

Frailty and Adverse Outcomes After SARS-CoV-2 Infection in Elderly Patients on Maintenance Hemodialysis: A Cohort Study

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Purpose: Frailty is an important geriatric syndrome associated with aging and adverse events, especially in patients with severe infection. To help guide prognosis for elderly patients undergoing maintenance hemodialysis (MHD) who experience acute infection, this study investigated whether baseline (pre-infection) frailty may be associated with adverse outcomes in elderly patients undergoing MHD who suffer SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection.

Patients and Methods: Patients (aged ≥ 60 y) receiving MHD had been assessed for overall frailty and the 5 frailty components based on the Fried Frailty Phenotype scale within 3 months prior to SARS-CoV-2 infection.

Results: There were 59 and 98 patients in the frail and non-frail groups, respectively. Three months after SARS-CoV-2 infection, 21 (13.4%) and 45 (28.7%) patients had died or were in hospital. The multivariate COX proportional risk model suggested that the all-cause mortality rate in patients judged overall frail or with low activity was significantly higher compared with that of the non-frail ($P = 0.049$; 0.003). The multivariate logistic regression analysis showed that hospitalization 3 months after SARS-CoV-2 infection was associated with both overall frailty and low activity (OR 2.276, 95% CI: 1.034–5.010, $P = 0.041$; OR 2.809, 95% CI: 1.311–6.020, $P = 0.008$, respectively).

Conclusion: Overall frailty and specifically low activity were significantly associated with all-cause mortality and hospitalization in this elderly MHD population after SARS-CoV-2 infection. Early assessment of frailty and effective interventions are recommended to improve the prognosis of patients receiving MHD who are at higher risk of acute infection.

Keywords: SARS-CoV-2, COVID-19, hemodialysis, frailty, elderly, prognosis

Introduction

In recent years hemodialysis has increasingly been used globally for the treatment of chronic kidney disease in the elderly. In China, the proportion of patients aged 65 or older on hemodialysis is as high as 28.91%,¹ and the social and economic burden is correspondingly high. In addition, coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) virus has been a serious challenge to public health.² The risk of mortality due to SARS-CoV-2 infection is higher for people with comorbidities such as chronic kidney disease.^{3,4}

The influence of frailty within a setting of comorbidities has gained more attention over the last few decades. The prevalence of frailty in elderly patients undergoing maintenance hemodialysis (MHD) is reportedly between 35% and 72%.^{5–7} These studies suggest that frail patients who require MHD also experience higher rates of falls, hospitalization, and mortality.

In general, patients under MHD who suffer viral infections similar to SARS-CoV-2 are more prone to adverse events, which affect their prognosis. However, the influence of frailty, specifically, on prognosis in these patients is not known. In addition, few researchers have studied a correlation between frailty and adverse prognosis after SARS-CoV-2 infection.

Results have been controversial. Tylicki et al⁸ found that in hospitalized patients under MHD with SARS-CoV-2 infection there was a positive association between the admission Clinical Frailty Scale score and all-cause mortality. Yet, Hendra et al⁹ reached the opposite conclusion.

The current cohort study investigated an association between baseline frailty status and adverse outcomes of elderly patients under MHD after SARS-CoV-2 infection.

Materials and Methods

Beijing Friendship Hospital affiliated with Capital Medical University granted ethics approval for this study (2022-P2-120-01). All the enrolled patients provided informed consent for participation in the study. Our study complies with the Declaration of Helsinki.

Study Design and Study Population

The cohort comprised elderly patients (aged ≥ 60 y) at the Blood Purification Center of Beijing Friendship Hospital affiliated with Capital Medical University, who had received MHD for at least 3 months, and who had been judged either frail or non-frail according to a baseline Fried Frailty Phenotype (FFP) scale score.¹⁰ In addition, within 3 months of the baseline assessment for frailty, all these patients experienced natural SARS-CoV-2 infection, specifically between 7 and 31 December 2022, during the COVID-19 pandemic. The diagnoses of SARS-CoV-2 infections were conducted at the outpatient or emergency department, and were based on Nucleic Acid Testing. Furthermore, only patients who provided informed consent for participation in the study were included.

Patients with any of the following were excluded: severe trauma or long-term hospitalization; or malignant wasting diseases such as muscle atrophy, amputation, or advanced malignant tumor.

To investigate an association between frailty and adverse outcomes after SARS-CoV-2 infection in patients undergoing MHD, the subjects in this cohort were classified as either frail or non-frail, and compared based on various relevant parameters.

