

Effects of Frailty Status on Hospitalization Risk and Healthcare Costs among Patients Undergoing Maintenance Haemodialysis: A Retrospective Cohort Study

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Research Article

Keywords: Frailty, Maintenance haemodialysis, Hospitalization risk, Medical costs

Posted Date: October 11th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10878451/v1>

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Additional Declarations: No competing interests reported.

Abstract

Background

Frailty is common in patients on maintenance haemodialysis(MHD), but its link to healthcare use, is not well understood. This study examined how frailty affects hospitalization outcomes in these patients.

Methods

A retrospective cohort study at a tertiary teaching hospital in East China examined MHD patients from August 2020 to October 2021. Frailty was assessed using the Fried frailty phenotype, categorizing patients as non-frail, pre-frail, or frail. Participants were monitored until October 1, 2025, focusing on all-cause hospitalization frequency and costs. A negative binomial regression model analyzed the link between frailty and hospitalization frequency, while Tobit regression models assessed the relationship with hospitalization costs. Sensitivity analyses used Fine–Gray competing risk models.

Results

A total of 738 patients were included. Compared with non-frail patients, pre-frail and frail patients had significantly higher hospitalization frequencies (IRR = 1.59, 95% CI: 1.354–1.890; and IRR = 2.50, 95% CI: 2.063–3.050, respectively; both $P < 0.001$). Fine–Gray competing risk analyses showed that pre-frail patients had an increased risk of hospitalization (SHR = 1.280, 95% CI: 1.102–1.487; $P = 0.001$), with frail patients facing an even greater risk (SHR = 1.616, 95% CI: 1.322–1.975; $P < 0.001$). Tobit regression analyses showed that hospitalization costs rose by an average of USD 5,354 in pre-frail patients and USD 15,400 in frail patients compared to non-frail patients, indicating a dose-response relationship. Log-transformed cost analyses confirmed these results.

Conclusions

Frailty independently linked to more frequent and costly hospitalizations in MHD patients. Early detection and management could lower healthcare use and costs for this vulnerable group.

Introduction

Chronic kidney disease (CKD) is a major global public health challenge, affecting approximately 10% of the population worldwide [1]. China has the greatest number of patients with CKD, with an estimated 132.3 million affected individuals [2]. As the disease progresses, approximately 0.04% of patients develop end-stage renal disease and require renal replacement therapy to sustain life, among which haemodialysis is the most commonly used treatment modality [3]. By the end of 2022, the Chinese National Renal Data System reported that the number of patients receiving maintenance haemodialysis

(MHD) had reached 0.844 million, with a continuing upwards trend [4]. China's large and continuously growing population of MHD (Maintenance Hemodialysis) patients has imposed a heavy burden on the national healthcare system. Optimizing the allocation of medical resources has become a pressing public health issue that requires urgent resolution.

Nevertheless, this long-term treatment paradigm is associated with a host of significant clinical challenges in clinical practice. Patients undergoing MHD are prone to increased protein catabolism because of multiple factors, including chronic microinflammation, metabolic acidosis, and the accumulation of uraemic toxins [5]. In addition, prolonged sedentary behaviour and reduced physical activity further impair muscle protein synthesis and physical performance, thereby increasing the susceptibility to frailty [6]. Frailty is a clinical syndrome characterized by a decreased physiological reserve and multisystem dysregulation, leading to a reduced ability to withstand stressors and maintain homeostasis [7]. This increased vulnerability to stress is associated with an increased risk of adverse outcomes, including falls, cognitive impairment, disability, and mortality [8]. Our previous study demonstrated that the prevalence of frailty among patients undergoing MHD was as high as 57.5% [9]. Frailty not only substantially compromises health outcomes in this population but also consumes considerable healthcare resources, imposing a substantial socioeconomic burden.

Research conducted in Western countries and select Asian regions, such as the Republic of Korea, has consistently shown a strong association between frailty status and various adverse clinical outcomes in patients undergoing maintenance hemodialysis (MHD), including all-cause mortality, vascular access complications, and increased fall risk [10–12]. Some of these studies have also explored the relationship between frailty and healthcare resource utilization, revealing that frailty is linked to a higher risk of hospitalization and increased medical expenses among MHD populations [13, 14, 15]. However, these investigations have primarily been conducted within the healthcare systems of high-income countries, which differ significantly from the Chinese healthcare system in terms of health insurance policies, hospitalization admission criteria, and dialysis care delivery models. Additionally, the sociodemographic and clinical baseline characteristics of Chinese MHD patients differ from those of Western cohorts, potentially introducing variability in the extent of frailty's impact on hospitalization-related outcomes [16]. Existing research on frailty within Chinese chronic kidney disease (CKD) cohorts has predominantly concentrated on the prevalence of frailty and its associations with clinical outcomes, such as mortality and fall incidents [9, 10]. Nonetheless, a significant gap persists in the real-world evidence (RWE) that systematically examines the relationship between frailty status, hospitalization frequency, and overall healthcare expenditure in this population.

