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Original Article

Functional Predictors of Frailty and Kidney Disease Burden in Patients with End-stage Renal Disease Receiving Dialysis

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Abstract

Objectives: In patients receiving dialysis, the prevalence of frailty can be as high as 73%; however, systematic identification of frailty and the relation to disease burden is not standard practice. This study examined whether functional outcome measures would predict frailty and kidney disease burden among patients receiving dialysis, which would enable more efficient assessments. **Methods**: The study included twenty-eight patients receiving dialysis to analyze the number of falls in the past year, Timed Up and Go time, and 30-second sit-to-stand repetitions as predictors of the (a) Fried frailty score and (b) Kidney Disease Quality of Life burden of kidney disease subscale score. **Results**: The functional outcome measures were significant predictors of frailty score (R^2 = 0.784, F = 29.4, P < .001). The number of falls in the past year was a significant predictor of kidney disease burden (R^2 = 0.22, F = 7.20, P = .01). **Conclusions**: The results provide evidence for the use of higher Timed Up and Go times and fewer 30-second sit-to-stand repetitions as predictors of the Fried frailty score. An increased number of self-reported falls in the past year predicted a higher burden of kidney disease.

Keywords: Frailty, Disease Burden, Functional Outcome Measures, Renal Disease, Dialysis

Introduction

In patients with end-stage renal disease who receive dialysis the prevalence of frailty can be as high as 73%[1]. The presence of frailty is associated with decreased health-related quality of life, thus higher disease burden, in renal disease populations[2]. Despite this, systematic identification of frailty is not standard practice, nor is there agreement on what tests and measures should be part of the comprehensive assessment of frailty and disease burden in this population[3]. Further research is needed to define optimal strategies for frailty screening in chronic kidney disease to reduce disease burden and improve quality of life[4-6].

Frailty is a complex construct that is difficult to define due to the number of body systems and variables involved. In 2001, frailty was defined as a clinical geriatric syndrome and phenotype, distinct from disability and comorbidity, having at least three of five characteristics: unintentional weight loss, decreased grip strength, slow gait speed, exhaustion, and decreased physical activity[7,8]. A 2012 systematic review found a 10.7% prevalence of frailty in the community-dwelling older adult population, which increases with age[9]. Once thought to inevitably lead to death and associated with societal burdens, the natural course of frailty varies greatly. While only a small proportion of frail individuals return spontaneously to a non-frail state as found in a 4.5-year longitudinal study, frailty can be reversible with opportunities for prevention and remediation[10]. Frailty prevention requires early identification of people at risk and effective remediation requires early detection and action.

Chronic kidney disease is an increasing health problem in the United States causing frailty deficits and decreased

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quality of life[11]. Approximately 37 million Americans are affected by chronic kidney disease, with approximately 800,000 individuals classified as end-stage renal disease[12]. Of those with end-stage renal disease, 71% require dialysis[12]. The high prevalence of frailty among patients with end-stage renal disease is expected as the biomarkers of inflammation, neuroendocrine dysregulation, immune senescence, and sarcopenia are similar for both physical frailty and end-stage renal disease[13,14].

Frailty has been linked to an increased burden of kidney disease, resulting in decreased quality of life in patients with end-stage renal disease receiving dialysis[2]. Hall et al. studied the quality of life themes that mattered most to these patients finding a connection between physical well-being, social support, and the burden of kidney disease[15]. The participants described physical well-being as being able to do things independently, having symptom control, maintaining physical health, and being alive; while having social support meant receiving logistical support, having emotional support, and socialization. These results highlight the association between the burden of kidney disease and the functional limitations inherent in the progression of end-stage renal disease[16]. Therefore, assessing functional status in relation to frailty and the burden of kidney disease is essential.

The Timed Up and Go and 30-second sit-to-stand tests have been found to be predictors of frailty in community-dwelling older adults and may be helpful measures if they can predict frailty, kidney disease burden, or both[17,18]. A recent study found that gait speed, Timed Up and Go, and 5-times sit-to-stand test were able to discriminate frail and non-frail individuals with end-stage renal disease receiving dialysis[3]. However, the 30-second sit-to-stand test may be more appropriate than the 5-times sit-to-stand for those with activity limitations and has been found to be a reliable test for patients with end-stage renal disease[19]. Falls are a predictor of mortality in patients with end-stage renal disease and are associated with decreased mobility and increased disease burden[20]. Therefore, the purposes of this study were to determine if the functional measures Timed Up and Go time, 30-second sit-to-stand repetitions, and number of falls in the past year predicted (a) frailty (defined as the Fried Frailty Score) and (b) kidney disease burden (defined by the burden of kidney disease subscale from the Kidney Disease Quality of Life 36-item short form survey) among patients with end-stage renal disease receiving dialysis.

