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Original Article

Simple self-report FRAIL scale might be more closely associated with dialysis complications than other frailty screening instruments in rural chronic dialysis patients

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SUMMARY AT A GLANCE

The simple FRAIL scale scores introduced in this manuscript might demonstrate a closer relationship with dialysis-related complications. This is the first study establishing the utility of different self-report questionnaires for assessing frailty in chronic dialysis patients.

ABSTRACT:

Aim: **Despite the perceived importance of frailty, few studies focus on its impact on rural patients undergoing chronic dialysis. Comparison of different self-report questionnaires in assessing frailty among these patients has not been attempted before.**

Methods: **A prospectively enrolled chronic dialysis cohort from a rural centre was recruited for analysis. Six types of self-report questionnaires were administered to these patients. Clinical and dialysis-related laboratory parameters were collected. Correlation analyses between questionnaire results and dialysis complications were performed, and variables demonstrating significant correlations were entered into multivariate regression models to determine their independent associations.**

Results: **Six types of questionnaire (Strawbridge questionnaire, Edmonton Frail Scale, simple FRAIL scale, Groningen Frail Indicator, G8 questionnaire, and Tilburg Frail Indicator) were provided to rural patients undergoing chronic dialysis. Scores from each questionnaire showed significant association with each other, except the G8 questionnaire. Scores from the simple FRAIL scale correlated significantly with age ($P = 0.02$), female gender ($P = 0.03$), higher Liu's comorbidity index ($P = 0.02$), lower serum albumin ($P = 0.03$) and creatinine levels ($P < 0.01$), and higher ferritin levels ($P = 0.02$). The other five questionnaires did not show consistently significant relationships with important dialysis-related complications. Multivariate linear regression analysis identified an independently negative association between serum albumin and the simple FRAIL scale results ($P = 0.01$).**

Conclusion: **This is the first study establishing the utility of different self-report questionnaires for assessing frailty in chronic dialysis patients. The simple FRAIL scale scores might demonstrate a closer relationship with dialysis-related complications.**

Frailty describes a status of accumulating health deficits during the aging process, leading to loss of the ability to cope with physical or psychological stress. Presence of frailty in the geriatric population correlates with higher risks of hospitalization and institutionalization after discharge, and an overall higher risk of mortality.[1–3] The prevalence of frailty in the elderly increases from 7% to 10% in those aged over 65 years and to 20–40% among octogenarians.[4]

Screening for frailty has become a crucial measure to optimize care for geriatric patients with such phenotype. Most experts agree that comprehensive geriatric assessment (CGA) could be a confirmatory procedure in establishing

frailty; however, conducting a complete CGA is often time-consuming and unavailable in the primary care setting.[5] A two-step approach is proposed to assess patients suspected to be frail: initial screening for the presence of frailty, followed by more comprehensive tests.[5,6] Such screening instruments mostly involve self-report questionnaires or postal questionnaires, instead of biological assessments or performance-based measures.

Compared with studies of frailty in the general geriatric population, there are significantly fewer studies focusing on frailty in chronic dialysis patients. The application of the frailty construct to patients with end-stage renal disease (ESRD) has the potential to enhance the predictability of adverse outcomes among these patients. Furthermore, proven beneficial interventions for frail geriatric patients might similarly improve outcomes of frail dialysis patients.[7] In chronic dialysis patients, available reports concerning frailty mostly used the criteria of Woods *et al*. modified from Fried's original specifications (unintentional weight loss, weakness, exhaustion, and low activity).[4,8] However, the Fried frailty index requires performance-based assessments including dynamometer-measured grip strength, timed walk speed over a pre-specified distance, and other indexes of physical activity, all of which could be time-consuming and inconvenient for both the dialysis patients and nephrologists. Consequently, a self-report questionnaire-based assessment of frailty might be more friendly and practical for ascertaining frailty in chronic dialysis patients, especially in those with advanced age and who are living in rural areas.[9] Currently, the most suitable or efficacious questionnaire-based tool for diagnosing frailty remains unclear. None of the existing self-report questionnaires have been tested in the dialysis population. We aimed to investigate the applicability of existing self-report questionnaires in chronic rural dialysis patients by examining correlations between self-reported findings and complications from dialysis.

MATERIALS AND METHODS

Study design, setting, and clinical data collection

This study protocol was approved by the NTUH ethics committee (NO.201403006RINB). All enrolled patients provided informed consent.

