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Prevalence and associated factors of frailty among Southern Chinese Han patients on haemodialysis: a multicentre, observational cross-sectional study

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ABSTRACT

Objectives Frailty has been extensively studied in the general population. However, there is little information on frailty among patients undergoing haemodialysis (HD) in China. This study analysed the prevalence and associated factors of frailty among Southern Chinese Han patients on HD.

Design Observational cross-sectional study.

Setting Three HD centres in Southern China.

Participants Three hundred patients who underwent regular HD between June 2019 and October 2019.

Main outcomes and measures Frailty was assessed using the Tilburg indicator of frailty (TFI) questionnaire, and the psychological status of the respondents was evaluated by the Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS).

Results Seventy-five per cent of participants were in the frailty group, and the TFI score of HD patients was 6.89±2.87, with 8.15±2.06 in the frailty group and 2.87±1.31 in the non-frailty group. Frailty patients had higher SDS and SAS scores, and were more likely to suffer depression and anxiety than non-frailty patients. Multivariate logistic regression analysis excluding depression and anxiety showed that age, Charlson Comorbidity Index (excluding end-stage renal disease), a nuclear family (compared with living alone), and albumin were independently associated with frailty (all p<0.05). In the model including depression and anxiety, age, diabetes mellitus, living as a couple (compared with living alone), a nuclear family (compared with living alone), an extended family (compared with living alone), low phosphorus, depression and anxiety were associated with frailty by multivariate logistic regression analysis (all p<0.05).

Conclusions Approximately three-quarters of patients with HD in Southern China are frail, often accompanied with depression and anxiety. Age, diabetes mellitus, family structure, phosphorus, depression and anxiety were associated with frailty.

Strengths and limitations of this study

- We analysed the prevalence and associated factors of frailty among Southern Chinese Han patients on haemodialysis (HD), which has not been investigated in detail to date.
- The Tilburg indicator of frailty has been extensively studied among community-dwelling people aged 65 years or older, although it has rarely been used to assess frailty among patients undergoing HD.
- The sample size included in this study was relatively small, and dialysis-related indicators and nutritional information were lacking.

INTRODUCTION

Frailty, an age-related fragile state that is characterised by lack of physiological reserve and decreased ability to resist stress, was first described and verified by Fried *et al* in the elderly population.[1 2] As a unique domain associated with, but distinct from, comorbidities and disabilities, frailty can lead to an increased risk of adverse outcomes, including falls, fractures, hospitalisation, disability, cognitive decline, dementia and poor quality of life.[3–10] Frailty has been extensively studied in the general population, with a weighted overall prevalence of approximately 10% among community-dwelling people aged 65 years or older.[1 11] However, there is a relatively limited number of studies showing an increase in the prevalence of frailty in high-risk groups, such as patients with cardiovascular disease, cancer, surgery and end-stage renal disease (ESRD).[12–15]

The prevalence of frailty in patients with chronic kidney disease (CKD) is significantly higher than that in the general elderly population,[11 16] and the prevalence increases as renal function declines, with the highest prevalence among patients with ESRD.[15–20] CKD is associated with malnutrition, chronic inflammation, metabolic acidosis and low physical activity, and these factors directly or

indirectly contribute to accelerated ageing and may lead to frailty development.[20–22] Predialysis patients can show significant muscle atrophy, which is the main reason for weakness in CKD patients.[23] When combined with frailty, it further increases the risk of falls, fractures, hospitalisation, cognitive impairment and mortality in patients with CKD.[16 18 24–26]

The most commonly used method to assess frailty is the Fried phenotype frailty scale based on a biological model[1]; however, because this physical frailty tool might lead to fragmentation of care, some researchers have emphasised the multi-factorial nature of frailty.[27 28] The Tilburg indicator of frailty (TFI) was developed using a complete conceptual model covering three dimensions: physical, psychological, and social frailty.[28] The TFI is a standardised self-reported questionnaire that can be administered in several ways, such as face-to-face interviews, emails, chat applications in mobile phones or telephone calls, whereas Fried's phenotype scale requires face-to-face interviews to objectively assess physical performance, which requires professional expertise. The TFI has been extensively studied in terms of psychometric properties and it has shown reliability and validity, making it particularly useful for both laypeople and professionals.[29] However, the TFI has rarely been used to assess frailty among patients undergoing dialysis, and the prevalence of frailty among haemodialysis (HD) patients using the TFI in southern China remains unclear.