Therefore, using real-world data, this study aimed to systematically evaluate the associations between the frailty status and both hospitalization frequency and total hospitalization costs among patients undergoing MHD and to examine potential dose–response relationships. The findings are expected to provide evidence to inform resource allocation and the development of preventive intervention strategies.

Materials and Methods

Study population

This study was designed as a retrospective cohort study. Patients who received haemodialysis treatment between August 2020 and October 2021 at a tertiary teaching hospital in East China were included. Baseline frailty assessments were completed for all participants during this period. To minimize selection bias, consecutive sampling was employed to recruit patients who met the predefined inclusion and exclusion criteria. Additionally, two independent investigators were assigned the responsibility of verifying the eligibility of each participant for enrollment. The inclusion criteria were as follows: age ≥ 18 years, dialysis duration ≥ 3 months, and receiving haemodialysis three times per week, with each session lasting 3–4 hours. The exclusion criteria included active malignancy, missing baseline frailty assessment data, and kidney transplantation or transfer to another dialysis centre within 3 months of follow-up.

This study was approved by the Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine ([2025B] IIT Ethical Approval No. 1457). Given the retrospective nature of this study, which is based on historical data, the requirement for informed consent was waived by the ethics committee. All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Data collection

The data collected included demographic characteristics, clinical information, and laboratory parameters. The demographic data included age, sex, and educational level. Clinical variables included primary kidney disease, comorbidities (hypertension and diabetes mellitus), dialysis duration, and body mass index (BMI). Laboratory parameters included the levels of haemoglobin, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), serum albumin, C-reactive protein (CRP), serum calcium, serum phosphorus, parathyroid hormone (PTH), urea clearance index (Kt/V), and serum creatinine. Data were obtained from the hospital electronic medical records system, the haemodialysis management system, and the laboratory database. Laboratory data were obtained from the most recent predialysis samples before the study endpoint. All laboratory samples were collected prior to the first dialysis session of the week and promptly delivered for testing within 2 hours of collection. To address potential information bias, a double data entry procedure was employed for all datasets to ensure data accuracy. Prior to the commencement of formal data analysis, all patient-related information was thoroughly de-identified; personally identifiable information (PII) was substituted with unique study identification codes, access to the data was limited to research purposes only, and stringent confidentiality protocols were adhered to throughout the complete data management process.

Assessment of frailty status

Frailty status was assessed using the classic Fried frailty phenotype [17], which includes five components: unintentional weight loss, slow walking speed, reduced grip strength, low physical activity, and self-reported exhaustion. Each component was scored as 1 point if present, yielding a total score ranging from 0 to 5. Patients were classified as non-frail (score = 0), pre-frail (score = 1–2), or frail (score ≥ 3).

Follow-up and outcome measures

Participants were followed from the date of the baseline frailty assessment until October 1, 2025, or until death, kidney transplantation, or transfer to another dialysis centre, whichever occurred first. The follow-up duration was calculated in person-years.

The outcomes of interest included the all-cause hospitalization frequency and total hospitalization costs. Healthcare cost data were obtained from the medical insurance settlement system and included direct medical expenditures related to hospitalization, such as bed charges, diagnostic examinations, treatment procedures, and medication costs.

BMI was calculated as weight (kg) divided by height squared (m^2).

Kt/V was calculated using the following formula:

$$\text{Kt/V} = -\ln(R - 0.008t) + (4 - 3.5R) \times \text{UF/W},$$

where R is the ratio of the postdialysis blood urea nitrogen level to the predialysis blood urea nitrogen level, t is the duration of dialysis (hours), $\ln$ denotes the natural logarithm, UF is the ultrafiltration volume (L), and W is the postdialysis body weight (kg).

Handgrip strength was measured before dialysis using a CAMRY EH101 electronic dynamometer (Guangdong Xiangshan Weighing Apparatus Group Co., Ltd., China). Measurements were performed three times, and the mean value was recorded. For patients with an autologous arteriovenous fistula, measurements were taken on the arm without the fistula; for patients with central venous catheters, the dominant hand was used. All the data were collected by trained research personnel and independently verified by two investigators to ensure the accuracy of the data.

Statistical analysis

All the statistical analyses were performed using R software (version 4.4.0). Continuous variables with a normal distribution are presented as means $\pm$ standard deviations ($\bar{x} \pm \text{SD}$), and differences between groups were compared using one-way analysis of variance (ANOVA). Continuous variables with a nonnormal distribution are presented as medians (interquartile ranges) [M(Q1, Q3)], and comparisons

between groups were conducted using the Kruskal–Wallis H test. Categorical variables are presented as counts (percentages) [n (%)], and comparisons between groups were performed using the χ^2 test; when the expected frequency was < 5, Fisher's exact test was applied. The ordinal variables were analysed using the Kruskal–Wallis H test.

