Frailty and associated risk factors in patients with chronic kidney disease on dialysis

Gabriela Dutra Gesualdo (https://orcid.org/0000-0002-0125-6468) [1]
Juliana Gomes Duarte (https://orcid.org/0000-0001-7678-038X) [2]
Marisa Silvana Zazzetta (https://orcid.org/0000-0001-6544-767X) [2]
Luciana Kusumota (https://orcid.org/0000-0001-9290-3722) [3]
Fabiana de Souza Orlandi (https://orcid.org/0000-0002-5714-6890) [2]

Abstract *The objective of this article is to determine the relationship between frailty and socio-demographic/clinical characteristics in patients with chronic kidney disease on dialysis. A cross-sectional study was conducted with 107 participants. Descriptive, correlation and logistic regression analyses were performed, with the level of significance set to 5% (p < 0.05). The prevalence of frailty was 47.66%. Frailty was negatively correlated with cognition (r = -0.30; p = 0.002), functioning on instrumental activities of daily living (r = -0.41; p = 0.000) and hematocrit level (r = -0.19; p = 0.04). The proportion of frailty increased with the age of the participants (OR = 1.03; 95%CI: 1.004-1.069; p = 0.02). Individuals with chronic kidney disease on dialysis had high percentages of frailty, which was associated with an older age and correlated with cognition, functioning on instrumental activities of daily living and a lower hemotocrit level.*

Key words *Adult Health, Health of the Elderly, Frailty, Chronic Kidney Failure, Dialysis*

[1] Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo (USP). Rodovia Washington Luís, km 235, SP-310. 13565-905 São Carlos SP Brasil. fabi_ferreira@yahoo.com.br
[2] Departamento de Gerontologia, Universidade Federal de São Carlos. São Carlos SP Brasil.
[3] Departamento de Enfermagem Geral e Especializada, USP. São Paulo SP Brasil.

Introduction

Chronic diseases require interventions and a change in lifestyle in a continual care process that does not always lead to a cure. Such diseases constitute a considerable public health problem and correspond to 72% of the causes of death[1]. One such condition is chronic kidney disease (CKD), which is a serious health problem that is considered a growing "epidemic"[2].

CKD is defined as an abnormality is renal structure and/or function for more than three months, with implications for one's health. It is necessary to clarify the cause of the disease and define its stage to identify the risk of negative outcomes, such as kidney failure and death[3].

Patients on dialysis for CKD undergo severe changes in their social life, work, eating habits and sexual life, which can exert a negative impact on both physical and emotional wellbeing. CKD imposes limitations that can distance patients from their social groups, leisure activities and even their families. These factors can make the patient frail, leading to a reduction in quality of life[4].

Frailty syndrome has a multidimensional nature and is characterized by vulnerability to stressors, with reductions in strength, endurance and physiological functions. This condition increases the risk of adverse events, such as dependence, hospitalization, institutionalization and death[5,6].

CKD increases the chances of frailty in comparison to individuals with normal kidney function and those with other chronic diseases, such as diabetes, chronic obstructive pulmonary disease, cancer and rheumatoid arthritis[7]. Patients with CKD experience reductions in quality of life, cognition, physical activity and muscle mass, with highly prevalent symptoms, such as fatigue, nausea and anorexia[8].

The prevalence of frailty increases as the glomerular filtration rate (GFR) diminishes. Indeed, 14% of patients with CKD are frail, whereas 10% of community-dwelling elderly individuals have the frailty phenotype[9]. The prevalence among patients who begin dialysis is high and frailty is an important construct in this dimension, as it is strongly associated with adverse outcomes[10].

The identification of frailty and associated risk factors in patients with CKD on dialysis enables improving care in the public and private health systems to establish more concrete, viable interventions. The present study is justified by the importance of investigating this issue in Bra-zil, as strategies directed at the control of frailty syndrome can enable better health for the elderly.