The current study was conducted at the National Taiwan University Hospital Jinshan branch (NTUH-JS), the only regional centre that serves the entire Jinshan county in the rural area of New Taipei city (approximately 20 000 residents over 50 square kilometres).[9] ESRD patients under maintenance haemodialysis in NTUH-JS for 3 months or longer were prospectively enrolled over a period of 6 months. Patients unable to respond due to severe dementia or pre-existing major neurologic illnesses were excluded. We collected data regarding demographics (age, gender, body mass index [BMI]), socioeconomic status (education, marriage status, disposable monthly income), geospatial separation (distance between NTUH-JS and patients' residences), dialysis vintage, and aetiology of ESRD on enrolment. Comorbidity index was calculated according to established formulae.[10] Laboratory data including haemograms, serum biochemistry/electrolyte panels, nutritional profiles (albumin, creatinine, lipid profiles), iron profiles, and dialysis adequacy (represented by single pool Kt/V values), were checked.

Administration of frailty screening instruments

Patients were evaluated by at least two independent nurse researchers. Six types of established self-report questionnaires, aided by Chinese translation, for assessing the presence of frailty were administered simultaneously to participants after enrolment and blood tests. The questionnaires consisted of the Strawbridge frailty questionnaire (SF), the Edmonton Frail Scale (EFS), the 5-item simple FRAIL scale questionnaire, the Groningen Frailty Indicator (GFI), the G8 questionnaire, and the Tilburg Frailty Indicator (TFI). The Chinese-translated versions of all six questionnaires were internally verified, and all the staffs have concordance on the translations more than 90% of the time. Forward and backward translations were performed by experts in this field. Minor diversities were resolved by consensus between the staffs, study nurses, and external experts.

The six self-report screening questionnaires have been proven to demonstrate fair construct validity. They encompass one or more frailty domains using different scoring systems. SF is based on four functional domains (physical, nutritive, cognitive, and sensory functions), containing a total of 16 variables.[11] Subjects scoring 3 or higher on at least one item in any domain are considered to be frail in that domain, while frailty is qualified if more than one domain is positive. The EFS has nine domains (cognition, general health status, functional independence, social support, medication use, nutrition, mood, continence, and functional performance), with scores between 0 and 17 (maximal severity).[12] Those scoring ≥8 are classified as frail.[12] The simple FRAIL scale was proposed by the International Association of Nutrition and Aging, including five brief questions summarized by the acronym 'FRAIL' (Fatigue, Resistance, Ambulation, Illness, and Loss of weight).[13] Participants with scores higher than 2 out of 5 are categorized as frail, while those scoring 1 or 2 are identified as being pre-frail, an intermediate status. GFI was characterized by the inclusion of psychosocial components (four domains: physical, cognitive, social, and psychological), and has a scoring range between 0 and 15.[14] Those with GFI scores ≥4 are deemed frail according to previous studies.[14,15] The G8 questionnaire is a recently formulated instrument for determining CGA need in geriatric oncology patients, including the following items: appetite loss, weight loss, mobility, neuropsychological problems, BMI, medication use, self-perceived health status, and age.[16] A score of ≤14 out of 17 indicates frailty, with the lower scores indicating higher severity. Finally, TFI has been developed by a Dutch group that aims to describe the frailty phenotype (three domains: physical, psychological, and social).[17] Presence of frailty is determined if scores are ≥5 out of 15. As the best instrument describing the frailty phenotype in geriatric or dialysis patients remains unclear, we elected to choose these six questionnaires, owing to their simplicity for administration and fair validity in primary care settings.[18]

The results of all questionnaires were summarized in a tabular format. Each participant was given his/her total score for each questionnaire, and was further dichotomized as being frail or not.

Statistical analysis

Statistical analyses were performed using SPSS 18.0 software (SPSS, Chicago, IL, USA). Categorical variables were described using the case number with percentage in parentheses, and group comparisons were performed using the χ^2 test. Continuous variables were expressed as mean ± standard deviation, with group comparisons performed by an independent *t*-test or Mann–Whitney *U*-test. We first assessed the associations between the scoring results of the six questionnaires and clinical variables as well as dialysis-related complications using the Pearson's correlation coefficient. Dialysis-related complications included malnutrition, anaemia, inflammation, divalent ion imbalances/abnormal mineral bone parameters, dialysis inadequacy, and abnormal fluid status. Variables demonstrating significant associations with any of the frailty questionnaire findings, or those deemed relevant, were selected to enter multivariate analyses. Subsequent multivariate-adjusted regression models, incorporating demographic profiles, comorbidities, socioeconomic variables, and frailty instrument components, with dependent variables from dialysis-related complications, were constructed to analyze any independent associations between frailty components. A two-sided $P < 0.05$ was considered statistically significant.