A Poisson regression model was initially fitted to examine the association between the frailty status and hospitalization frequency. If the ratio of deviance to degrees of freedom exceeded 2, indicating overdispersion, a negative binomial regression model was used instead. The incidence rate ratios (IRRs) and 95% confidence intervals (CIs) are reported, and the logarithm of the actual follow-up time (in years) was included as an offset to adjust for differences in the observation duration. Considering that all-cause mortality represents a competing risk factor that may affect hospitalization events, Fine–Gray competing risk models were further employed for sensitivity analysis, and subdistribution hazard ratios (SHRs) with 95% CIs were calculated to verify the robustness of the primary results.

All healthcare cost data were originally recorded in Chinese yuan (CNY) and converted to US dollars (USD) using the annual central parity rate published by the People's Bank of China, corresponding to each patient's actual hospitalization year (2020–2025 rates: 6.46, 5.87, 5.13, 7.05, 7.075, and 7.19 CNY/USD, respectively) to reduce potential bias from inflation and exchange rate fluctuations. Since 17.5% of patients had zero hospitalization costs (left-censored data), the association between the frailty status and hospitalization costs was analysed primarily using covariate-adjusted Tobit regression models. Additionally, unadjusted base models and log-transformed Tobit models were constructed for validation, and bootstrap resampling (1,000 iterations) was performed to further assess robustness. Marginal effects of frailty on hospitalization costs were estimated by creating a standardized patient and adjusting for relevant covariates.

All adjusted models controlled for the following potential confounders: age, sex, dialysis duration, comorbidities (hypertension and diabetes mellitus), and serum albumin, CRP, haemoglobin, PTH, serum phosphorus, and Kt/V levels. For variables with less than 5% missing data, including Kt/V, total cholesterol levels, triglyceride levels, HDL-C levels, LDL-C levels, VLDL-C levels, and BMI, multiple imputation was applied. A two-sided significance level of $\alpha = 0.05$ was used, and P values < 0.05 were considered to indicate statistical significance.

Results

Baseline characteristics

A total of 800 patients undergoing MHD were initially screened. Of these, 20 patients with dialysis durations < 3 months, 3 patients aged < 18 years, 10 patients with an active malignancy, 14 patients with missing baseline frailty assessment data, and 15 patients who underwent kidney transplantation or who were transferred to another dialysis centre within 3 months of follow-up were excluded. Ultimately, 738 MHD patients were included in the analysis. Among them, 252 (34.15%) were classified as non-frail, 317

(42.95%) as pre-frail, and 169 (22.90%) as frail. The median ages of the non-frail, pre-frail, and frail patients were 58.00 years (interquartile range [IQR]: 47.00–69.00), 62.00 years (IQR: 50.00–71.00), and 63.00 years (IQR: 51.00–74.00), respectively, with statistically significant differences among the groups ($P = 0.012$). The detailed results are presented in Table 1.

Table 1
Baseline characteristics of the non-frail, pre-frail, and frail patients undergoing MHD

Characteristic	Overall N = 738	Non-Frail N = 252	Pre-Frail N = 317	Frail N = 169	p value ¹
Sex, n (%)					0.100
Female	280 (38)	109 (43)	110 (35)	61 (36)	
Male	458 (62)	143 (57)	207 (65)	108 (64)	
Age, median (IQR)	61.00 (49.00– 71.00)	58.00 (47.00– 69.00)	62.00 (50.00– 71.00)	63.00(51.00– 74.00)	0.012
Education, n (%)					0.240
Primary	139 (19)	44 (17)	64 (20)	31 (18)	
Secondary	172 (23)	70 (28)	70 (22)	32 (19)	
High school	245 (33)	83 (33)	108 (34)	54 (32)	
College or above	182 (25)	55 (22)	75 (24)	52 (31)	
Primary disease, n (%)					0.660
Glomerulonephritis	448 (61)	155 (62)	195 (62)	98 (58)	
Diabetes	166 (22)	51 (20)	75 (24)	40 (24)	
Others	124 (17)	46 (18)	47 (15)	31 (18)	
Hypertension, n (%)	524 (71)	174 (69)	234 (74)	116 (69)	0.340
Diabetes, n (%)	205 (28)	62 (25)	92 (29)	51 (30)	0.370
Dialysis duration (months), median (IQR)	53.00 (19.00– 104.00)	61.00 (21.00– 112.50)	46.00 (19.00– 98.00)	53.00 (15.00– 103.00)	0.070
BMI (kg/m ²), median (IQR)	20.96 (18.92– 23.66)	21.08 (18.88– 24.08)	21.09 (19.10– 23.61)	20.69 (18.44– 22.84)	0.290
Haemoglobin (g/L), median (IQR)	109.50 (101.00– 117.00)	109.00 (100.00– 117.00)	110.00 (101.00– 117.00)	109.00 (102.00– 117.00)	0.980
Triglycerides (mmol/L), median (IQR)	1.57 (1.06– 2.50)	1.59 (1.08– 2.57)	1.63 (1.05– 2.51)	1.46 (1.00– 2.34)	0.220

Note: IQR, interquartile range; SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; PTH, parathyroid hormone; Kt/V, urea clearance index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.