The purpose of this study was to explore the prevalence of frailty, including physical, psychological and social frailty, and its associated factors among HD patients in southern China.

METHODS

Study population

Between June 2019 and October 2019, 623 patients who had been on regular HD for more than 3 months were enrolled from three HD centres (the First Affiliated Hospital of Jinan University, the Guangzhou Red Cross Hospital and Jihua Affiliated Hospital of Jinan University) as the cohort for this cross-sectional study. The exclusion criteria were as follows: (1) patients aged <18 years; (2) those diagnosed with dementia, Alzheimer's disease or schizophrenia; (3) patients undergoing treatment for other acute and critical conditions; (4) those who refused the questionnaire survey; (5) inability to communicate and complete the questionnaire; (6) a deficiency of clinical data and (7) an incomplete or unqualified questionnaire.

A total of 323 patients were excluded for the following reasons: 25 patients were younger than 18 years of age; 49 patients were diagnosed with dementia, Alzheimer's disease or schizophrenia; 48 patients were being treated for other acute and critical conditions; 87 patients refused the questionnaire survey; 65 patients showed inability to communicate and complete the questionnaire; 35 patients had a deficiency of clinical data; and 14 questionnaires were incomplete or unqualified (online supplemental figure 1).

In total, 300 HD patients were enrolled in the study. The causes of renal disease were as follows: 79 patients (26.33%) had primary glomerular nephropathy, 83 patients (27.67%) had diabetic kidney disease, 35 patients (11.67%) had hypertensive nephropathy, 58 patients (19.33%) had obstructive nephropathy, 10 patients (3.33%) had polycystic kidney disease and 35 patients (11.67%) had other causes.

Patient and public involvement

No patient involved.

Measurements

Data collection

Data collection was performed using a questionnaire. A trained investigator conducted face-to-face, self-reported and semistructured interviews with patients. We also recorded demographic data including age, gender, primary renal disease and complications, duration of HD, blood pressure, dry weight body mass index (BMI), education status, marital status, family structure and payment pattern. Laboratory data (including haemoglobin, albumin, total cholesterol, triglycerides, high sensitivity C reactive protein (hsCRP), calcium, phosphorus and intact parathyroid hormone (iPTH)) were collected before dialysis and immediately on patient admission. All the experimental indices were measured on a 7180 Biochemical Automatic Analyzer (Hitachi, Tokyo, Japan).

Frailty

Frailty was assessed using the TFI questionnaire, consisting of fifteen self-reported questions covering three domains. Among them, the physical domain included eight items, the psychological domain included four items, and three items were in the social domain. The answer categories for each item were 0 (no) and 1 (sometimes or yes). Participants with an overall score of 5 or higher were included in the frailty group.[28 30–32] The cut-off scores of physical, psychological and social frailty were 3, 2 and 2, respectively.[28 33]

Psychological status

The Self-Rating Depression Scale (SDS)[34] and the Self-Rating Anxiety Scale (SAS)[35] were used to evaluate the psychological status of the respondents. According to the Chinese norm, the threshold value of the SDS score was 53; 53–62 was mild depression, 63–72 was moderate depression, and ≥73 was severe depression.[36 37] SAS scores ranging from 50 to 59 were diagnosed as mild anxiety, those from 60 to 69 as moderate anxiety, and ≥70 as severe anxiety according to the Chinese norm.[37]

Charlson Comorbidity Index

We used the Charlson Comorbidity Index (CCI) and age-adjusted CCI (aCCI) to quantify comorbidities. According to the CCI score, the patients' comorbidities were classified into three groups according to severity:

mild (1–2 points), moderate (3–4 points) and severe (≥5 points).[38 39]

Statistical analyses

Continuous variables are presented as the mean±SD, and non-parametric variables are presented as the median and IQR. Categorical variables are expressed as frequency and percentage. Logarithmic transformation of iPTH in regression analysis was performed because of the skewed distribution.