RESULTS

Clinical features of the enrolled chronic dialysis patients

A total of 46 rural patients undergoing chronic dialysis were recruited; their clinical data are shown in Table 1. The average age of participants was comparatively higher than the average age of the chronic dialysis population, and 43% were male. About 75% of patients were illiterate or received elementary school education only, compatible with their rural residence background. Half of the patients had a poor economic status, with a monthly disposable income less than 10 000 New Taiwan Dollars (roughly 333 US dollars). More than 80% of the patients had hypertension, followed in incidence by diabetes mellitus (DM), heart failure, and a history of malignancy. Most of the patients developed ESRD due to DM nephropathy (39%).

Frailty status among rural patients undergoing chronic dialysis

All patients completed the six questionnaires successfully, aided by family members, nurse researchers, and nephrologists. The G8 questionnaire identified the highest proportion of patients to be frail (38 [82.6%]), followed by the SF (32 [69.6%]), GFI (25 [54.3%]), EFS (20 [43.5%]), and TFI (14 [30.4%]) (Table 1). The simple FRAIL scale identified the lowest proportion of patients to be frail (9 [19.6%]).

The distribution of functional insufficiency in the domains described in each questionnaire is shown in Table 2. Physical domain disability constituted the most common finding (>90%) among rural patients undergoing chronic dialysis who used the GFI and TFI, while physical domain disability was the second most common finding using the SF, after sensory dysfunction. Half of the patients exhibited disability in the sensory domain (visual and hearing impairment) by the SF, while sensory dysfunction was also detected in the physical domain items by the GFI and TFI. Disability in the nutritive domain was the least common finding (<10%) (assessed by the SF and EFS). However, when the item 'body weight loss' or 'appetite loss' were included, the percentage of patients with nutritive deficiency increased to 20–30% (assessed by the G8 questionnaire). Nearly half of the chronic dialysis patients (40–50%) exhibited social domain disability, as assessed by the EFS, GFI, and TFI. For the psychological domain, the different instruments derived a wide range of estimates from the dialysis patients, ranging from 13% (the G8 questionnaire) to 72% (the TFI). The phenotype-based simple FRAIL scale, contrary to the other five instruments, identified that chronic dialysis patients most commonly had difficulties in the resistance (59%) and ambulation (46%) domains.

Relationship between frailty status and dialysis complications among rural patients undergoing chronic dialysis

Each questionnaire identified a different subset of frail dialysis patients (Tables 1 and 3). The distance between the residences and dialysis clinics was significantly shorter for SF-identified frail dialysis patients ($P = 0.04$), but their dialysis clearance was better ($P = 0.02$) than that of non-frail dialysis patients. EFS-identified frail dialysis patients were significantly older ($P = 0.01$) and had lower serum creatinine levels ($P = 0.02$). Simple FRAIL scale-identified frail dialysis patients were significantly older ($P = 0.02$) and were more likely to be female ($P = 0.03$), have concurrent heart failure ($P = 0.02$), have a higher comorbidity index ($P = 0.02$), and lower serum albumin ($P = 0.03$), lower serum creatinine ($P < 0.01$), and significantly higher serum ferritin ($P = 0.02$) levels. GFI-identified frail dialysis patients had higher haemoglobin levels ($P = 0.04$) and lower transferring saturation ($P = 0.04$). G8 questionnaire-identified dialysis patients had significantly lower BMI ($P = 0.36$), while TFI-identified frail dialysis patients did not have significant differences in clinical or dialysis complications compared to non-frail patients.

We subsequently performed correlation analyses between the scores of each frailty assessment, as well as between assessment results and clinical/laboratory parameters. The results showed that all instruments displayed fair associations, except the G8 questionnaire (Table 4). Specifically, scores of the EFS, simple FRAIL scale, GFI, and TFI significantly correlated with those of other instruments, except the G8 questionnaire (Table 4). The G8 questionnaire scores were only significantly correlated with the SF scores ($P = 0.01$).