Data Collection and Procedures

Trained physicians conducted the geriatric assessments of the patients, and the data was collected from the electronic database of the hospital. The main investigators verified the final data. Baseline characteristics included demographics, medication, and medical history. The following laboratory tests were performed: blood cells, hemoglobin, albumin, uric acid, plasma electrolytes, blood lipids, urea nitrogen, serum creatinine, parathyroid hormone, and urea removal rate (URR).

Assessment of Frailty

The 5 components of the FFP were respectively included in the assessments of the patients' frailty status:¹⁰ unintentional weight loss; slow walking speed; weakness; exhaustion; and low activity level. One point was scored for each criterion met, and ≥ 3 points was defined as frailty.

Specifically, weight loss was defined as unintentional if it was as much as 4.5 kg, or 5% of body weight, within the past 12 months. Walking speed was adjudged by the time required to walk 4.57 meters. Walking speed was considered slow if 6 seconds were required for men and women of heights 1.59 and 1.73 meters, respectively, or 7 seconds for men and women shorter than or equal to these heights.

Using a hand-held dynamometer, weakness was measured according to the grip strength of the patient's dominant hand, or the hand without an arteriovenous fistula, depending on the patient's sex and body mass index (BMI). For women with a BMI of ≤ 23.0 , 23.1–26.0, 26.1–29, or >29.0 kg/m², weakness was defined as a grip strength of, respectively, ≤ 17.0 , ≤ 17.3 , ≤ 18.0 , and ≤ 21 kg. For men with a BMI of ≤ 24.0 , 24.1–26.0, 26.1–28.0, and >28 kg/m², weakness was considered a grip strength of ≤ 29.0 , ≤ 30.0 , ≤ 31.0 , and ≤ 32.0 kg.

The CES-D (Center for Epidemiologic Studies Depression Scale)¹¹ was employed to determine the presence of exhaustion. Briefly, patients were asked how often they had felt in the previous week that “everything I did was an effort” or “I could not get going.” If their answer was 3 to 4 days, or 5 to 7 days, this was accounted a sign of exhaustion.

Similarly, the low activity component of the FFP was judged based on the patient's self-report of weekly physical activity. For women, low activity was considered an expenditure of less than 270 kcal/week, or fewer than approximately 2 hours of walking. For men, low activity was less than 383 kcal/week, or fewer than 2.5 hours of walking.

Nutritional Assessment

The assessment of nutrition was calculated based on the Geriatric Nutrition Risk Index (GNRI).¹² $GNRI = [14.89 \times \text{albumin, g/dL}] + [41.7 \times (\text{body weight/ideal body weight})]$. The ideal weight was calculated as: $(\text{height, m}^2) \times 22$. If the patient's weight exceeded the ideal body weight, then $(\text{body weight/ideal body weight})$ was set to 1 (one).¹²

Outcome

The follow-up period ended on 31 March 2023. The main outcome was all-cause mortality at 3 months after SARS-CoV-2 infection. The secondary outcome was hospitalization.

Statistical Analysis

Categorical variables were compared using the chi-square or Fisher's exact test, and data are reported as number (percentage). Continuous variables were compared using Student's *t*-test or the Mann-Whitney U-test. Normally distributed data are reported as mean \pm standard deviation, and skewed distribution data as median (interquartile range [IQR]).

Univariate and multivariable Cox proportional hazards models were used to analyze the association between frailty status and all-cause mortality. Furthermore, associations between each of the 5 frailty components of the FFP and all-cause mortality were determined, and univariate and multivariable logistic regression analyses were applied to determine the influence of overall frailty status and frailty components on the rate of hospital admissions. The univariate analysis included factors with a significance of $P < 0.05$. These factors, and dialysis duration, were incorporated into the multivariate study. The URR was substituted for nitrogen and serum creatinine. All statistical analyses were conducted with SPSS 26.0 software. Statistical significance was considered $P < 0.05$.

Results

Baseline Characteristics and Frailty Status of Patients

Among 178 patients aged 60 years or older receiving MHD in our Blood Purification Center in December 2022, 164 were confirmed by nucleic acid test to have SARS-CoV-2 infection. Among them, 21 were excluded as follows: 14 patients tested negative for SARS-CoV-2 infection; and 4, 2, and 1 due to long-term hospitalization or severe trauma, malignant tumor, and missing important data, respectively (Figure 1). Finally, 157 patients were included, 80 (51.0%) men, with a median age of 67 years (IQR 63–74 y; Table 1).

The most common etiology of end stage renal disease was chronic glomerulonephritis (21.7%), then diabetic nephropathy (15.3%) and hypertensive renal disease (14.0%; Table 1). The most frequently used dialysis access (89.9%) was arteriovenous fistula. The most common patients' choice of dialysis mode was hemodialysis combined with hemodiafiltration (HDF; 46.5%) 3 times/week. The most common comorbidities were hypertension (92.4%), coronary heart disease (43.9%), and sleep disorders (39.5%). Only 9 (5.7%) patients received the vaccine.