The Student's t-test, analysis of variance or the non-parametric test was used to compare continuous variables between groups where appropriate. Differences between categorical variables were analysed using a chi-square test or double-tailed Fisher's exact test depending on applicability.

A multivariate logistic regression model was used to study the association of indices of frailty with age, gender, and all variables, with significant associations (p<0.05) examined using univariate logistic regression analysis. The social demographic information was incorporated into the logistic regression analyses to account for the effects of these uncontrollable social factors. Considering that TFI includes psychological frailty, two multivariate logistic regression models were used: model 1 excluding depression and anxiety and model 2 including depression and anxiety.

All values were two tailed, and a p<0.05 was considered statistically significant. Data were analysed using IBM SPSS Statistics V.25.0 for Windows (IBM).

RESULTS

Demographic and clinical characteristics of the study population

The mean age of patients was 61.96 years, and 61.33% of patients were male. The median duration of HD was 33 months, and the mean dry weight BMI was 22.20. In the non-frailty group, 6.67% of patients lived alone, 20.00% were in a couple, 37.33% in a nuclear family, and 36.00% had an extended family. The prevalence of the family structure in the frailty group was 14.22% living alone, 28.00% in a couple, 17.78% with a nuclear family and 40.00% with an extended family (table 1).

Patients with frailty were older, had a longer duration of HD, had a higher prevalence of diabetes mellitus (DM), CCI and aCCI, and lower serum albumin and phosphorus than those in the non-frailty group (p<0.05; table 1).

Prevalence of frailty among HD patients

Of all participants, 75.00% were categorised as frail. The TFI score of HD patients was 6.89±2.87, with 8.15±2.06 in the frailty group and 2.87±1.31 in the non-frailty group. In the frailty group, the physical, psychological, and social scores were 4.80±1.43, 2.42±1.10 and 1 (IQR 0–2), respectively, which were significantly higher than those of the non-frailty group (1.77±0.76, 0.73±0.97 and 0 (IQR 0–1), respectively, all p<0.001). Among frailty patients, the prevalence of the three domains of frailty was 94.67%, 78.67%, and 27.11% for physical frailty, psychological frailty, and social frailty, respectively, whereas in the non-frailty group, the prevalence was 17.33%, 25.33%, and 5.33%, respectively (all p<0.001, figure 1).

Overlap between frailty, depression and anxiety

There was a higher prevalence of psychological disorders in frailty participants. The score was 58.17±9.05 for SDS and 49.62±6.35 for SAS, with 72.00% of HD patients diagnosed with depression and 52.67% with anxiety. Frailty patients had higher SDS and SAS scores and were more likely to suffer from depression and anxiety than non-frailty patients (all p<0.001; table 1). There was overlap between frailty, depression, and anxiety: approximately half of the HD patients were frail with both depression and anxiety. Only 9% were frail without depression or anxiety, 3.33% were frail with depression but no anxiety, and 17.67% were frail with anxiety but no depression. 14.33% did not suffer from frailty, depression or anxiety (figure 2).

Approximately 80% of patients with mild depression had frailty, and the percentage of frailty in participants with moderate to severe depression reached 95% or higher. Among patients with mild to moderate anxiety, >90% suffered from frailty (online supplemental figure 2).

Factors associated with frailty

62.35% of middle-aged (45–59 years) and 85.64% of elderly (≥60 years) patients with HD had frailty, which was higher than the prevalence in younger (<45 years of age) groups (50.00%, both p<0.001). The prevalence of frailty was highest in patients with a duration of HD ≤1 year (85.86% vs 64.56% in duration of HD 1–3 years group, p=0.001; 85.86% vs 72.95% in duration of HD >3 years group, p=0.02). The percentage of patients with frailty was higher in those with DM than in those without DM (85.71% vs 66.74%, p<0.001). According to CCI (excluding ESRD) scores, patients' comorbidities were classified into three groups: none, mild, and moderate and severe. Compared with the mild or moderate and severe comorbidity groups, patients without comorbidities had a lower prevalence of frailty (77.88% vs 58.33%, p=0.003; and 88.00% vs 58.33%, p<0.001, respectively). Patients living alone or in a couple had a higher prevalence of frailty than those living in a nuclear family (86.49% vs 58.82%, p=0.004; 80.77% vs 58.82%, p=0.004; figure 3).