Table 1 Baseline characteristics of dialysis patients, divided according to the presence of frailty or not

Features	Total	SF		EFS		Simple FRAIL		GFI		G8		TFI	
		Frail+	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*
Demographic profiles													
Age (years)	67.3 ± 11.9	67.8 ± 12.9	65.6 ± 9.5	72.1 ± 7.8*	63.3 ± 13.3*	75.3 ± 9.1*	65.1 ± 11.8*	68.1 ± 14	66 ± 9	66.9 ± 12.5	68.1 ± 9.1	69.6 ± 13.3	66 ± 11.3
Gender (male)	20 (43)	12 (38)	8 (57)	7 (35)	13 (50)	1 (11)*	19 (51)*	7 (28)	13 (62)	16 (42)	4 (50)	5 (36)	15 (47)
Dialysis vintage (years)	2.6 ± 2.5	2.6 ± 2.5	2.7 ± 2.5	2.9 ± 2.4	2.4 ± 2.5	3.9 ± 2.6	2.3 ± 2.4	2.8 ± 2.8	2.4 ± 2	2.9 ± 2.6	1.1 ± 1.0	2.8 ± 1.9	2.5 ± 2.7
BMI (kg/m^2)	22.9 ± 3.0	22.9 ± 3.4	22.9 ± 1.7	23.2 ± 2.7	22.7 ± 3.2	23.6 ± 2	22.7 ± 3.2	23.3 ± 3.4	22.4 ± 2.4	22.5 ± 3.1	24.9 ± 1.4	23.1 ± 2.9	22.8 ± 3.1
Education													
None	19 (41)	14 (44)	5 (36)	11 (55)	8 (31)	4 (44)	15 (41)	10 (40)	9 (43)	15 (39)	4 (50)	6 (43)	13 (41)
Elementary	17 (37)	14 (44)	3 (21)	6 (30)	11 (42)	3 (33)	14 (38)	10 (40)	7 (33)	15 (39)	2 (25)	6 (43)	11 (35)
Junior high	5 (11)	2 (6)	3 (21)	2 (10)	3 (11)	1 (11)	4 (11)	3 (12)	2 (10)	4 (11)	1 (13)	2 (14)	3 (9)
Senior high	3 (7)	1 (3)	2 (14)	1 (5)	2 (8)	1 (11)	2 (5)	1 (4)	2 (10)	2 (5)	1 (13)	0 (0)	3 (9)
College	2 (4)	1 (3)	1 (8)	0 (0)	2 (8)	0 (0)	2 (5)	1 (4)	1 (4)	2 (5)	0 (0)	0 (0)	2 (6)
Socioeconomic profiles													
Marriage (married)	43 (93)	30 (94)	13 (93)	18 (90)	25 (96)	8 (89)	35 (95)	24 (96)	19 (90)	35 (92)	8 (100)	12 (86)	31 (97)
Monthly disposable income (NTD 10000 or above)	24 (52)	18 (56)	6 (43)	10 (50)	14 (54)	4 (44)	20 (54)	17 (68)	7 (33)	20 (53)	4 (50)	9 (64)	15 (47)
Residence from dialysis clinic (km)	6.7 ± 6.9	5.3 ± 6.6*	9.8 ± 7*	6.0 ± 5.8	7.2 ± 7.8	5.7 ± 6.3	6.9 ± 7.1	6 ± 6	7.5 ± 8	6.8 ± 6.7	6.2 ± 8.6	4.9 ± 5.4	7.5 ± 7.4
Comorbidities													
DM	21 (46)	16 (50)	5 (36)	10 (50)	11 (42)	6 (67)	15 (41)	13 (52)	8 (38)	17 (45)	4 (50)	7 (50)	14 (44)
HTN	39 (85)	28 (88)	11 (79)	17 (85)	22 (85)	8 (89)	31 (84)	23 (92)	16 (76)	33 (87)	6 (75)	12 (86)	27 (84)
HF	8 (17)	5 (16)	3 (21)	3 (15)	5 (19)	4 (44)*	4 (11)*	5 (20)	3 (14)	7 (18)	1 (13)	4 (29)	4 (13)
LC	4 (9)	2 (6)	2 (14)	2 (10)	2 (8)	1 (11)	3 (8)	2 (8)	2 (10)	4 (11)	0 (0)	1 (7)	3 (9)
Malignancy	5 (11)	4 (13)	1 (7)	3 (15)	2 (8)	2 (22)	3 (8)	3 (12)	2 (10)	3 (8)	2 (25)	1 (7)	4 (13)
Liu's dialysis comorbidity index	1.5 ± 1.8	1.3 ± 1.4	1.8 ± 2.5	1.5 ± 1.4	1.5 ± 2	2.7 ± 1.4*	1.2 ± 1.7*	1.6 ± 1.6	1.3 ± 2	1.4 ± 1.7	1.8 ± 2.4	1.6 ± 1.6	1.4 ± 1.9
Etiology of ESRD													
DMN	18 (39)	13 (41)	5 (36)	9 (45)	9 (35)	5 (56)	13 (35)	11 (44)	7 (33)	14 (37)	4 (50)	5 (36)	13 (41)
CGN	4 (9)	2 (6)	2 (14)	1 (5)	3 (11)	0 (0)	4 (11)	2 (8)	2 (10)	2 (5)	2 (25)	1 (7)	3 (9)
Others†	21 (46)	15 (47)	6 (42)	8 (40)	13 (50)	4 (44)	17 (46)	12 (48)	9 (43)	19 (50)	2 (25)	8 (57)	13 (41)
Unknown	3 (6)	2 (6)	1 (8)	2 (10)	1 (4)	0 (0)	3 (8)	0 (0)	3 (14)	3 (8)	0 (0)	0 (0)	3 (9)

