate of patients with CGN.¹⁸

In contrast, the USRDS showed that DN was the principal cause of ESRD,

followed by HTN.⁵ Furthermore, a multi-center prospective cohort study conducted in Japan showed that the all-cause mortality associated with HTN patients was as high as that for patients with DN, and that the prognosis of patients with ESRD secondary to HTN was as poor as that of patients with DN.¹⁹ When blood pressure and blood glucose concentration were not well controlled, patients with HTN or DN showed further deterioration of renal function and the development of complications, including hyperkalemia, infection, and congestive heart failure. Similarly, a 9-year cohort study conducted in Japan showed that the presence of diabetes mellitus predisposes toward all-cause mortality in patients undergoing hemodialysis.²⁰ Consistent with this, reductions in systolic blood pressure and glycosylated hemoglobin A1c prolong the survival of patients with DN.²¹ Thus, the management of blood pressure and blood glucose is essential for patients undergoing MHD.

BMI and serum albumin are important indicators of nutritional status, and are closely associated with malnutrition, inflammation, chronic protein-energy wasting, and even all-cause mortality.^{22,23} Consistent with the findings of the DOPPS,²⁴ we found that low baseline BMI and serum albumin concentration are independently associated with a higher risk

of mortality. Moreover, because of insufficient erythropoietin or the accumulation of toxins in the circulation, patients undergoing MHD tend to develop renal anemia to varying extents, involving a lower hemoglobin concentration, a lower platelet count, and less hematopoiesis. A recent clinical study showed that low transferrin saturation and a high ferritin concentration are predictors of cerebrovascular and cardiovascular disease and mortality in patients undergoing MHD.²⁵ Notably, we have shown that low TIBC and platelet count are associated with a higher risk of all-cause mortality. Iron use disorders would aggravate any anemia, and thrombocytopenia would increase the risks of bleeding and infection. In addition, we have shown that high iPTH and NT-pro BNP concentrations are associated with a high mortality rate in patients undergoing MHD. As the duration of dialysis and the age of the participants increased, there was progressive deterioration of calcium and phosphorus metabolism in patients undergoing hemodialysis, but hyperphosphatemia and hypocalcemia would stimulate the secretion and release of PTH, leading to secondary hyperparathyroidism, osteoporosis, and even cardiovascular events.^{26,27} NT-proBNP concentration is widely used to assess cardiac function, and high concentrations are associated not only with CVD-related, but also non-CVD-related mortality.²⁸ Consistent with the findings of Kara *et al.*,²⁹ we found that a low spKt/V is associated with a higher risk of death in patients undergoing MHD. The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Hemodialysis has recommended a target spKt/V of 1.4 per hemodialysis session for patients being treated three times weekly, and a minimum spKt/V of 1.2.³⁰ Sahutoglu *et al.* also found that a high spKt/V (>1.4) was associated with lower

1-year mortality in a small cohort of patients undergoing MHD.³¹ Further studies are required to assess the association between the effectiveness of hemodialysis and mortality.

The findings of the present study should be viewed in light of its limitations. Because it was a single-center retrospective cohort study, a number of potentially confounding factors could not be accounted for. In addition, it had a small sample size, there was a lack of information regarding other causes of death, and the effects of various dialysis modes were not investigated. Therefore, further multi-center, large-scale, prospective studies should be conducted to identify further risk factors for mortality in patients undergoing MHD.

In conclusion, the mean annual mortality rate of patients undergoing MHD at our center was 7.4%. In these patients, the prevalence of cardiovascular events as a cause of death decreased between 2015 and 2018. In contrast, death from cerebrovascular events increased in prevalence between 2016 to 2018, which implies that more attention should be paid to screening and preventative measures for cerebrovascular diseases. Long-term dialysis was closely associated with specific primary kidney diseases, and specifically the survival time and prognosis of patients with CGN were significantly better than those of patients with HTN or DN. Low BMI, spKt/V, albumin, platelet count, and TIBC; and high iPTH and NT-proBNP concentration were found to be independent risk factors for all-cause mortality in patients undergoing MHD.

Declaration of conflicting interest


The authors declare that there is no conflict of interest.

Funding

The authors disclosed receipt of the following financial support for the research, authorship,

and publication of this article: This study was funded by the Natural Science Foundation of China (No. 81870501) and the Shanghai Science and Technology Commission Fund (No. 19411967800).