A multivariate logistic regression analysis was performed to identify factors independently associated with frailty. In a multivariate adjusted model excluding depression and anxiety, the analysis showed that age, CCI (excluding ESRD), a nuclear family (compared with living alone) and albumin were independently associated with frailty (all p<0.05). In the model including depression and anxiety, age, DM, living in a couple (compared with living alone), a nuclear family (compared with living

Table 1 Differences of demographic and clinical characteristics between frailty patients and non-frailty patients

	Non-frailty (N=75)	Frailty (N=225)	Total (N=300)	P value
Age	53.93±13.13	64.64±12.82	61.96±13.68	<0.001
Age groups				<0.001
<40 years	17 (22.67%)	17 (7.56%)	34 (11.33%)	
40–49 years	32 (42.67%)	53 (23.56%)	85 (28.33%)	
≥60 years	26 (34.67%)	155 (68.89%)	181 (60.33%)	
Gender				0.784
Male	47 (62.67%)	137 (60.89%)	184 (61.33%)	
Female	28 (37.33%)	88 (39.11%)	116 (38.67%)	
Duration of HD (months)	36 (24–60)	24 (12–60)	33 (12–60)	0.115
Duration of HD groups				0.004
≤1 year	14 (18.67%)	85 (37.78%)	99 (33.00%)	
1–3 years	28 (37.33%)	51 (22.67%)	79 (26.33%)	
>3 years	33 (44.00%)	89 (39.56%)	122 (40.67%)	
Dry weight BMI	22.31±3.78	22.16±3.56	22.20±3.61	0.763
Education status				0.151
Primary school or illiteracy	17 (22.67%)	81 (36.00%)	98 (32.67%)	
Junior high school	22 (29.33%)	63 (28.00%)	85 (28.33%)	
Senior high school	19 (25.33%)	40 (17.78%)	59 (19.67%)	
College education or above	17 (22.67%)	41 (18.22%)	58 (19.22%)	
Marital status				0.020
Single	6 (8.00%)	6 (2.67%)	12 (4.00%)	
Married	65 (86.67%)	187 (83.11%)	252 (84.00%)	
Divorced or widowed	4 (5.33%)	32 (14.22%)	36 (12.00%)	
Family structure				0.003
Living alone	5 (6.67%)	32 (14.22%)	37 (12.33%)	
A couple	15 (20.00%)	63 (28.00%)	78 (26.00%)	
A nuclear family	28 (37.33%)	40 (17.78%)	68 (22.67%)	
An extended family	27 (36.00%)	90 (40.00%)	17 (39.00%)	
Payment pattern				0.317
Self-paying or medical insurance for residents	15 (20.00%)	65 (28.89%)	80 (26.67%)	
Medical insurance for employees	50 (66.67%)	132 (58.67%)	182 (60.67%)	
Medical insurance at public expense	10 (13.33%)	28 (12.44%)	38 (12.67%)	
Diabetes mellitus	19 (25.33%)	114 (50.67%)	133 (44.33%)	<0.001
CCI (excluded ESRD)	1.09±1.60	2.03±1.61	1.80±1.66	<0.001
CCI (excluded ESRD) groups				<0.001
No complications	40 (53.33%)	56 (24.89%)	96 (32.00%)	
Minor	23 (30.67%)	81 (36.00%)	104 (34.67%)	
Medium and severe	12 (16.00%)	88 (39.11%)	100 (33.33%)	
aCCI (excluded ESRD)	2.25±1.82	4.05±2.22	3.60±2.26	<0.001
HGB	104.37±18.79	100.94±18.55	101.80±18.64	0.169
ALB	38.63±7.65	36.21±4.17	36.82±5.35	0.001
Total cholesterol	4.19±1.14	4.13±1.04	4.14±1.06	0.689
Triglyceride	2.35±1.81	2.13±1.42	2.19±1.53	0.280
hsCRP	3.90±3.05	4.48±3.48	4.33±3.38	0.225