Data were expressed as mean ± standard deviation for continuous variables, or number with percentages in parentheses for categorical variables. *$P < 0.05$. †Including lupus, unresolving acute kidney injury, chronic interstitial nephritis, obstructive uropathy, allograft failure. BMI, body mass index; CGN, chronic glomerulonephritis; DM, diabetic mellitus; DMN, diabetic mellitus nephropathy; ESRD, end-stage renal disease; HF, heart failure; HTN, hypertension; LC, liver cirrhosis; NTD, New Taiwan Dollar.

Table 2 Results of frailty questionnaires administered to the current chronic dialysis cohort

Questionnaires	Domain categories†								
	Physical		**Nutritive**			**Cognitive**		**Sensory**	
SF	30.4% (+)		6.5% (+)			19.6% (+)		52.2% (+)	
	Cognition	**General health status**	**Functional independence**	**Social support**	**Medication use**	**Nutrition**	**Mood**	**Incontinence**	**Functional performance**
EFS	34.8% (+)	100% (+)	47.8% (+)	45.7% (+)	93.5% (+)	6.5% (+)	37% (+)	6.5% (+)	71.7% (+)
	Fatigue		**Resistance**		**Ambulation**		**Illness**	**Loss of weight**	
Simple FRAIL	23.9% (+)		58.7% (+)		45.7% (+)		13% (+)	2.2% (+)	
	Physical		**Cognitive**			**Social**		**Psychological**	
GFI	95.7% (+)		39.1% (+)			45.7% (+)		43.5% (+)	
	Loss of appetite	**Weight loss**	**Mobility**	**Neuropsychological problems**		**BMI**	**Medication use**	**Self-perceived health**	**Age‡**
G8	28.3% (+)	32.6% (+)	23.9% (+)	13% (+)		43.5% (+)	91.3% (+)	78.3% (+)	17.4% (+)
	Physical			**Psychological**			**Social**		
TFI	91.3% (+)			71.7% (+)			54.3% (+)		

†Positivity in each domain signifies the presence of functional inadequacy of any items in that domain. ‡Positivity if age ≧ 80 according to the domain specification. BMI, body mass index.

EFS, Edmonton Frailty Scale; FRAIL, Fatigue, Resistance, Ambulation, Illness, Loss of weight; G8, G8 questionnaire; GFI, Groningen Frailty Indicator; SF, Strawbridge Frailty questionnaire; TFI, Tilburg Frailty Indicator.

As the simple FRAIL scale demonstrated potential associations with more clinical parameters and dialysis complications than the other instruments, we focused on the relationship between the simple FRAIL scale and dialysis complications, especially those related to nutrition. Multiple regression analyses, using serum albumin levels as dependent variables, demonstrated a significant negative association between the presence or absence of frailty (assessed by the simple FRAIL scale) and albumin levels ($P = 0.01$). Another approach using the presence or absence of frail/pre-frail similarly demonstrated that being frail or pre-frail was negatively associated with albumin levels ($P = 0.04$). A sensitivity analysis also showed that the simple FRAIL scale scores demonstrated a significantly negative association with albumin levels as a continuous variable ($P < 0.01$).