Materials and Methods

A cross-sectional exploratory research design was used to generate a predictive correlational model to address the purposes of the study. Participants were recruited from adults receiving dialysis at the Wise Health System Dialysis Center in Decatur, TX, a 24-chair, single-center outpatient facility. Inclusion criteria were adults aged 18 years or older who had been receiving dialysis for at least 1 year. Participants were excluded if they were unable to walk at least 10 meters with or without an assistive device. The census of the dialysis center at the time of the study was 77 patients and 28 participants were tested and analyzed (Figure 1).

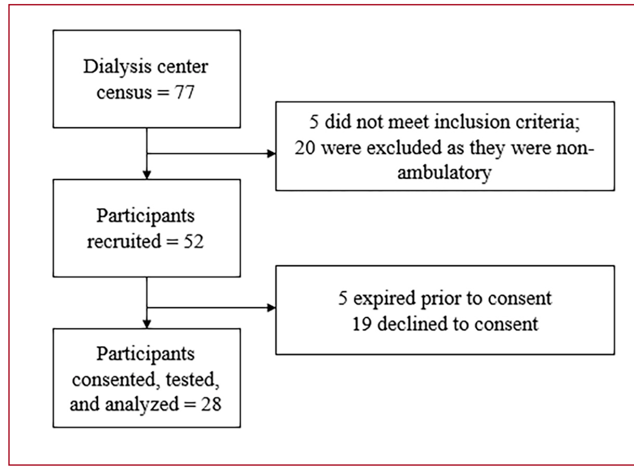

Figure 1. Participant Recruitment Flow Diagram.

Data was collected for the outcome variables (Fried frailty score and burden of kidney disease subscale from the Kidney Disease Quality of Life 36-item short form survey) and the predictor variables (Timed Up and Go time, 30-second sit-to-stand repetitions, and number of falls in the past year). Participants were scheduled for a data collection session 30 minutes prior to a regularly scheduled dialysis appointment. This session was conducted by the first author in a private treatment area of the dialysis center. All assessments were performed in a standardized order to minimize fatigue: gait speed, exhaustion question, grip strength, International Physical Activity Questionnaire Short Form, Timed Up and Go, the 4-item burden of kidney disease subscale from the Kidney Disease Quality of Life 36-item short form survey, fall history questionnaire, and 30-second sit to stand test. Dry weight was extracted from the medical record.

The first outcome variable was the Fried frailty score, calculated by the total number of positive findings from the measures of gait speed, exhaustion, grip strength, physical inactivity, and unintentional weight loss[7]. In the 2001 hallmark article, Fried et al. found this phenotype was independently predictive of falls, worsening mobility, hospitalization, and death[7]. The phenotype has been tested for validity and reliability across multiple settings, pathologies, and countries[21,22].

Gait speed is a measure of functional capacity with well documented predictive value for major health-related outcomes among older adults and thus considered a vital sign[23]. The test was performed over a 10 meter walkway as described in the literature[23]. A gait speed less than 0.8 m/s, the cut-off value for community ambulation, was defined as a positive finding for frailty[23].

Exhaustion was measured by asking the question “Over the past month, do you feel tired most of the time?” An answer of “Yes” has been shown to have a 20% increase in the 10-year mortality rate in older adults[24]. A “Yes” answer was defined as a positive finding.

Grip strength measured using a grip strength dynamometer is a reliable direct measure of isometric hand and forearm strength and a marker of muscle status and sarcopenia[25,26]. Following a protocol described for patients receiving dialysis, the average maximum force over three trials was recorded in kilograms[27]. An average grip strength that was less than the age-predicted normative value was defined as a positive frailty finding[28].

Physical inactivity was determined by the 7-item International Physical Activity Questionnaire Short Form (IPAQ-SF) that asks about number of days and time spent participating in vigorous activity, moderate activity, walking, and sitting with examples activities provided[29]. The summary score is expressed in physical activity metabolic equivalent of task (MET)-min per week and each participant was then classified as having low, moderate, or high physical activity level according the IPAQ-SF analysis instructions[30]. A classification of low activity level was defined as a positive finding for frailty.