Based on the total FFP score, the subjects were classified as frail (59, 37.6%) or non-frail (98, 62.4%; Figure 2). The most common components of the FFP were weakness (64.3%), exhaustion (57.3%), and slow walking speed (35.7%; Figure 3).

Compared with the non-frail group, the frail group was significantly older and had longer dialysis duration (Table 1). The frail group was further characterized by a higher rate of choosing HD alone (3 times/week) as the dialysis mode; lower serum potassium, albumin, GRNI score, urea nitrogen, serum creatinine, and URR; and higher prevalence of peripheral vascular disease (PVD) and chronic pulmonary disease (CPD).

Frailty and All-Cause Mortality

Among the total study population of 157 patients, at the end of the follow-up 21 (13.4%) had died, specifically 16 (10.2%) and 5 (3.2%) patients in the frail and non-frail groups, respectively (Figure 4). The univariate COX proportional

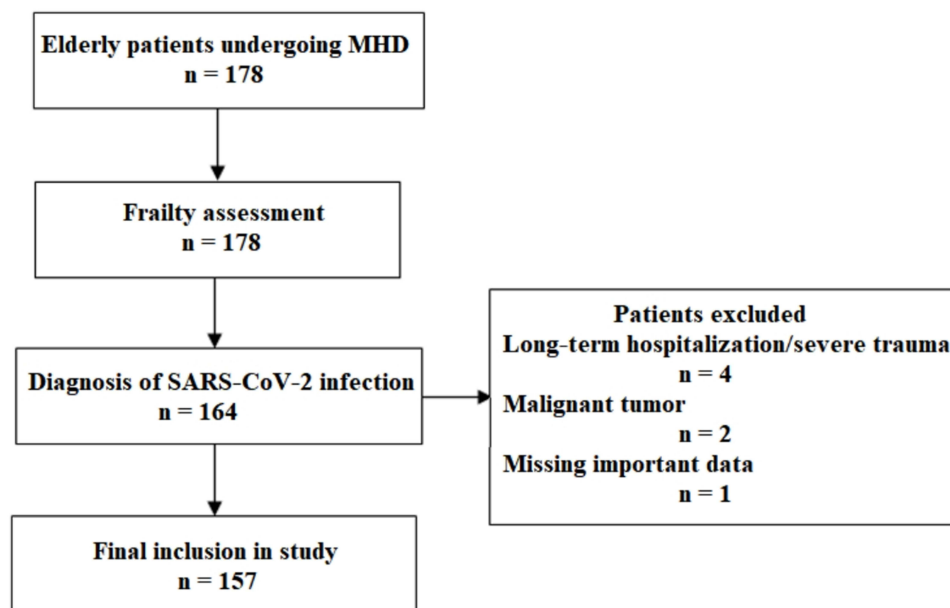


Figure 1 Study inclusion and exclusion flowchart.

risk model showed that among the FFP components, frailty ($P = 0.001$), low activity ($P < 0.001$), weakness ($P = 0.047$), and slow walking speed ($P = 0.001$) were significant risk factors for all-cause mortality (Table 2). The subsequent multivariate COX regression analysis showed that, after adjusting for age, dialysis duration, URR, GNRI, serum

Table 1 Baseline Demographics and Clinical Characteristics of Elderly Patients Undergoing MHD^a

	All Subjects	Non-Frail (Control)	Frail	P
Subjects, n	157	98	59	–
Age, y	67.0 (63.0–74.0)	65.0 (62.75–70.0)	74.0 (66.0–79.0)	<0.001
Male sex, n (%)	80 (51.0)	53 (54.1)	27 (45.8)	0.313
BMI, kg/m ²	22.49 (20.63–24.97)	22.43 (20.95–24.94)	22.51 (20.29–25.34)	0.936
GNRI score	100.96 (96.38–104.01)	101.89 (98.39–104.83)	97.54 (93.70–102.30)	<0.001
Dialysis duration, y	8.0 (5.0–15.0)	7.0 (4.0–12.0)	12.0 (5.0–18.0)	0.005
Vaccination rate, n (%)	9 (5.7)	6 (6.1)	3 (5.1)	1.000
Primary kidney disease, n (%)				0.468
Chronic glomerulonephritis	34 (21.7)	24 (24.5)	10 (16.9)	
Diabetes nephropathy	24 (15.3)	13 (13.3)	11 (18.6)	
Hypertensive nephropathy	22 (14.0)	15 (15.3)	7 (11.9)	
Polycystic kidney	18 (11.5)	10 (10.2)	8 (13.6)	
Drug-induced renal damage	10 (6.4)	4 (4.1)	6 (10.2)	
Other	49 (31.2)	32 (32.7)	17 (28.8)	
Vascular access, n (%)				0.279
AVF	141 (89.9)	90 (91.8)	51 (86.4)	
CVC	16 (10.2)	8 (8.2)	8 (13.6)	
Dialysis mode, n (%)				0.006
HD+HDF	73 (46.5)	54 (55.1)	19 (32.2)	
Hemodialysis	59 (37.6)	27 (27.6)	32 (54.2)	
HDF	10 (6.4)	8 (8.2)	2 (3.4)	
Other	15 (9.6)	9 (9.2)	6 (10.2)	