Characteristic	Overall N = 738	Non-Frail N = 252	Pre-Frail N = 317	Frail N = 169	p value ¹
Total cholesterol (mmol/L), median (IQR)	3.41 (2.93–4.15)	3.40 (2.89–4.20)	3.50 (2.99–4.19)	3.35 (2.89–4.01)	0.430
HDL-C (mmol/L), median (IQR)	0.93 (0.77–1.18)	0.94 (0.73–1.17)	0.92 (0.78–1.15)	0.95 (0.80–1.21)	0.400
LDL-C (mmol/L), median (IQR)	1.67 (1.26–2.23)	1.65 (1.27–2.20)	1.70 (1.29–2.27)	1.69 (1.20–2.24)	0.690
VLDL-C (mmol/L), median (IQR)	0.71 (0.49–0.99)	0.68 (0.50–0.99)	0.74 (0.51–1.02)	0.64 (0.46–0.91)	0.070
Albumin (g/L), median (IQR)	40.00 (37.40–42.00)	40.15 (37.80–42.10)	39.90 (37.30–41.90)	39.40 (37.10–42.10)	0.500
CRP (mg/L), median (IQR)	2.00 (0.83–5.30)	2.00 (0.70–4.83)	2.00 (0.91–5.30)	2.00 (0.90–6.60)	0.430
Calcium (mmol/L), median (IQR)	2.26 (2.14–2.39)	2.25 (2.15–2.41)	2.26 (2.15–2.39)	2.24 (2.13–2.36)	0.330
Phosphorus (mmol/L), Median (IQR)	1.64 (1.34–2.04)	1.68 (1.39–2.04)	1.60 (1.32–2.01)	1.67 (1.30–2.08)	0.520
PTH (pg/mL), median (IQR)	189.00 (101.00–318.00)	188.00 (99.90–313.20)	187.00 (104.20–330.00)	191.40 (90.90–297.00)	0.650
Kt/V, median (IQR)	1.57 (1.36–1.76)	1.60 (1.36–1.83)	1.55 (1.35–1.71)	1.56 (1.38–1.76)	0.370
Creatinine (μmol/L), mean ± SD	890.78 ± 260.73	920.45 ± 264.81	893.49 ± 245.50	841.46 ± 276.24	0.019
Event type, n (%)					< 0.001
No event	121 (16)	70 (28)	48 (15)	3 (1.8)	
Hospitalization	584 (79)	178 (71)	258 (82)	148 (88)	
Note: IQR, interquartile range; SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; PTH, parathyroid hormone; Kt/V, urea clearance index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.					

Characteristic	Overall N = 738	Non-Frail N = 252	Pre-Frail N = 317	Frail N = 169	p value ¹
Death	31 (4.2)	4 (1.6)	9 (2.9)	18 (11)	
Follow-up years, median (IQR)	3.47 (1.25– 5.17)	4.10 (1.92– 5.17)	3.47 (1.42– 5.17)	1.58 (0.58– 3.88)	< 0.001
Hospitalization cost (USD), median (IQR)	7,327.89 (1,456.52– 18,738.27)	2,725.98 (0.00– 9,420.18)	8,512.27 (2,071.65– 18,821.61)	13,945.08 (6,391.19– 25,397.61)	< 0.001
Hospitalization frequency, median (IQR)	3.00 (1.00– 5.00)	1.00 (0.00– 4.00)	3.00 (1.00– 5.00)	4.00 (2.00– 6.00)	< 0.001
Note: IQR, interquartile range; SD, standard deviation; BMI, body mass index; CRP, C-reactive protein; PTH, parathyroid hormone; Kt/V, urea clearance index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.					

Association between frailty and hospitalization frequency

According to unadjusted negative binomial regression analyses, compared with non-frail patients, pre-frail patients had a significantly higher hospitalization rate (IRR = 1.599, 95% CI: 1.354–1.890; $P < 0.001$), and the increase was more pronounced among frail patients (IRR = 2.507, 95% CI: 2.063–3.050; $P < 0.001$). After adjustment for age, sex, dialysis duration, hypertension, diabetes mellitus, and serum albumin, CRP, haemoglobin, PTH, serum phosphorus, and Kt/V levels, these associations remained statistically significant (pre-frail: IRR = 1.593, 95% CI: 1.345–1.887; $P < 0.001$; frail: IRR = 2.498, 95% CI: 2.056–3.039; $P < 0.001$). The detailed results are presented in Fig. 1 and Table 2.

Table 2

Negative binomial regression analysis of the association between the frailty status and hospitalization frequency

Group	Unadjusted Model		Adjusted Model [§]	
	IRR (95% CI)	P value	IRR (95% CI)	P value
non-frail	1.00 (Reference)	-	1.00 (Reference)	-
pre-frail	1.599 (1.354–1.890)	< 0.001	1.593 (1.345–1.887)	< 0.001
Frail	2.507 (2.063–3.050)	< 0.001	2.498 (2.056–3.039)	< 0.001
Notes: [§] The model was adjusted for the following covariates: age, sex, dialysis duration, hypertension, diabetes, albumin level, C-reactive protein level, haemoglobin level, parathyroid hormone level, phosphate level, and urea clearance index. All models included log(actual follow-up years) as an offset term to standardize the hospitalization rate.				