Continued

Table 1 Continued

	Non-frailty (N=75)	Frailty (N=225)	Total (N=300)	P value
Calcium	2.24±0.20	2.19±0.21	2.20±0.21	0.118
Phosphorus	2.08±0.59	1.85±0.65	1.91±0.64	0.007
iPTH	54.36 (23.87–259.03)	47.20 (20.10–193.60)	50.60 (21.45–203.75)	0.167
SDS score	50.49±7.57	60.72±8.00	58.17±9.05	<0.001
Depression	28 (37.33%)	188 (83.56%)	216 (72.00%)	<0.001
SAS score	44.73±4.88	51.25±5.94	49.62±6.35	<0.001
Anxiety	13 (17.33%)	145 (64.44%)	158 (52.67%)	<0.001

P value for analysis of comparison between non-frailty patients and frailty patients.
aCCI, age-adjusted Charlson comorbidity Index; ALB, albumin; BMI, body mass index; CCI, Charlson Comorbidity Index; DBP, diastolic blood pressure; ESRD, end-stage renal disease; HD, haemodialysis; HGB, haemoglobin; hsCRP, high-sensitivity C reactive protein; iPTH, intact parathyroid hormone; SAS, Self-Rating Anxiety Scale; SDS, Self-Rating Depression Scale.

alone), an extended family (compared with living alone), phosphorus, depression and anxiety were associated with frailty according to the multivariate analysis (all p<0.05; table 2).

DISCUSSION

This study analysed frailty and psychological status among southern Chinese Han patients on HD, and the results showed that the TFI score was 6.89±2.87 and approximately three-quarters of participants were frail. There was overlap between frailty, depression, and anxiety in HD patients. Frailty patients had higher SDS and SAS scores, and were more likely to suffer from depression and anxiety than non-frailty patients. Approximately half of the patients with frailty had both depression and anxiety. Along with the aggravation of depression or anxiety, the prevalence of frailty in patients with HD increased gradually. Multivariate logistic regression analysis showed that age, DM, family structure, phosphorus, depression and anxiety were associated with frailty, which was consistent with previous studies.

Frailty is a medical syndrome that was proposed in recent years and is characterised by a decline in physical strength, endurance and physiological function, which increases the vulnerability of individuals, including the inability to self-care and death.[1 2] Frailty is not only associated with quality of life, rehospitalisation and mortality among community-dwelling elders, but also with the comprehensive management, long-term outcomes and mortality of chronic diseases, including cardiovascular disease, stroke, ESRD and cancer.[2 7 12–15] The Fried phenotype focuses on physical frailty, and thus, may lead to the fragmentation of nursing.[27] In addition to physical items, the TFI scale measures psychological and social frailty.[28] The TFI has shown excellent psychometric performance among community-dwelling elders in the Netherlands, with better psychometric characteristics than other frailty measurement tools such as the Sherbrooke Postal Questionnaire, the Groningen Frailty Indicator and the SHARE-FI.[28 40 41] Because of its validity, reliability, and convenience, the TFI scale has been widely used and translated into Chinese.[32]

CKD patients have underlying potential pathophysiological factors of frailty, including anaemia, malnutrition,

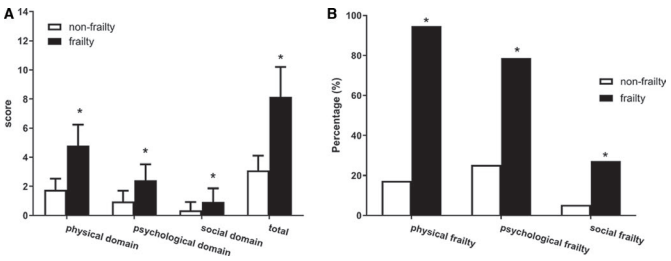

Figure 1 Distribution of TIF scores and frailty in HD patients. *Indicated comparison with non-frailty group, p<0.05. HD, haemodialysis; TFI, Tilburg indicator of frailty.