(Continued)

Table 1 (Continued).

	All Subjects	Non-Frail (Control)	Frail	P
Comorbidities, n (%)				
Hypertension	145 (92.4)	92 (93.9)	53 (89.8)	0.539
Coronary heart disease	69 (43.9)	41 (41.8)	28 (47.5)	0.492
Peripheral vascular disease ^b	16 (10.2)	5 (5.1)	11 (18.6)	0.007
Cerebrovascular disease ^c	13 (8.3)	7 (7.1)	6 (10.2)	0.713
Chronic pulmonary disease	21 (13.4)	8 (8.2)	13 (22)	0.013
Diabetes	53 (33.8)	32 (32.7)	21 (35.6)	0.706
Sleep disorder	62 (39.5)	38 (38.8)	24 (40.7)	0.813
Multiple medications, n (%)	142 (90.4)	90 (91.8)	52 (88.1)	0.445
WBC, ×10 ⁹ /L	5.80 (4.83–7.23)	5.85 (4.87–7.48)	5.71 (4.70–7.14)	0.576
NLR, %	3.21 (2.63–4.32)	3.11 (2.61–4.19)	3.33 (2.63–4.44)	0.451
GR, %	67.82 ± 7.72	67.93 ± 7.75	67.27 ± 7.71	0.604
LY, %	21.10 (16.30–24.45)	21.75 (16.38–24.35)	19.90 (16.20–25.00)	0.377
RBC, ×10 ¹² /L	3.74 (3.53–4.03)	3.72 (3.52–3.98)	3.79 (3.53–4.11)	0.144
HB, g/L	115.0 (110.0–121.0)	116.0 (110.0–121.0)	114.0 (110.0–122.0)	0.967
PLT, ×10 ⁹ /L	175.68 ± 52.78	176.15 ± 50.93	174.90 ± 56.15	0.886
Albumin, g/L	40.50 (38.35–42.40)	41.30 (39.60–42.73)	39.50 (36.70–41.10)	<0.001
Uric acid, μmol/L	370.70 (313.15–418.50)	377.10 (326.40–422.55)	360.40 (301.90–414.00)	0.090
Calcium, mmol/L	2.31 (2.19–2.42)	2.31 (2.19–2.42)	2.31 (2.18–2.40)	0.970
Phosphorus, mmol/L	1.69 (1.41–2.09)	1.69 (1.39–2.10)	1.70 (1.47–2.07)	0.616
CHOL, mmol/L,	4.05 ± 0.94	4.09 ± 0.91	3.99 ± 1.01	0.523
TG, mmol/L	1.21 (0.91–1.82)	1.30 (1.03–1.86)	1.11 (0.83–1.61)	0.061
HDL, mmol/L	1.09 (0.91–1.31)	1.07 (0.88–1.31)	1.09 (0.98–1.34)	0.284
LDL, mmol/L	2.17 (1.78–2.72)	2.28 (1.89–2.73)	6.47 (5.60–9.41)	0.192
Glucose, mmol/L	6.87 (5.69–9.01)	6.47 (5.60–9.41)	7.49 (5.97–8.91)	0.165
Sodium, mmol/L	137.94 ± 2.69	137.88 ± 2.71	138.05 ± 2.68	0.713
Potassium, mmol/L	4.79 (4.41–5.15)	4.90 (4.51–5.24)	4.60 (4.27–5.02)	0.010
Osmotic pressure, mOsm/L	306.90 (301.90–312.90)	307.50 (302.23–313.60)	305.60 (299.70–311.80)	0.055
Urea nitrogen, mmol/L	23.30 ± 5.42	24.51 ± 5.12	21.30 ± 5.35	<0.001
Serum creatinine, μmol/L	875.19 ± 193.19	934.66 ± 180.95	776.41 ± 172.41	<0.001
Parathyroid hormone, pg/mL	258.90 (139.65–470.70)	268.35 (145.67–470.25)	236.80 (129.10–472.50)	0.720
URR, %	69.71 (65.97–73.98)	70.39 (66.19–75.25)	68.79 (65.48–72.21)	0.031

Notes: ^aData is reported as median (IQR), unless noted otherwise; ^bIncluding peripheral vascular stenosis, occlusion, and gangrene; ^cExcluding lacunar infarction and ischemic white matter changes.