Sensitivity analysis

In the Fine–Gray competing risk model, death was treated as a competing event to assess the association between the frailty status and hospitalization events. The results showed that pre-frail patients had a higher subdistribution hazard ratio (SHR) for hospitalization (SHR = 1.280, 95% CI: 1.102–1.487; P = 0.001), whereas frail patients exhibited an even higher risk (SHR = 1.616, 95% CI: 1.322–1.975; P < 0.001), indicating that the frailty status was an independent risk factor for hospitalization. After adjustment for age, sex, dialysis duration, hypertension status, diabetes mellitus status, serum albumin level, CRP level, haemoglobin level, PTH level, serum phosphorus level, and Kt/V, the associations remained statistically significant. In addition, an older age (SHR = 1.006, 95% CI: 1.001–1.011; P = 0.017) and higher PTH levels (SHR = 1.0003, 95% CI: 1.0002–1.0004; P < 0.001) were associated with an increased risk of hospitalization. The detailed results are presented in Table 3.

Table 3

Fine–Grey competing risk analysis of the association between the frailty status and hospitalization events

Variable	SHR	95% CI	p value
non-frail	1.00 (reference)	-	-
pre-frail	1.280	1.102–1.487	0.001
Frail	1.616	1.322–1.975	< 0.001
Age	1.006	1.001–1.011	0.017
Sex	0.964	0.820–1.133	0.659
Dialysis duration	1.000	0.998–1.001	0.618
Hypertension	0.946	0.802–1.115	0.505
Diabetes	1.169	0.986–1.386	0.072
Albumin level	0.985	0.964–1.006	0.156
CRP level	0.997	0.991–1.003	0.258
Haemoglobin level	0.997	0.991–1.003	0.329
Phosphorus level	0.944	0.824–1.081	0.405
PTH level	1.0003	1.0002–1.0004	< 0.001
Kt/V	1.036	0.871–1.234	0.691

Note: SHR, subdistribution hazard ratio; CI, confidence interval; CRP, C-reactive protein; PTH, parathyroid hormone; Kt/V, urea clearance index.

Association between the frailty status and hospitalization costs

In the unadjusted base Tobit model (Wald $\chi^2 = 28.43$, $P < 0.001$), hospitalization costs were significantly higher among pre-frail and frail patients than among non-frail patients. Specifically, pre-frail patients incurred an average increase of USD 5,750 in hospitalization costs (95% CI: 694–10,805; $P = 0.026$), whereas frail patients experienced an average increase of USD 15,980 (95% CI: 10,088–21,873; $P < 0.001$).

After adjustment for age, sex, and multiple additional covariates, the Tobit model remained statistically significant ($\chi^2 = 44$, $P < 0.001$). Compared with the non-frail patients, hospitalization costs increased by an average of USD 5,354 among pre-frail patients (95% CI: 282–10,427; $P = 0.039$) and by USD 15,400 among frail patients (95% CI: 9,483–21,316; $P < 0.001$), demonstrating a clear dose–response relationship. In addition, patients with diabetes mellitus incurred significantly higher hospitalization costs, with an average increase of USD 6,637 (95% CI: 1,297–11,976; $P = 0.015$). Other covariates, including age, sex, BMI, hypertension, dialysis duration, and laboratory indicators, were not significantly associated with hospitalization costs.

According to the log-transformed Tobit model, hospitalization costs of pre-frail patients were, on average, 1.629 log-units higher than those of non-frail patients (95% CI: 0.919–2.339; $P < 0.001$), while the costs of frail patients increased by 2.788 log-units (95% CI: 1.955–3.622; $P < 0.001$). Serum albumin levels were positively associated with log-transformed hospitalization costs, with an increase of 0.105 log-units per unit increase in the albumin concentration (95% CI: 0.018–0.192; $P = 0.018$). No statistically significant associations were observed for other covariates, including age, sex, or diabetes mellitus ($P > 0.05$ for all). The detailed results are presented in Table 4. After adjustment for age, sex, BMI, comorbidities, and key laboratory indicators, marginal effect estimates for a standardized patient showed that the predicted hospitalization cost was USD 3,842 for non-frail patients. The predicted hospitalization cost for pre-frail patients was USD 9,196, representing an increase of USD 5,354 (139.4%) compared with that for non-frail patients; thus, hospitalization costs for pre-frail patients were approximately 2.4 times higher than those for non-frail patients. For frail patients, the predicted hospitalization cost was USD 19,242, corresponding to an increase of USD 15,400 (400.8%) compared with non-frail patients. After controlling for covariates, hospitalized frail patients were predicted to incur approximately fivefold higher hospitalization costs than non-frail patients were.