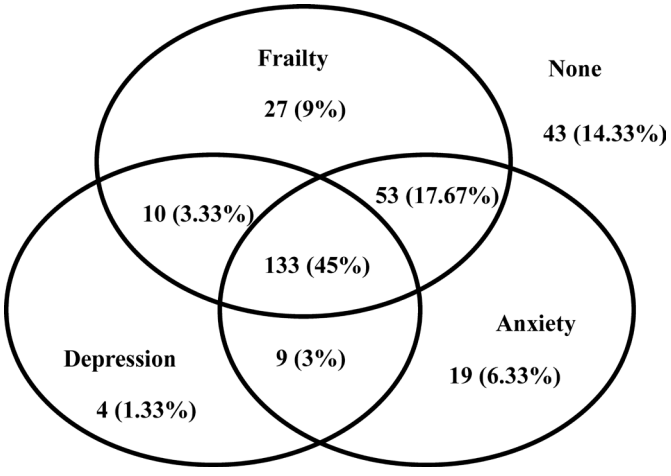

Figure 2 The overlap of frailty, depression and anxiety was displayed through a Venn diagram. The percentages represented the proportion of the total population with only frailty, depression and anxiety as well as the overlap of these three factors. Frailty was defined as ≥5 scores by the Tilburg indicator of frailty. Depression was defined as ≥53 scores by the Self-Rating Depression Scale, and anxiety was defined as ≥50 scores by the Self-Rating Anxiety Scale. A total of 300 HD participants were enrolled and the size of each subgroup was indicated in parentheses. HD, haemodialysis.

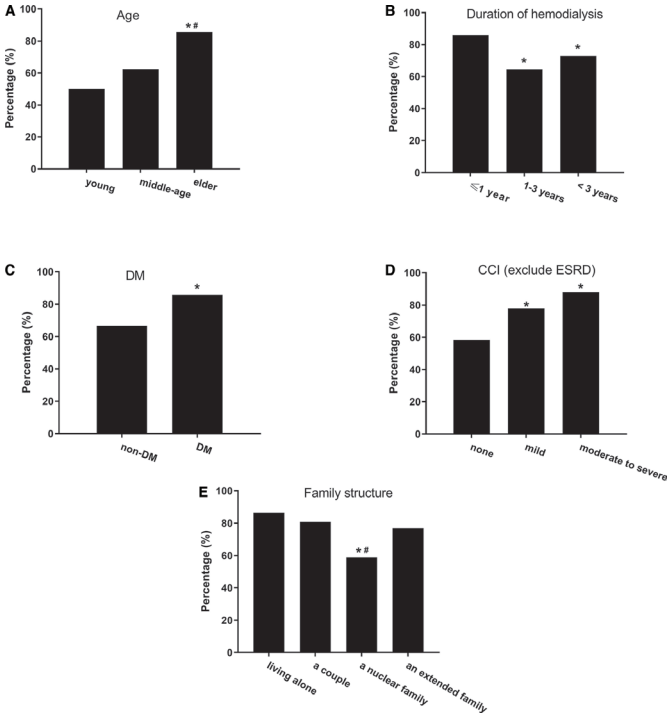

Figure 3 Percentage of frailty among HD patients in different age, duration of HD, DM, CCI (excluded ESRD) and family structure groups. (A) In different age group, *indicated comparison with the young group, p<0.05; #indicated comparison with middle-aged group, p<0.05. (B) In different duration of HD group, *indicated comparison with the duration of HD ≤1-year group, p<0.05; #indicated comparison with the duration of HD 1–3 years group, p<0.05. (C) In different DM group, *indicated comparison with the non-DM group. (D) In different CCI (excluded ESRD) group, *indicated comparison with the none group, p<0.05; #indicated comparison with mild group, p<0.05. (E) In different family structure group, *indicated comparison with the living alone group, p<0.05; #Indicated comparison with living in a couple group, p<0.05). CCI, Charlson Comorbidity Index; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, haemodialysis.