Abbreviations: AVF, arteriovenous fistula; CHOL, cholesterol; CVC, central venous catheterization; GR, neutrophil granulocyte; HB, hemoglobin; HD, hemodialysis; HDL, high density lipoprotein; LDL, low density lipoprotein; LY, lymphocyte; NLR, neutrophil lymphocyte ratio; PLT, platelet; RBC, red blood cell; TG, triglyceride; WBC, white blood cell.

potassium, and history of PVD or CPD, frailty remained significantly associated with all-cause mortality ($P = 0.049$). Regarding an association between FFP components and all-cause mortality, after adjusting for covariates, patients with low activity had a 37.5% higher rate of all-cause mortality compared with the control ($P = 0.003$).

Frailty and Hospitalization

Forty-five (28.7%) of the patients, that is, 26 (16.6%) in the frail group and 19 (12.1%) in the non-frail group, were admitted to the hospital or visited the emergency department for 24 hours or more (Table 3; Figure 4). The univariate logistic regression analysis showed that frailty ($P = 0.001$) including low activity ($P = 0.001$), and low walking speed ($P = 0.030$) were risk factors for hospitalization. After adjusting for age, dialysis duration, URR, serum potassium, and

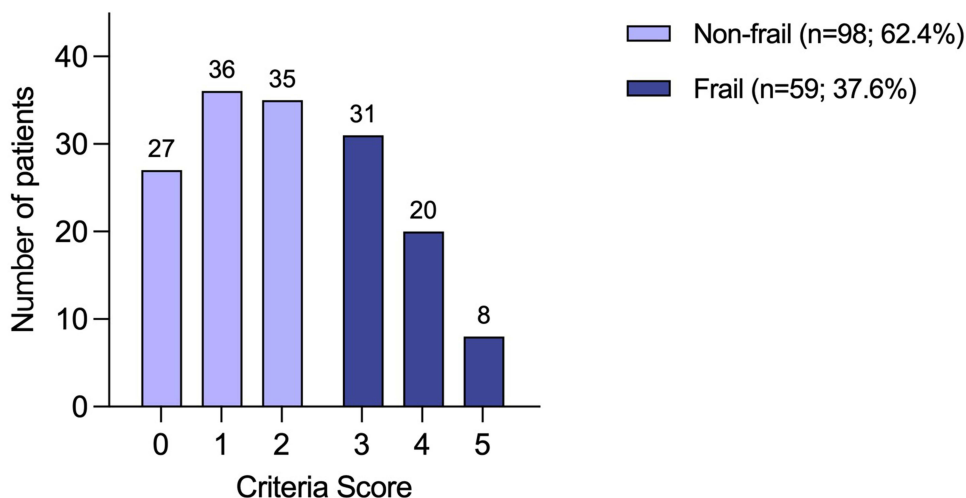


Figure 2 Prevalence of frailty in elderly hemodialysis patients according to the FFP.

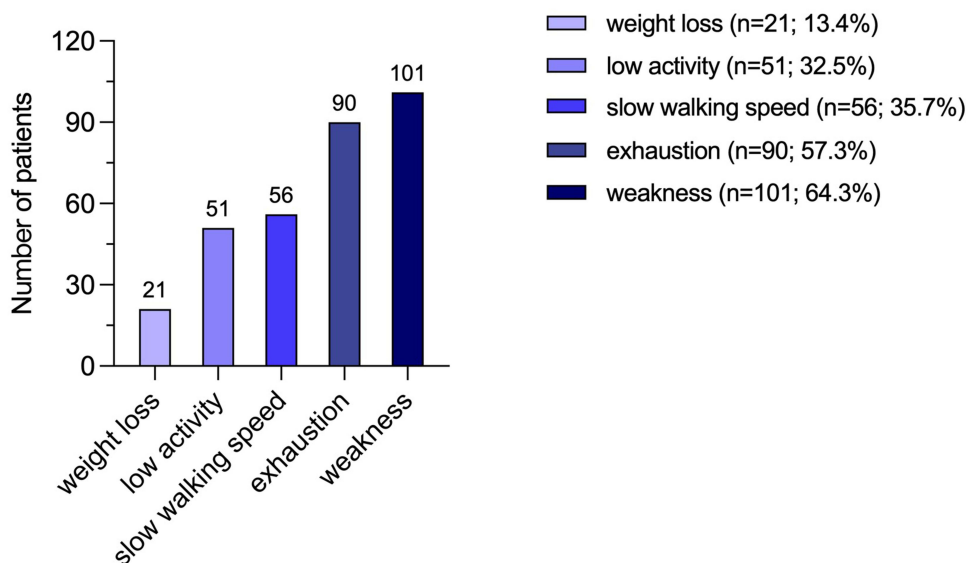


Figure 3 Number and percentage of subjects within each frailty component.