Unintentional weight loss was determined by calculating the difference between current and 1-year-prior estimated dry weight measurements, with a weight loss of greater than 5% of estimated dry weight defined as a positive finding[7]. Estimated dry weight in kilograms is a value clinically determined by the nephrologist prior to every dialysis session to determine how much fluid the dialysis treatment should remove[31].

The frailty score represents a summative score and was used as an interval/ratio variable with a range of 0 to 5. Research has found a one-point increase in frailty score can represent an 87% increase in mortality in patients with chronic kidney disease, therefore a summative score was used for analysis rather than an ordinal classification status of non-frail, pre-frail, or frail[32].

The second outcome variable was the burden of kidney disease subscale score from the Kidney Disease Quality of Life 36-item short form survey. Participants responded to four statements covering issues such as time spent dealing with their kidney disease, the burden of managing their disease, and the frustration with dealing with their disease[33]. Each statement was rated on a 5-point Likert-type scale ranging from definitely true to definitely false[33]. Responses were averaged and then transformed to a 0 to 100 scale according to the analysis instructions, with higher scores representing a higher quality of life and lower burden of kidney disease[2,33,34]. Normative values for this score among patients of all races with end-stage renal disease receiving dialysis has been found to be 52.8[35].

The three predictor variables were analyzed at the interval/ratio level: Timed Up and Go in seconds, 30-second sit to stand test (repetition count), and self-reported falls history (number of falls recalled in the past 12 months). The normal-paced Timed Up and Go (measuring the time required to rise from a chair, walk 3 meters at one’s normal pace, and return to a seated position in a chair) has been found to be reliable measure of functional mobility in patients receiving dialysis[36]. For descriptive purposes, a time of greater than 13.5 seconds was used as the cut-off score for fall risk in community-dwelling older adults[37]. The 30-second sit-to-stand test (counting the number of sit-to-stand repetitions participants completed in 30 seconds from a standard chair with their arms folded across their chest) has been found to be a reliable assessment of functional mobility in patients receiving dialysis[19]. Age-related normative values were used for descriptive purposes[38]. Falls history was assessed retrospectively with a questionnaire asking participants how many falls had occurred in the past 12 months[39].

Data analyses, conducted using SPSS version 28 (IBM), included two multiple regression models testing whether any of the predictor variables (Timed Up and Go time, the number of 30-second sit-to-stand repetitions, and number of falls in the past year) would have a statistically significant relationship with (a) Fried frailty score or (b) Kidney Disease Quality of Life 36-item short form survey burden of kidney disease subscale score. The three predictor variables were initially entered into each of the two models as a single block and then non-significant predictors removed. Global ANOVA interpretation was based on $\alpha = .05$. Interpretation of the individual predictors of the model was based on $\alpha = .05$.

Results

The average participant was an older, frail White male who had been on dialysis for 3.6 years, presented with a high kidney disease burden, and walked without an assistive device (see Table 1). Prior to conducting the regression analyses, the assumptions for linear regression were examined and all were met. Therefore, the two multiple linear regression analyses proceeded as planned. The overall model predicting frailty score from all three predictor variables was significant ($R^2 = 0.78$, $F = 29.4$, $P < .001$) and accounted for 78.4% of the variance. Of the predictor variables, 30-second sit-to-stand repetitions (B = -0.11; 95% CI, -0.17 to -0.04) and Timed Up and Go time (B = 0.09; 95% CI, 0.03 to 0.16) were significant predictors of frailty score (Table 2). However, fall history was not a significant predictor of frailty ($P = .97$). Therefore, the regression model was revised to perform a hierarchical

Table 1. Participant Characteristics.

Variable	*M*	*SD*	Min	Max	Frequencies	
					n	%
Age (years)	66.7	13.6	42.80	91.65		
Gender						
Male					19	67.9
Female					9	32.1
Ethnicity and race						
White alone					24	85.7
Hispanic or Latino					3	10.7
Black alone					1	3.5
Assistive device used						
None					15	53.6
Rolling walker/ rollator					9	32.1
Cane/ quad cane					4	14.3
Years on dialysis	3.57	2.71	1.02	10.29		
Burden of Kidney Disease (score)[a]	47.54	26.42	0	100		
Frailty score (score)[b]	4[c]		1	5		
Gait speed (m/s)	0.74	0.26	0.31	1.35		
Grip strength (kg)						
Entire sample	22.06	7.15	7.67	35.67		
Male	25.01	6.08	15.33	35.67		
Female	15.82	5.00	7.67	22.33		
Physical activity level						
Low					17	60.7
Moderate					8	28.6
High					3	10.7
Exhaustion						
Yes					22	78.6
No					6	21.4
Estimated dry weight difference (%)[d]	-1.42	6.11	-21.38	10.00		
Timed Up and Go (s)[e]	15.66	5.96	7.25	27.20		
30-second sit to stand (repetitions)[f]	4.64	5.95	0	19		
Falls in the past year (count)	2.61	2.47	0	8		