DISCUSSION

In this study, we demonstrated that frailty assessment with the simple FRAIL scale was significantly correlated with clinical parameters (age, comorbidities) and dialysis complications, including hypoalbuminaemia and inflammation (higher ferritin). After adjustment, presence of frailty or pre-frailty (by the simple FRAIL scale) and the frail severity correlated significantly with serum albumin levels in chronic dialysis patients. These findings suggested the possibility of better utility for simple FRAIL scale compared to other self-report questionnaires in ascertaining frailty in dialysis patients, and further shed light on the potential pathways through which frailty might lead to an adverse outcome.

The estimated prevalence of frailty in this study was between 30% and 82%. The first study of frailty in dialysis patients used Fried's criteria for classification, and found 67.7% of them to be frail, with higher prevalence as age increases.[7] Another study similarly found a 73% prevalence of frailty in dialysis patients.[19] On the contrary, recent reports have identified only 13% to 30% of prevalent dialysis cohorts to be frail, using the same Fried frail index.[20,21] Consequently, the wide range of frailty prevalence estimated by the self-report questionnaires in the current study yielded comparable results to the literature.

Factors associated with frailty in the general geriatric population included advanced age, female, presence of DM/hypertension, and potentially chronic inflammation.[22,23] Recognized frailty contributes to a subsequently elevated risk of adverse outcomes. For chronic dialysis patients, similar factors demonstrate such associations (age, gender, peripheral vascular disease, and arrhythmia), but there are reports indicating that dialysis-specific features (excess fluid and fat mass) also correlate with frailty.[20,21] In this study, using different self-report based questionnaires, we also found that frailty correlated with demographic profiles (age, gender) and parameters including albumin, creatinine, and ferritin levels (Tables 1 and 3). Consequently, self-report based frailty instruments could display close associations with important clinical and laboratory indexes, akin to those

Table 3 Serum laboratory profiles of the current cohort according to the presence of frailty or not