history of CPD, the multivariate logistic regression analysis showed that frailty ($P = 0.041$) and low activity ($P = 0.008$) were independent risk factors for hospitalization.

Effect of Age on Mortality and Hospitalization

Age was an independent risk factor for 3-month all-cause mortality ($P = 0.002$) and hospitalization ($P = 0.025$).

Discussion

This was a cohort study of 157 patients receiving MHD who had been assessed for baseline frailty within 3 months prior to diagnosis of SARS-CoV-2 infection during the COVID-19 epidemic. To determine a prognosis for such patients, we investigated associations between the condition of frailty and outcome parameters at the 3-month follow-up after infection. The prevalence of frailty was 37.6%, and nearly one-third of the patients' activity levels were not up to standard.

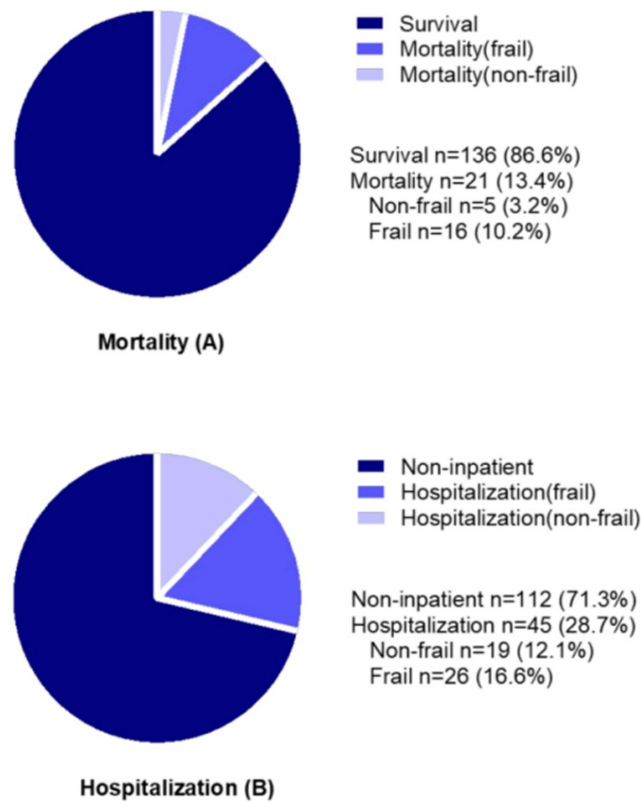


Figure 4 Mortality and hospitalization in the frail and non-frail groups.

The frailty rate determined by the present study is higher than the 34.7% previously reported at our center in 2019.⁶ This may be due, at least partially, to the COVID-19 pandemic. A systematic review showed that the restrictions, quarantines, and lockdowns imposed during the COVID-19 pandemic greatly affected the lifestyles and physical activity

Table 2 Univariate and Multivariable Cox Regression Analysis of Associated Factors with All-Cause Mortality

	Unadjusted		Model 1 ^a		Model 2 ^b	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Age	1.131 (1.070–1.195)	0.002	1.101 (1.035–1.171)	0.002	1.103 (1.041–1.169)	0.001
Frail	5.720 (2.093–15.629)	0.001	2.988 (1.005–8.881)	0.049	–	–
Low activity	7.318 (2.677–20.009)	<0.001	–	–	4.747 (1.682–13.399)	0.003
Weakness	3.454 (1.017–11.728)	0.047	–	–	–	0.986
Slow walking speed	4.844 (1.878–12.496)	0.001	–	–	–	0.853
Weight loss	1.077 (0.317–3.657)	0.905	–	–	–	–
Exhaustion	1.930 (0.748–4.974)	0.174	–	–	–	–
URR	0.944 (0.900–0.991)	0.019	–	0.159	–	0.059
GNRI	0.938 (0.895–0.983)	0.007	–	0.314	–	0.384
Potassium	0.424 (0.208–0.863)	0.018	–	0.250	–	0.463
PVD	3.024 (1.106–8.267)	0.031	–	0.232	–	0.354
CPD	3.370 (1.360–8.351)	0.009	–	0.223	–	0.155
Dialysis duration	1.048 (0.993–1.106)	0.090	–	0.469	–	0.540

(Continued)

Table 2 (Continued).