chronic inflammation and low physical activity, especially in patients with ESRD.[20–22 42] A study identified frailty status in 7% of elderly adults, 14% of predialysis patients and 42% of ESRD patients on HD.[43] According to the Fried model, 52.6% of Japanese HD patients are classified into pre-frailty and 21.4% into frailty categories.[44] In the USA, 67.7% of 2275 dialysis patients were considered frail according to the United States Renal Data System.[45] Indeed, the prevalence of frailty increases with the progression of CKD.[42] In this study, frailty was identified in 75% of HD patients in Southern China, which is similar to the incidence in developed countries (approximately 67.7%–74%).[24 43 45–48] In addition, some studies reported that frailty is common in a large number of non-elderly patients on HD, and frailty is a strong independent predictor of hospitalisation and mortality regardless of age.[24 45]

Because the concept of frailty was developed among community-dwelling elderly, age is the most important risk factor for frailty.[1 2 4 10] Traditional risk factors such as age, comorbidities and DM were validated in this study. However, unlike previous studies, women were not more prone to frailty, which could be due to the different populations included. Johansen *et al* showed that in addition to age, female gender, comorbidities (atherosclerotic heart disease, heart failure) and DM, race (non-white), Hispanic ethnicity, HD via a catheter, serum albumin, and hospitalisation within the prior year were closed related to frailty.[48 49] Malnutrition has been identified as an important factor involved in frailty.[43 50] The present multivariate logistic regression model 1 showed that serum albumin was associated with frailty, and only phosphorus was related to frailty in model 2, both of which reflect the nutritional status of patients to a certain extent. This might indicate that the effect of low serum albumin or serum phosphorus on frailty was not independent from other related factors, such as strict dietary restrictions, inflammation and comorbidities.[49] Additional indicators of nutritional status, including normalised protein catabolic rate, waist-to-hip ratio and subcutaneous fat thickness, should be examined in future studies to explore the relationship between nutrition and frailty in HD patients. Given that inflammation, nutrition, and hospitalisation are potentially modifiable factors, this might be useful for selecting interventions to prevent and improve frailty.

Unlike the Fried phenotype, which is limited to objective physical measures, the TFI incorporates psychological and social factors. A cross-sectional study from the Urban Health Centres Europe project showed that 67.03% of community-dwelling older adults who live alone have a significantly higher incidence of frailty than those who live with others (47.80%, p<0.001).[31] Therefore, this study analysed the family structure of HD patients. We found that patients who live alone or in a couple had a higher prevalence of frailty than those who live in a nuclear family. The results of the multivariate logistic regression analysis showed that living in a nuclear family (compared with living alone) was independently correlated with frailty. This could be explained by the additional support of a nuclear family, which is beneficial for patients' psychological and social well-being. These results suggest that we should pay more attention to the family structure of patients and provide social support, including the intervention of social workers when necessary.

Psychological abnormalities and frailty are both affected by older age, chronic inflammation, anaemia and other chronic diseases, and have many of the same risk factors, hence the addition of the psychological domain to the TFI scale.[28 41] Depression and frailty are widespread in the elderly population, with cross-sectional studies showing a fourfold increased risk of depression in elder patients diagnosed with frailty. The opposite association was also observed, with depressed people having a fourfold higher risk of becoming frail.[51] A recent study reported that the prevalence of depression is as high as 51% and is an independent predictor of the TFI score and frailty in patients with atrial fibrillation.[52] Depression, anxiety and frailty

Table 2 Logistic regression analysis for the factors related to frailty (0=non-frailty, 1=frailty)

Variables	OR	95% CI of OR		P value
		Lower	Upper	
Model 1 (adjusted R^2=0.181)				
Age	1.044	1.019	1.070	<0.001
CCI (excluded ESRD)	1.392	1.124	1.723	0.002
Family structure				0.024
A couple (compared with live alone)	0.343	0.100	1.176	0.089
A nuclear family (compared with live alone)	0.170	0.052	0.557	0.003
An extended family (compared with live alone)	0.330	0.103	1.053	0.061
ALB	0.918	0.845	0.996	0.041
Model 2 (adjusted R^2=0.330)				
Age	1.048	1.020	1.077	0.001
DM	2.443	1.176	5.075	0.017
Family structure				0.031
A couple (compared with live alone)	0.219	0.052	0.925	0.039
A nuclear family (compared with live alone)	0.122	0.030	0.493	0.003
An extended family (compared with live alone)	0.207	0.053	0.814	0.024
Phosphorus	0.551	0.316	0.961	0.036
Depression (0=no, 1=yes)	8.136	3.588	18.448	<0.001
Anxiety (0=no, 1=yes)	3.333	1.621	6.854	0.001