[a]Smaller numbers indicate lower functional mobility. [b]Higher numbers indicate increased frailty. [c]Mode. [d]Negative values represent weight loss from one year prior. [e]Higher times indicate lower functional mobility. [f]Lower number of repetitions indicate lower functional mobility.

Table 2. Multiple Regression Analysis for Predictors of Frailty and Burden of Kidney Disease.

Variables	B	95% CI for B	β	*t*	*P*
Frailty[a]					
Predictor variables included in the final model					
30-second sit to stand repetitions	-0.11	-0.17 to -0.04	-0.50	-3.31	.01
Timed Up and Go time	0.09	0.03 to 0.16	0.45	3.19	.01
Predictor variable not included					
Falls in the past year	0.01	-0.11 to 0.12	0.01	0.04	.97
Burden of kidney disease[b]					
Predictor variable included in the final model					
Falls in the past year	-4.98	-8.80 to -1.17	-0.47	-2.68	.01
Predictor variables not included					
30-second sit to stand repetitions	1.05	-1.53 to 3.64	0.24	0.84	.41
Timed Up and Go time	1.35	-1.02 to 3.72	0.30	1.17	.25

[a] $R^2 = 0.78$ for step 1, $P < .001$; $\Delta R^2 = 0.00$ for step 2, $P = .97$
[b] $R^2 = 0.22$ for step 1, $P = .01$; $\Delta R^2 = 0.04$ for step 2, $P = .51$

analysis with 30-second sit to stand repetitions and Timed Up and Go time in the first block and reported fall rate as the second block. In this analysis, the final overall model was unchanged showing no effect of reported fall rate, ($\Delta R^2 = 0$). These results show that frailty increased with fewer sit-to-stand repetitions (β = -.50) and longer Timed Up and Go times (β = .45).

The overall model predicting kidney disease burden score from all three predictor variables was not significant ($R^2 = 0.26$, $F = 2.80$, $P = .06$). However, the number of falls in the past year (B = -4.98; 95% CI, -8.8 to -1.17) was a significant predictor of the burden of kidney disease (Table 2). Although the overall model was not statistically significant, fall history emerged as an independent predictor. Therefore, the regression model was revised to a hierarchical analysis with the number of falls in the past year as the first block and the mobility measures entered in the second block. In this analysis, the final overall model was significant with the number of falls in the past year accounting for 21.7% of the variance of the burden of kidney disease subscale score ($R^2 = 0.22$, $F = 7.20$, $P = .01$). These results show that as the reported fall rate decreases (β = -.47) the subscale score increases; indicating a lower burden of kidney disease and thus a higher quality of life.

Discussion

This study examined the relationship between functional performance, frailty, and disease burden in individuals with end-stage renal disease receiving dialysis. The primary findings indicate that impaired functional performance, specifically longer Timed Up and Go times and fewer 30-second sit-to-stand repetitions, was associated with higher frailty scores. A higher number of self-reported falls was associated with greater kidney disease burden, whereas functional mobility measures were not predictive. The findings of this study reinforce the importance of functional assessment in this population and highlight distinct relationships between physical frailty and perceived disease burden.

Our results are consistent with prior literature demonstrating that performance-based measures such as gait speed, Timed Up and Go, and sit-to-stand tests discriminate frailty status in individuals receiving dialysis[3]. Importantly, the present study supports the clinical utility of the 30-second sit-to-stand test in this population, as 54% of participants were unable to complete even a single repetition, suggesting significant functional limitations with timed sit-to-stand tests. These findings support the Timed Up and Go and 30-second sit-to-stand as practical indicators of declining function and increasing frailty in patients with end-stage renal disease.