	Unadjusted		Model 1 ^a		Model 2 ^b	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
Dialysis mode		0.935	–	–	–	–
HD+HDF	Reference		–	–	–	–
HDF	1.106 (0.427–2.867)	0.835	–	–	–	–
HD	1.660 (0.359–7.685)	0.517	–	–	–	–
Others	1.059 (0.229–4.902)	0.942	–	–	–	–

Notes: ^aAssociation between frailty and all-cause mortality, adjusted for age, dialysis duration, GNRI, serum potassium, URR, and medical history of PVD and CPD; ^bAssociation between frailty components and all-cause mortality, adjusted for age, dialysis duration, GNRI, serum potassium, URR, and medical history of PVD and CPD. **Abbreviation:** HD, hemodialysis; CPD, chronic pulmonary disease; GNRI, Geriatric Nutrition Risk Index; HD, hemodialysis; HDF, hemodiafiltration; PVD, peripheral vascular disease; URR, urea removal rate.

Table 3 Univariate and Multivariable Logistic Regression Analyses of Associated Factors with Hospitalization

	Unadjusted		Model 1 ^a		Model 2 ^b	
	OR (95% CI)	P	OR (95% CI)	P-value	OR (95% CI)	P
Age	1.088 (1.035–1.143)	0.001	1.064 (1.008–1.123)	0.025	1.070 (1.016–1.127)	0.010
Frail	3.276 (1.598–6.714)	0.001	2.276 (1.034–5.010)	0.041	–	–
Low activity	3.598 (1.737–7.453)	0.001	–	–	2.809 (1.311–6.020)	0.008
Slow walking speed	2.194 (1.079–4.463)	0.030	–	–	–	0.633
Weakness	2.076 (0.954–4.519)	0.066	–	–	–	–
Weight loss	0.995 (0.360–2.751)	0.992	–	–	–	–
Exhaustion	1.515 (0.741–3.097)	0.254	–	–	–	–
URR	0.939 (0.892–0.989)	0.017	–	0.164	–	0.114
Potassium	0.546 (0.311–0.960)	0.036	–	0.381	–	0.480
CPD	2.623 (1.026–6.707)	0.044	–	0.313	–	0.231
Dialysis duration	1.026 (0.977–1.078)	0.298	–	0.882	–	0.862
PVD	2.108 (0.734–6.057)	0.166	–	–	–	–
GNRI	0.959 (0.912–1.008)	0.102	–	–	–	–
Dialysis mode		0.778	–	–	–	–
HD+HDF	Reference		–	–	–	–
HDF	1.451 (0.677–3.111)	0.338	–	–	–	–
HDs	1.310 (0.306–5.602)	0.716	–	–	–	–
Others	1.528 (0.461–5.063)	0.488	–	–	–	–

Notes: ^aAssociation between frailty and hospital admissions, adjusted for age, dialysis duration, serum potassium, URR, and medical history of CPD; ^bAssociation between frailty components and hospital admissions, adjusted for age, dialysis duration, serum potassium, URR, and medical history of CPD. **Abbreviation:** HD, hemodialysis; CPD, chronic pulmonary disease; GNRI, Geriatric Nutrition Risk Index; HDF, hemodiafiltration; PVD, peripheral vascular disease; URR, urea removal rate.

of the elderly, and the rate of frailty increased.¹³ The elderly who live alone and socialize little were also more susceptible.¹⁴ Similarly, researchers in Spain who studied patients with MHD linked lower physical function, social function, and physical activity to the influence of the COVID-19 pandemic.¹⁵ During the COVID-19 epidemic, elderly patients receiving MHD were less physically active and thus at higher risk of frailty.

Frail patients have poor physiological reserves, low resistance to microbial attacks, and are more prone to adverse outcomes after various acute stress events.^{10,16} For example, frail elderly patients have a higher risk of postoperative complications, comorbidities, hospitalization, and mortality (30-day and long-term).¹⁷ In another study, frailty in elderly patients presented an independent risk of adverse events after trauma.¹⁸ A determination of frailty also has great prognostic value in a setting of acute infection. For example, frail elderly patients had a high rate of mortality or

functional decline within 30 days of hospitalization for pneumonia, which was independent of pneumonia severity; a frailty assessment could inform the widely used standard of pneumonia severity (CURB-65).^{19,20}

Relevant to the present study, acute SARS-CoV-2 infection could cause damage to multiple systems in elderly patients,²¹ and frail elderly patients had a higher risk of mortality after infection.²² If clinicians can improve the frailty of elderly patients, the outcome of emergency events may also improve.