Model 1: multivariable adjusted, without depression (0=no, 1=yes) and anxiety (0=no, 1=yes).
Model 2: multivariable adjusted, including depression (0=no, 1=yes) and anxiety (0=no, 1=yes).
Variables of univariate regression analysis include age, gender (male=1, female=2), duration of HD groups (1=≤1 year, 2=1–3 years, 3=>3 years), education status (1=primary school or illiteracy, 2=junior high school, 3=senior high school, 4=college education or above), married status (1=single, 2=married, 3=divorced or widowed), family structure (1=live alone, 2=a couple, 3=a nuclear family, 4=an extended family), payment pattern (1=self-paying or medical insurance for residents, 2=medical insurance for employees, 3=medical insurance at public expense), BMI, DM, CCI (excluded ESRD), HGB, ALB, total cholesterol, triglyceride, hsCRP, calcium, phosphorus, iPTH, depression (0=no, 1=yes) and anxiety (0=no, 1=yes).
All variables with significant associations in univariate regression analysis were included in multivariate regression analysis.
ALB, albumin; BMI, body mass index; CCI, Charlson Comorbidity Index; DBP, diastolic blood pressure; DM, diabetes mellitus; ESRD, end-stage renal disease; HD, haemodialysis; HGB, haemoglobin; hsCRP, high-sensitivity C reactive protein; iPTH, intact parathyroid hormone.

often coexist in chronic diseases, although their correlation has not been investigated in detail. In this study, we showed that frailty, depression, and anxiety overlap in patients on HD. Patients with frailty had higher SDS and SAS scores, as well as a higher incidence of depression and anxiety than those without frailty. Approximately 50% of frailty patients had both depression and anxiety, and the prevalence of frailty increased gradually with the progression of depression or anxiety. The severity of depression was positively associated with more severe symptoms of frailty. The clinical assessment of patients with HD should include measures of anxiety and depression to prevent the occurrence and severity of frailty. In clinical practice, healthcare providers should recognise that HD patients with coexisting frailty need additional therapeutic intervention based on their individual needs and expectations.

This study has several strengths. First, we analysed the prevalence and associated factors of frailty among Southern Chinese Han patients on HD, which has little insight available to date. Second, we studied adults of all ages from three centres rather than limiting the analysis to older adults undergoing HD. Thirdly, we analysed the relationship between frailty and depression and anxiety in HD patients. The study also had limitations, including the relatively small number of enrolled patients and the lack of dialysis-related indicators and nutritional assessment. In addition, 53.83% of patients from these HD centres were excluded from the study cohort, which might lead to bias in analysis of the prevalence of frailty among the entire cohort of HD patients. Although the TFI is a prospective measurement of a validated, easy to operate frailty scale, the Fried phenotype frailty scale remains the most commonly used tool in patients with chronic diseases. The use of the TFI in the Chinese language in HD patients requires further confirmation. The primary outcome of this study was the result of a subjective evaluation, and frailty was not evaluated objectively. Thus, the actual incidence of frailty may be influenced by the current psychological state and may be overestimated. Finally, this was an observational study, and we cannot firmly establish a cause and effect relationship between the associated factors and frailty. Additional large scale and follow-up studies are needed.

CONCLUSIONS

In conclusion, we confirmed that approximately three-quarters of southern Chinese Han patients on HD are frail, and frailty is often accompanied by depression and anxiety. Because HD patients visit the hospital regularly every week and frailty is associated with the accumulation of risk factors, early detection and intervention are important to improve quality of life and the long-term prognosis. Additional multicentre large-scale studies, including prospective longitudinal studies, further detailed assessments and interventional assessment, are necessary to investigate the factors associated with frailty.

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