The high prevalence of frailty observed in this sample further underscores the vulnerability of individuals receiving dialysis. Over 60% of participants met criteria for frailty, which is consistent with previously reported rates in end-stage renal disease populations[1]. Notably, even small increases in frailty score have been associated with substantial increases in mortality risk in individuals with chronic kidney disease[32]. Therefore, interpreting frailty as a continuous summative score, rather than as a categorical classification, may provide greater prognostic value and sensitivity to change over time. This perspective supports the integration of repeated frailty assessments into clinical practice to monitor disease progression and responses to intervention.

These findings support multidimensional models of frailty that distinguish physical and psychosocial domains[40]. The Fried frailty phenotype primarily reflects the physical domain of frailty, encompassing deficits in strength, mobility, endurance, and activity level[7,22]. The observed relationships between Timed Up and Go times, 30-second sit-to-stand repetitions, and frailty scores reinforce that these measures are capturing impairments within the physical domain of frailty.

However, these functional performance measures may not fully capture the psychosocial components of frailty that influence overall disease burden. In contrast to the findings related to frailty score, falls history alone was a significant predictor of kidney disease burden. This suggests that adverse events, rather than baseline functional limitations, may have a greater impact on perceived quality of life in this population. The role of falls in this population is particularly important given the high number of reported falls recorded in this study, which exceeded values found in both community-dwelling older adults and individuals with chronic kidney disease[41,42]. The findings suggest that while individuals may adapt to gradual mobility decline, falls may act as threshold events that worsen perceived health and disease burden, impacting psychosocial frailty.

From a clinical perspective, these findings support the role of physical therapy in the early identification and management of frailty in individuals receiving dialysis. Functional outcome measures such as the Timed Up and Go, 30-second sit-to-stand test, and retrospective falls assessment are feasible, low-cost tools that can be implemented in clinical settings to screen for both physical and psychosocial domains of frailty. Early identification of frailty can facilitate targeted interventions aimed at improving strength, mobility, and overall functional capacity, potentially slowing disease progression and reducing adverse outcomes.

This study contributes to the growing body of literature supporting the integration of frailty assessment into dialysis care. Future research should focus on establishing optimal assessment frequency, determining responsiveness to interventions, and identifying strategies to reduce disease burden and improve quality of life. Further study of psychosocial contributors to disease burden is warranted, as they may not be captured by physical performance measures alone.

Limitations

The primary limitation of this project was the recruitment of participants. The study was conducted in a small, semi-rural dialysis center and this may have impacted external validity and generalizability of the results. At the time of data collection, the total census of hemodialysis patients was 77 patients, fewer than the typical census of approximately 100 patients. There was a lack of diversity in the consented sample of this study compared to nationwide characteristics for persons with end-stage renal disease on dialysis. The participants' self-reported racial and ethnic distribution lacked diversity but corresponded to the demographics found in Wise County, Texas census data[43]. However, these proportions did not parallel national end-stage renal disease demographics[12].

An additional limitation involved the collection of data regarding falls. Each individual's history of falls was determined by a retrospective questionnaire asking them how many times they had fallen in the past year. While a recent combined analysis of three fall rate models included retrospective falls history, prospective falls assessment leads to more accurate data[39,44]. The retrospective falls data collected in this study may have been affected by a number of issues. Retrospective fall reporting may have introduced recall bias, as participants may have forgotten falls or misremembered details. Cognitive impairments with older adults would also have an effect on accurate fall reporting. Additionally, social desirability may have led participants to underreport falls due to fear of being perceived as frail. Evidence has shown that 50% of recurrent fallers underreport falls when assessed retrospectively as compared to prospectively.44 These factors may have impacted the influence of falls history on the regression results.

Conclusions

The findings of this study support the use of efficient, objective functional measures as part of frailty screening in patients receiving dialysis. Incorporating these measures into clinical practice may help guide targeted interventions aimed at improving physical function and reducing disease burden. Further research is needed to clarify the role of physical therapy in dialysis care and to optimize its integration for this vulnerable population.

Ethics approval

Prior to beginning the study, Institutional Review Board (IRB) approval was obtained through the Texas Woman's University IRB (IRB-FY2022-428).

Consent to participate

Written informed consent was obtained from every participant.

Authors' contributions

Rick Ward, as part of his dissertation work, conceptualized and designed the study, conducted participant recruitment, collected data, and wrote the final

manuscript. Mary Thompson, Elaine Trudelle-Jackson, and Kelli Brizzolara, as part of the dissertation committee, contributed to study design and provided critical revisions to the manuscript. All authors read and approved the final version of the manuscript.

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