Lab data	Total	SF		EFS		Simple FRAIL		GFI		G8		TFI	
		Frail+	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*	*Frail+*	*Frail–*
Haemogram													
White blood cells (K/μL)	6.8 ± 2.6	6.5 ± 2.8	7.3 ± 2.4	7.1 ± 2.9	6.5 ± 2.5	8.1 ± 2.3	6.4 ± 2.6	7.1 ± 2.7	6.4 ± 2.6	7.1 ± 2.6	5.3 ± 2.5	7.3 ± 2.2	6.5 ± 2.8
Haemoglobin (g/dL)	9.5 ± 1.5	9.5 ± 1.5	9.5 ± 1.6	9.3 ± 1.9	9.7 ± 1.2	9.3 ± 1.9	9.5 ± 1.5	9.9 ± 1.1*	9 ± 1.8*	9.5 ± 1.6	9.4 ± 1	9.7 ± 1.5	9.4 ± 1.6
Biochemical parameters													
Albumin (mg/dL)	3.8 ± 0.3	3.8 ± 0.3	3.8 ± 0.4	3.7 ± 0.4	3.8 ± 0.3	3.5 ± 0.2*	3.8 ± 0.3*	3.7 ± 0.3	3.8 ± 0.4	3.8 ± 0.3	3.8 ± 0.4	3.7 ± 0.2	3.8 ± 0.4
Creatinine (mg/dL)	10.5 ± 2.5	10.3 ± 2.3	10.9 ± 3.1	9.5 ± 2*	11.2 ± 2.6*	8.1 ± 1**	11.1 ± 2.4**	10.2 ± 2.2	10.8 ± 2.9	10.3 ± 2.5	11.3 ± 2.6	10 ± 2.2	10.7 ± 2.7
Na (meq/L)	136 ± 3.1	135 ± 2.7	137 ± 3.7	135 ± 2.5	136 ± 3.4	134 ± 2.7	136 ± 3.1	135 ± 3.2	137 ± 2.6	136 ± 3.2	136 ± 1.7	135 ± 2.1	136 ± 3.4
K(meq/L)	4.7 ± 0.9	4.6 ± 1	4.9 ± 0.8	4.7 ± 0.8	4.8 ± 1	4.6 ± 1.2	4.8 ± 0.8	4.7 ± 1	4.8 ± 0.8	4.7 ± 0.9	4.8 ± 0.8	4.4 ± 1	4.9 ± 0.9
Ca (mg/dL)	9 ± 0.9	9 ± 1	8.8 ± 0.6	9.1 ± 0.7	8.9 ± 1	9.2 ± 0.8	8.9 ± 0.9	9 ± 0.7	8.9 ± 1.1	9 ± 0.9	9 ± 0.7	9 ± 0.8	8.9 ± 0.9
P (mg/dL)	5.3 ± 1.4	5.4 ± 1.3	5.2 ± 1.8	5.2 ± 1.2	5.5 ± 1.6	5.1 ± 0.9	5.4 ± 1.5	5.5 ± 1	5.2 ± 1.8	5.4 ± 1.5	5.2 ± 1.3	5.4 ± 1	5.3 ± 1.6
Ca x P product	48.2 ± 15.1	49.1 ± 13.5	46.1 ± 18.7	46.9 ± 9.4	49.1 ± 18.5	46.8 ± 9.6	48.5 ± 16.3	49.2 ± 8.7	46.9 ± 20.5	48.4 ± 15.5	47 ± 13.8	47.8 ± 8	48.3 ± 17.4
Metabolic profiles													
Total cholesterol (mg/dL)	156 ± 36	156 ± 37	158 ± 34	166 ± 40	148 ± 31	169 ± 52	153 ± 31	162 ± 40	149 ± 31	156 ± 38	160 ± 25	164 ± 37	153 ± 36
LDL (mg/dL)	94 ± 29	94 ± 31	92 ± 23	101 ± 30	88 ± 28	104 ± 36	91 ± 27	100 ± 29	86 ± 27	93 ± 30	98 ± 20	102 ± 29	90 ± 29
Triglyceride (mg/dL)	135 ± 65	141 ± 72	120 ± 46	151 ± 64	122 ± 65	162 ± 65	128 ± 65	146 ± 67	121 ± 62	135 ± 66	135 ± 66	160 ± 75	123 ± 58
Iron profiles													
Ferritin (ng/mL)	664 ± 766	727 ± 889	520 ± 338	884 ± 1094	495 ± 279	1202 ± 1580*	534 ± 298*	584 ± 313	759 ± 1088	697 ± 834	508 ± 250	649 ± 386	671 ± 888
Transferrin saturation (%)	28.5 ± 15.8	29 ± 17.5	27.1 ± 10.9	29 ± 18.7	28 ± 13.3	31 ± 26.7	28 ± 12.1	24 ± 8.8*	34 ± 20.6*	30 ± 16.5	19 ± 4.4	23 ± 9	31 ± 17.6
Intact Parathyroid hormone (pg/mL)	335 ± 300	328 ± 266	349 ± 378	265 ± 199	388 ± 354	324 ± 239	337 ± 316	350 ± 273	317 ± 335	298 ± 295	510 ± 274	420 ± 258	297 ± 313
Kt/V	1.58 ± 0.24	1.63 ± 0.23*	1.46 ± 0.25*	1.54 ± 0.25	1.61 ± 0.24	1.59 ± 0.27	1.58 ± 0.24	1.6 ± 0.25	1.57 ± 0.24	1.6 ± 0.25	1.5 ± 0.21	1.62 ± 0.23	1.57 ± 0.25

Data were expressed as mean ± standard deviation. *$P < 0.05$. **$P < 0.01$. LDL, low-density lipoprotein; TSAT, transferrin saturation.

Table 4 Correlations between the assessment results of each questionnaire

Coefficient (*P*-value)	SF	EFS	Simple FRAIL	GFI	G8	TFI
SF		0.5 (<0.01)	0.66 (<0.01)	0.7 (<0.01)	−0.37 (0.01)	0.56 (<0.01)
EFS	0.5 (<0.01)		0.53 (<0.01)	0.64 (<0.01)	−0.04 (0.81)	0.45 (<0.01)
Simple FRAIL	0.66 (<0.01)	0.53 (<0.01)		0.49 (<0.01)	−0.27 (0.06)	0.43 (<0.01)
GFI	0.7 (<0.01)	0.64 (<0.01)	0.49 (<0.01)		−0.22 (0.13)	0.59 (<0.01)
G8	−0.37 (0.01)	−0.04 (0.81)	−0.27 (0.06)	−0.22 (0.13)		−0.03 (0.86)
TFI	0.56 (<0.01)	0.45 (<0.01)	0.43 (<0.01)	0.59 (<0.01)	−0.03 (0.86)	