Table 4

Association between the frailty status and hospitalization costs based on three Tobit regression models

Variable	Unadjusted Tobit model (USD) ¹		Adjusted Tobit model (USD) ²		Tobit of model log-transformed costs (ln-unit) ³	
	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value
Intercept	4,454 (624, 8,283)	0.023	-15,190 (-49,824--19,443)	0.390	0.029 (-4.842, 4.900)	0.991
non-frail	-	-	-	-	-	-
pre-frail	5,750 (694, 10,805)	0.026	5,354 (282–10,427)	0.039	1.629 (0.919, 2.339)	< 0.001
Frail	15,980 (10,088, 21,873)	< 0.001	15,400 (9,483–21,316)	< 0.001	2.788 (1.955, 3.622)	< 0.001
Age	-	-	45 (-130, 220)	0.616	0.020 (-0.005, 0.044)	0.116
Sex	-	-	1,080 (-4,024, 6,185)	0.678	-0.219 (-0.936, 0.499)	0.550
Dialysis duration	-	-	18 (-20, 56)	0.362	0.002 (-0.004, 0.007)	0.500
Hypertension	-	-	1,829 (-3,051, 6,708)	0.463	0.198 (-0.488, 0.884)	0.571
Diabetes	-	-	6,637 (1,297, 11,976)	0.015	0.409 (-0.344, 1.162)	0.287
Albumin level	-	-	389 (-231, 1,009)	0.219	0.105 (0.018, 0.192)	0.018
CRP level	-	-	-63 (-210, 83)	0.397	-0.018 (-0.038, 0.003)	0.086
Creatinine level	-	-	-5.9 (-16.6, 4.8)	0.297	0.0003 (-0.0015, 0.0015)	0.970

Variable	Unadjusted Tobit model (USD) ¹		Adjusted Tobit model (USD) ²		Tobit of model log-transformed costs (ln-unit) ³	
	β (95% CI)	p value	β (95% CI)	p value	β (95% CI)	p value
BMI			224 (-390, 837)	0.475	0.024 (-0.062, 0.110)	0.582
Phosphorus level	-	-	-1,223 (-5,540, 3,094)	0.579	-0.098 (-0.705, 0.509)	0.753
PTH level	-	-	0.98 (-5.9, 7.9)	0.780	0.0003 (-0.0006, 0.0013)	0.516
Kt/V	-	-	-290 (-5,017, 4,438)	0.904	-0.082 (-0.752, 0.589)	0.811
Note: Model 1 was unadjusted. Model 2 was adjusted for age, sex, diabetes mellitus, hypertension, serum albumin level, CRP level, BMI, serum phosphorus level, PTH level, and Kt/V. All monetary values were converted to US dollars (USD) using the annual central parity exchange rate between the Chinese yuan and the US dollar corresponding to each patient's hospitalization year. Model 3 was a log-transformed model; ln-units represent effect estimates for the natural logarithm-transformed dependent variable and can be interpreted as relative changes. CRP, C-reactive protein; BMI, body mass index; PTH, parathyroid hormone; Kt/V, urea clearance index.						

Discussion

The strong association between frailty and adverse clinical outcomes among patients undergoing MHD has been well documented in previous studies [18–20]. Building upon this evidence, the present study extended the analysis to healthcare utilization and the economic burden, thereby further validating and expanding the existing findings. We demonstrated that compared with non-frail patients, pre-frail and frail patients had a significantly higher risk of hospitalization, with increasing frailty status associated with a greater number of hospitalizations. These findings provide robust empirical evidence for the effect of frailty on healthcare utilization among patients undergoing MHD. Moreover, analyses of hospitalization costs revealed a significant positive association between the frailty status and medical expenditures, suggesting that frailty is an important correlate of an increased healthcare burden. Collectively, these results provide meaningful insights for optimizing health management strategies and reducing the economic burden on this vulnerable population.

Our findings showed that, compared with non-frail patients, hospitalization costs increased by USD 5,354 among pre-frail patients, while the increase was substantially greater among frail patients. These results are consistent with those reported by Johnston et al. [13], who demonstrated that the frailty status was associated with a significantly higher healthcare cost burden. Similarly, a previous study by Sy et al. [14] reported that, compared with non-frail patients, frail patients undergoing MHD incurred 22% higher total healthcare expenditures and 62.9% higher hospitalization costs, with an annual difference in hospitalization costs of approximately USD 11,500, findings that are consistent with our results. Importantly, our study further showed that even pre-frail patients had a 1.599-fold higher hospitalization rate than non-frail patients, and their hospitalization costs had already marginally but significantly increased. A large cohort study from South Korea examining the association between the frailty index and 10-year healthcare utilization and costs similarly revealed that pre-frail individuals had higher average total medical costs, inpatient costs, and outpatient costs than non-frail individuals [15]. These findings suggest that increased healthcare costs begin to emerge during the pre-frail stage. Therefore, clinical attention should not be limited to patients who have already progressed to frailty; pre-frail individuals may represent the most cost-effective target population for intervention [21]. Early interventions, such as nutritional support and exercise-based rehabilitation, may delay frailty progression [22] and facilitate a shift towards earlier disease prevention.