The present study showed that the 3-month all-cause mortality and hospitalization rates of elderly patients under MHD after SARS-CoV-2 infection were 13.4% and 28.7%, respectively. This was lower than the 35.4% and 76.2% rates reported previously.²³ Possible reasons for this discrepancy between the studies may be differences in ethnicity, age, and nutritional status of the enrolled patients, and the dialysis adequacy and the resources of the hospitals. In addition, the pathogenicity of the viral strain may have differed due to mutation. According to the Chinese Center for Disease Control and Prevention, the virus in our study was likely the Omicron variant. In addition, the dialysis access was via arteriovenous fistula (AVF) for 89.9% of the patients. Murt et al²⁴ concluded that AVFs contributed to higher survival in MHD patients with COVID-19. This may partially explain the lower all-cause mortality rate in our study.

The present study showed that the baseline frailty of elderly patients under MHD was significantly associated with all-cause mortality and hospitalization 3 months after SARS-CoV-2 infection. This is consistent with previous findings in adult patients undergoing dialysis. Bouwmans et al²⁵ reported that baseline frailty was an independent risk factor for 3-month mortality in hospital, and in the intensive care unit. Hilbrands et al²⁶ found that baseline frailty was associated with 28-day mortality. However, in another retrospective study,⁹ frailty was not associated with poor prognosis in adult patients under MHD care. These differences may be due to study population, frailty assessment tools, and follow-up time. Previous studies have assessed frailty based on the Clinical Frailty Scale, which is easy to use in the clinic but relies on the subjective judgment of the clinicians.²⁷ In the present research the FFP was applied to objectively reflect the patient's functional status.¹⁰ A correlation between frailty and adverse prognosis after acute viral infection in elderly patients under MHD needs further exploration in multi-center and large sample studies.

When analyzing the individual components of frailty in our patients 3 months after SARS-CoV-2 infection, we found a significant association between the score for the low activity component of the FFP and poor outcomes. Suzuki et al²⁸ showed that baseline low activity status and gradual decrease in activity levels were significantly associated with a higher risk of all-cause mortality and cardiovascular events in patients under MHD. Another study showed that in patients with advanced chronic kidney disease, higher levels of physical activity could reduce the risk of mortality.²⁹ Furthermore, multiple reviews regarding patients on dialysis have reported that physical activity could improve physical functions (grip strength and walking speed), fatigue and pain, depression, and quality of life.³⁰⁻³³ Therefore, we believe that physical activity can improve frailty, at least partially. Although the best pattern of activity is uncertain, we should still encourage patients to engage in appropriate physical activity based on a comprehensive consideration of their general situation.³⁰

The univariate analysis of the present study suggested that after SARS-CoV-2 infection low grip strength and low walking speed were associated with all-cause mortality, and low walking speed was also associated with hospitalization. Grip strength and walking speed can reflect muscle strength and performance³⁴ and are included in the diagnostic criteria for sarcopenia. Some researchers have proposed that these components were more prognostic than sarcopenia in patients under MHD.^{35,36} Johansen et al³⁷ reported that, in patients under MHD, all 5 components of the FFP were associated with all-cause mortality, and joint evaluation was the best approach. We conclude that geriatricians need to pay attention to all components of the FFP, and actively take interventional measures to improve each patient's prognosis.

The present study also found that age was an independent risk factor for adverse outcomes of elderly patients under MHD after SARS-CoV-2 infection. This result is consistent with previous research.^{8,9,23,38} Aging tends to develop into a chronic low-grade pro-inflammatory state, which is an important risk factor for morbidity, physical and cognitive disability, frailty, and death.³⁹ Yet frailty, as an alternative indicator of biological age, may be more predictive than actual age.⁴⁰

The present research is limited by its small sample size and data from a single medical center. However, our results regarding the association between baseline frailty and adverse outcomes in patients under MHD after acute events warrant verification by larger studies and multiple centers.

Conclusion

Frailty in patients aged 60 years or more and undergoing MHD should be assessed as a baseline measure, including the components of frailty. Low physical activity is an especially important prognostic factor for 3-month all-cause mortality and hospitalization in the event of an acute infection. Nephrologists and geriatric physicians should be cognizant of the high incidence and implications of frailty in elderly patients under MHD care. Early assessment, active intervention, and optimized management may improve patients' ability to cope and survive acute physical insults.

Data Sharing Statement

To protect the confidentiality of the participants, these data are not publicly available. The data supporting the results of this study may be provided by appropriate request of the corresponding author.

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Author Contributions

All the authors contributed significantly to this work whether by conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the final published version; agreed on the journal to which the article was submitted; and are accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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