ORCID iD

Yong Wu  <https://orcid.org/0000-0001-5449-8375>

References

- Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. *Lancet* 2013; 382: 260–272.
- Go AS, Chertow GM, Fan D, et al. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med* 2004; 351: 1296–1305.
- Chang CH, Fan PC, Kuo G, et al. Infection in Advanced Chronic Kidney Disease and Subsequent Adverse Outcomes after Dialysis Initiation: A Nationwide Cohort Study. *Sci Rep* 2020; 10: 2938.
- Hsieh HL, Hsu SC, Cheng HS, et al. The influence of atrial fibrillation on the mortality of incident ESRD patients undergoing maintenance hemodialysis. *PLoS One* 2020; 15: e0228405.
- Saran R, Robinson B, Abbott KC, et al. US Renal Data System 2017 Annual Data Report: Epidemiology of Kidney Disease in the United States. *Am J Kidney Dis* 2018; 71: A7.
- Okechukwu CN, Lopes AA, Stack AG, et al. Impact of years of dialysis therapy on mortality risk and the characteristics of longer term dialysis survivors. *Am J Kidney Dis* 2002; 39: 533–538.
- Iseki K, Tozawa M and Takishita S. Effect of the duration of dialysis on survival in a cohort of chronic haemodialysis patients. *Nephrol Dial Transplant* 2003; 18: 782–787.
- Sumida K, Yamagata K, Iseki K, et al. Different impact of hemodialysis vintage on cause-specific mortality in long-term hemodialysis patients. *Nephrol Dial Transplant* 2016; 31: 298–305.
- Dimkovic N, Djukanovic L, Marinkovic J, et al. Achievement of guideline targets in elderly patients on hemodialysis: a multicenter study. *Int Urol Nephrol* 2015; 47: 1555–1563.
- Issad B, Benevent D, Allouache M, et al. 213 elderly uremic patients over 75 years of age treated with long-term peritoneal dialysis: a French multicenter study. *Perit Dial Int* 1996; 16: S414–S418.
- Collins AJ, Foley RN, Herzog C, et al. Excerpts from the US Renal Data System 2009 Annual Data Report. *Am J Kidney Dis* 2010; 55: S1–420, a6–7.
- Ali OM, Sayed AA, Mohammed WS, et al. Cardiovascular System Affection and Its Relation to First-Year Mortality in Patients Initiating Maintenance Hemodialysis. *Int J Gen Med* 2020; 13: 379–385.
- Song KK, Zhao DL, Wang YD, et al. Analysis of Factors Associated with Death in Maintenance Hemodialysis Patients: A Multicenter Study in China. *Chin Med J (Engl)* 2017; 130: 885–891.
- Stirnadel-Farrant HA, Karaboyas A, Cizman B, et al. Cardiovascular Event Rates Among Hemodialysis Patients across Geographical Regions-A Snapshot from The Dialysis Outcomes and Practice Patterns Study (DOPPS). *Kidney Int Rep* 2019; 4: 864–872.
- Power A, Chan K, Singh SK, et al. Appraising stroke risk in maintenance hemodialysis patients: a large single-center cohort study. *Am J Kidney Dis* 2012; 59: 249–257.
- Ishiwatari A, Yamamoto S, Fukuma S, et al. Changes in Quality of Life in Older Hemodialysis Patients: A Cohort Study on Dialysis Outcomes and Practice Patterns. *Am J Nephrol* 2020; 51: 650–658.
- Lim WH, Wong G, McDonald SP, et al. Long-term outcomes of kidney transplant recipients with end-stage kidney disease attributed to presumed/advanced glomerulonephritis or unknown cause. *Sci Rep* 2018; 8: 9021.
- Litovkina O, Nekipelova E, Dvornyk V, et al. Genes involved in the regulation of vascular homeostasis determine renal survival rate in patients with chronic glomerulonephritis. *Gene* 2014; 546: 112–116.
- Inaguma D, Ito E, Takahashi K, et al. Impact of high mortality in incident dialysis

- patients due to hypertensive nephrosclerosis: a multicenter prospective cohort study in Aichi, Japan. *Clin Exp Nephrol* 2018; 22: 1360–1370.
20. Mori K, Nishide K, Okuno S, et al. Impact of diabetes on sarcopenia and mortality in patients undergoing hemodialysis. *BMC Nephrol* 2019; 20: 105.
 21. Hu F and Zhang T. Study on Risk Factors of Diabetic Nephropathy in Obese Patients with Type 2 Diabetes Mellitus. *Int J Gen Med* 2020; 13: 351–360.
 22. Herselman M, Esau N, Kruger JM, et al. Relationship between serum protein and mortality in adults on long-term hemodialysis: exhaustive review and meta-analysis. *Nutrition* 2010; 26: 10–32.
 23. Lukowsky LR, Kheifets L, Arah OA, et al. Nutritional predictors of early mortality in incident hemodialysis patients. *Int Urol Nephrol* 2014; 46: 129–140.
 24. Pifer TB, McCullough KP, Port FK, et al. Mortality risk in hemodialysis patients and changes in nutritional indicators: DOPPS. *Kidney Int* 2002; 62: 2238–2245.
 25. Kuragano T, Joki N, Hase H, et al. Low transferrin saturation (TSAT) and high ferritin levels are significant predictors for cerebrovascular and cardiovascular disease and death in maintenance hemodialysis patients. *PLoS One* 2020; 15: e0236277.
 26. Hiyamuta H, Yamada S, Taniguchi M, et al. Association of hyperphosphatemia with an increased risk of sudden death in patients on hemodialysis: Ten-year outcomes of the Q-Cohort Study. *Atherosclerosis* 2021; 316: 25–31.
 27. Li M, Ye ZC, Li CM, et al. The influence of cardiac valvular calcification on all-cause and cardiovascular mortality in maintenance hemodialysis patients. *Int Urol Nephrol* 2020; 52: 943–951.
 28. Kawagoe C, Sato Y, Toida T, et al. N-terminal-pro-B-type-natriuretic peptide associated with 2-year mortality from both cardiovascular and non-cardiovascular origins in prevalent chronic hemodialysis patients. *Ren Fail* 2018; 40: 127–134.
 29. Kara E, Sahutoglu T, Ahbap E, et al. The predictive value of malnutrition - inflammation score on 1-year mortality in Turkish maintenance hemodialysis patients. *Clin Nephrol* 2016; 86: 94–99.
 30. National Kidney Foundation. KDOQI Clinical Practice Guideline for Hemodialysis Adequacy: 2015 update. *Am J Kidney Dis* 2015; 66: 884–930.
 31. Sahutoglu T, Kara E, Ahbap E, et al. Test of the recommended dialysis dose on one-year mortality of nondiabetic maintenance hemodialysis patients; observations from a single dialysis unit. *Ren Fail* 2016; 38: 1174–1179.