EFS, Edmonton Frail Scale; Simple FRAIL, Fatigue, Resistance, Ambulation, Illness, and Loss of weight; G8, G8 questionnaire; GFI, Groningen Frailty Indicator; SF, Strawbridge frailty questionnaire; TFI, Tilburg Frailty Indicator.

reported by studies using the Fried frailty index. Judging from the ease of administration, we propose that there might be a role for screening frailty through these questionnaires in dialysis units or clinics.

In addition, we discovered that the simple FRAIL scale displayed a more consistent association with clinical variables and dialysis-related complications compared to the other five instruments in the study. Previous reports have also investigated this issue in the geriatric population. In a study comparing seven different frailty scales (including the EFS, simple FRAIL scale, GFI, and TFI) among community-dwelling adults, Theou *et al*. discovered that all of these scales demonstrated consistent relationships with clinical variables (age, gender), as well as outcomes.[24] Another study further described that the simple FRAIL scale exhibited a stronger predictive ability among the elderly for intermediate- and long-term disability, as well as prognosis, compared to other frail scales (Cardiovascular Health Study scale, Study of Osteoporotic Fractures scale, etc.).[25] Indeed, it has been suggested that the GFI and TFI demonstrate poor sensitivity and specificity for detecting frailty in an elderly survey.[26] On the contrary, the simple FRAIL scale has been credited for its simplicity (with five questions only) and efficiency for the identification of frailty among large groups of patients.[13] Furthermore, the simple FRAIL scale divides the tested cohort into tertiles (non-frail, pre-frail, frail), corresponding with a plausible temporal and biological evolution of frailty. These features lend support to our finding that the simple FRAIL scale might outperform the other five questionnaires regarding the associations between important clinical/laboratory parameters in dialysis patients. None of the previous studies have addressed the issue that different self-report questionnaires might have variable relationships with dialysis-related complications among chronic dialysis patients. We believe that the results of our pilot study will serve to inspire subsequent investigators in assessing frailty in dialysis patients, especially those living in rural areas.

Our finding that serum albumin levels had a significantly negative association with severity of frailty in dialysis patients is interesting and warrants further consideration. Kutner and colleagues similarly discovered that higher albumin levels were significantly associated with a lower risk of being frail (odds ratio 0.18).[20] We derived similar findings, but further extended it by using different approaches, including use of frailty questionnaire scores as continuous variables, and combining frailty and pre-frail into one variable. Aging might play an important role in the intertwined relationship between frailty and protein-energy malnutrition in ESRD patients. Age-associated factors, including decreased food intake, polypharmacy, dentition loss, increased prevalence of dementia, and sarcopaenia, have been reported to promote frailty and contribute to the malnutrition-inflammation syndrome. ESRD-related factors, including uraemic toxins, chronic inflammatory status, proteinuria with urinary nutrient loss, and hormonal (vitamin D or growth hormone) deficiency also assist in the development of frailty.[27] Consequently, frailty and protein-energy malnutrition, manifesting as hypoalbuminaemia, often co-exist and have the potential to drive each other under the influence of uraemia. The finding that the simple FRAIL scale scores correlated negatively with the levels of serum albumin and positively with the levels of ferritin, a potential inflammatory marker, strengthens this theory. We propose that this could explain the intimate relationship between frailty scores and albumin levels in this study.

Our study has strengths and limitations. To our knowledge, this might be the first study to evaluate the results of using self-report questionnaire in assessing frailty in rural ESRD patients, and the first to compare the utility of different self-report questionnaires in these patients. However, the modest number of cases and the clinical settings used to derive these findings limits the application of our results. In addition, the lack of data regarding clinical outcomes of these patients renders us unable to analyze whether questionnaire results correlate with patient prognosis. Future large-scale studies are needed to confirm the findings of this study.

CONCLUSION

Frailty is gradually being recognized as an important phenotype that correlates closely with disability and outcomes in both the geriatric population and patients undergoing chronic dialysis. A user- and recipient-friendly tool, the self-report frail questionnaire, is significantly under-utilized in chronic dialysis patients despite its promising applicability.

We hope that the results presented here will contribute to a broader adoption of these instruments in this population.

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