In the present study, the median follow-up age of frail patients was significantly older than that of non-frail patients, and age was identified as an independent risk factor for hospitalization. These findings may be related to the age-associated dysregulation of the hypothalamic–pituitary–adrenal axis, which exhibits a progressive decrease in function with ageing [23]. Such neuroendocrine alterations are closely linked to a reduced organ functional reserve, impaired stress resilience, and increased vulnerability to acute events, potentially contributing to an increased risk of hospitalization due to infections, cardiovascular events, and other complications [24]. Previous studies have reported an association between lower serum albumin levels and increased hospitalization risks [25]. In contrast, our study revealed a positive association between higher serum albumin levels and hospitalization costs. One possible explanation is that MHD patients with higher serum albumin levels generally have a better overall health status and longer survival, thereby increasing their likelihood of experiencing multiple hospitalization events over time. In addition, a greater physiological reserve and better treatment tolerance may allow these patients to undergo more intensive medical interventions, resulting in higher cumulative costs. Conversely, patients with end-stage disease and low serum albumin levels are more likely to receive conservative or palliative care with relatively lower costs. This difference in treatment intensity may further amplify differences in hospitalization expenditures.

Competing risk analyses also revealed that PTH levels were an independent risk factor for hospitalization, suggesting that hyperparathyroidism may be associated with a greater healthcare burden. Elevated PTH levels can lead to secondary hyperparathyroidism, which contributes to skeletal muscle atrophy and functional impairment, exacerbating decreases in grip strength and physical activity to thereby accelerate the progression of frailty, creating a vicious cycle [26]. Moreover, elevated PTH levels in MHD patients reflect systemic disturbances in mineral and bone metabolism [27], which are

frequently accompanied by vascular calcification, cardiovascular events, and sarcopenia [28], all of which may collectively increase the hospitalization risk. Therefore, PTH may serve as a potential biomarker for hospitalization-related resource utilization in MHD patients, highlighting the importance of addressing calcium–phosphorus metabolic disorders alongside targeted frailty management.

Several limitations of this study should be acknowledged. First, this single-centre retrospective cohort study was conducted at a tertiary hospital, which may limit the generalizability of the findings. Second, the frailty status was assessed only at baseline and was not monitored dynamically over time. Given the potentially reversible nature of frailty, this limitation may have attenuated the long-term effect estimates. Third, although we adjusted for age, sex, dialysis duration, comorbidities, and multiple biochemical indicators, residual confounding from unmeasured social determinants of health—such as family support, living environment, socioeconomic status, and health literacy—cannot be fully excluded. These factors may influence patients' self-management behaviours and healthcare utilization patterns. Future multicentre prospective studies incorporating psychosocial and socioeconomic variables are warranted to further validate the robustness of our findings.

Fourthly, while the Fried Frailty Phenotype is the most validated tool for assessing frailty in older adults and those on hemodialysis, certain aspects like physical activity and fatigue can be influenced by sociocultural factors, lifestyle, and disease symptoms. Hemodialysis patients often experience fatigue and reduced activity due to treatment schedules and symptoms, potentially leading to an overestimation of frailty. Additionally, personal perceptions of activity and health can skew symptom assessment. Future research should incorporate multidimensional approaches for a more thorough frailty evaluation.

A limitation of this study is that we used the annual official exchange rate from the People's Bank of China for currency conversion of inpatient expenditure data from 2020 to 2025. However, daily exchange rate fluctuations can affect the accuracy of medical cost estimates by introducing biases in currency conversion and influencing macroeconomic factors like the cost of imported medical supplies and medical service fees[29]. Therefore, it is advisable for future research to further investigate the potential confounding impact of exchange rate volatility on the precision of cost estimation outcomes.

In conclusion, this study demonstrates that frailty is an independent factor associated with an increased hospitalization risk and higher medical costs among patients undergoing MHD. As frailty advances, hospitalization rates and costs rise significantly, even in pre-frail patients. Thus, routine frailty screening and multidisciplinary interventions—such as nutrition, exercise, and psychological support—should be adopted in clinical practice to slow frailty progression, lower hospitalizations, and reduce economic impact.

Abbreviations

Chronic kidney disease	CKD
maintenance haemodialysis	MHD
interquartile range	IQR
standard deviation	SD
body mass index	BMI
C-reactive protein	CRP
parathyroid hormone	PTH
blood urea nitrogen	BUN
urea clearance index	Kt/V
high-density lipoprotein cholesterol	HDL-C
low-density lipoprotein cholesterol	LDL-C
very low-density lipoprotein cholesterol	VLDL-C
subdistribution hazard ratio	SHR
confidence interval	CI

Declarations

cknowledgements

We thank all the participants in this study for their support.

Author Contributions

The study was designed by J-P Y, G-L C and J-H F Interpretation, drafting and revision of the manuscript were performed by all authors. The decision to submit this manuscript for publication was jointly made by all the authors, and the manuscript was confirmed to be accurate and approved by all the authors.

Funding

This work was supported by the Discipline Construction Project Fund for Nursing Research.(FAHZU- No. 2025ZYHL24), General Research Project of Zhejiang Provincial Education Department (Natural Science Category) (Y202353913),and the Zhejiang Provincial Medical Association Special Fund for Clinical Medical Research (2025ZYC-A06).

Data availability

The datasets generated and/or analyzed in the current study are not publicly available because of patient privacy concerns but are available from the corresponding author upon reasonable request.

Ethical Considerations

This study was approved by the Ethics Review Committee of the First Affiliated Hospital of Zhejiang University School of Medicine ([2025B] IIT Ethics Approval No.1457). The research was conducted in compliance with the core principles outlined in the Declaration of Helsinki. This study is retrospective in nature, and the Ethics Committee has granted a waiver for the requirement of informed consent.

Consent for Publication

All the authors have read and approved the submitted manuscript and support its publication.

Declaration of Conflicts of Interest

We have no conflicts of interest to disclose.

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Figures

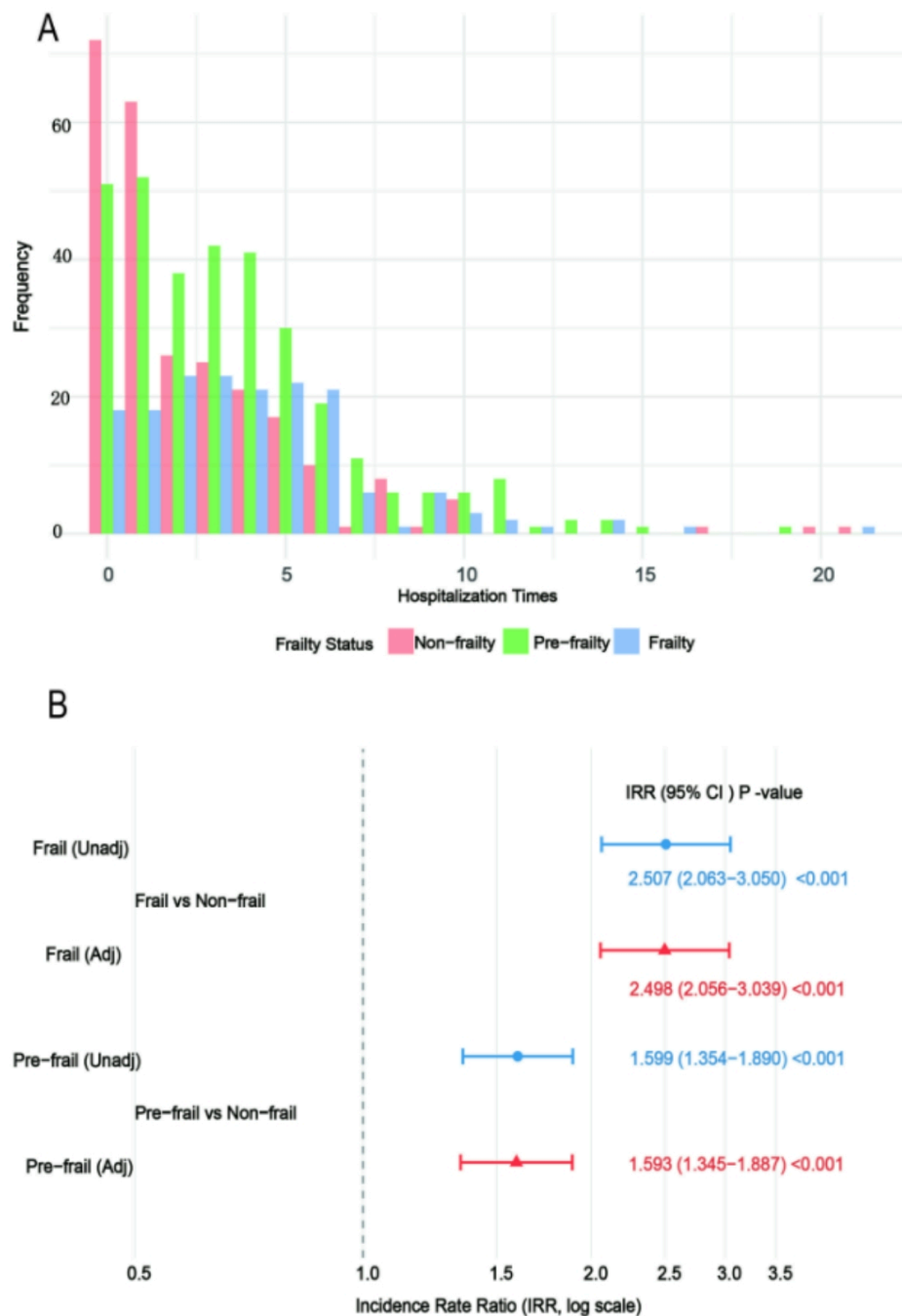


Figure 1

Distribution of the hospitalization frequency and forest plot of incidence rate ratios (IRRs) for patients stratified by frailty status. **A.** Boxplot showing the distribution of the hospitalization frequency across frailty groups. **B.** Forest plot of incidence rate ratios (IRRs) and their 95% confidence intervals derived from the negative binomial regression model. Reference group: non-frail patients.