It is important to conduct studies that identify patients with CKD on dialysis in situations of pre-frailty and frailty as well as associations with socio-demographic and clinical characteristics, considering the high prevalence of the syndrome in this population. Therefore, the aim of the present study was to determine associations between frailty and both socio-demographic and clinical characteristics in patients with chronic kidney disease on dialysis.

Methods

An observational, descriptive, quantitative, cross-sectional study was conducted involving patients with CKD at a dialysis service in the state of São Paulo (southeastern Brazil).

A non-probabilistic convenience sample was used, totaling 107 participants. Data collection took place between September and November 2014. The inclusion criteria were age 18 years or older, a medical diagnosis of CKD and being on dialysis for at least six months. Individuals with manifestations stemming from a stroke and those with severe vision or hearing impairment were excluded from the study. The data were collected prior to dialysis in a private room at the clinic in an evaluation lasting an average of one hour, during which we administered a questionnaire for the characterization of the participant, the Fried Frailty Phenotype criteria, Addenbrooke's Cognitive Examination – Revised (ACE-R) and the Lawton Scale.

Socio-demographic and clinical characteristics of the participants were collected using a questionnaire developed by our research group, which has been used in previous studies. This questionnaire addresses socio-demographic and economic characteristics (sex, age, self-declared skin color, schooling and family income) and clinical data (time on dialysis and hematocrit level).

Cognition was assessed using the ACE-R, which is a battery that can be administered to adults and seniors with high sensitivity and specificity for the determination of mild dementia. It is particularly useful for differentiating Alzheimer's disease from frontotemporal dementia. The ACE-R addresses five domains: orientation/attention (18 points), memory (26 points), verbal fluency (14 points), language (26 points) and visuospatial skills (16 points), which can be evaluated individually. The total score ranges from 0

to 100 points. The cutoff points for the total and domain scores (including the Mini Mental State Examination [MMSE], which was added to the ACE-R) were < 78 for the complete battery, < 17 points for orientation/attention, < 15 points for memory, < 8 points for verbal fluency, < 22 points for language, < 13 points for visuospatial skills and < 25 points for the MMSE[11].

Instrumental activities of daily living were evaluated using the Lawtwon Scale, which is employed to determine the functional performance of adults and seniors in terms of instrumental activities that enable maintaining an independent life, such as using the telephone, shopping, preparing meals, housekeeping, doing manual domestic chores, managing medications and managing finances. The score ranges from 7 (complete dependence) to 21 points (complete independence). Scores higher than seven and lower than 21 indicate partial dependence[12].

Frailty syndrome was investigated using the five items described as the components of the frailty phenotype[6]:

a) self-reported unintentional weight loss in the previous year (> 4.5 kg or > 5% of habitual weight);

b) sensation of exhaustion, evaluated using the following two questions: "How often in the past week have you felt that everything you did required considerable effort?" and "How often in the past week did you feel that you could not get going?" Answers of "most of the time" or "always" on at least one of these questions fulfilled this criterion of frailty;

c) weakness, evaluated based on grip strength measured using a manual dynamometer (Grip model, SAEHAN®) with the upper limb in which there is no arteriovenous fistula. The participants were instructed to exert maximum force on three trials. Those in the first quintile after adjusting for sex and body mass index were considered as having fulfilled this criterion of frailty;

d) slow gait speed, evaluated using a chronometer to measure the time (in seconds) required to travel a 4.6-m track. The mean of three consecutive trials was used, with adjustments made for sex and height;

e) low physical activity, self-reported based on the answer to the following question: "Do you think that you perform fewer physical activities than you did 12 months age?" An affirmative answer was considered as having fulfilled this frailty criterion.

Having three or more frailty criteria denoted frailty, fulfilling one or two criteria denoted pre-frailty and not fulfilling any of the criteria denoted non-frailty[6].

The data analysis involved descriptive statistics (measures of central tendency [mean, median, minimum and maximum] and dispersion [standard deviation]). Spearman's correlation coefficients were calculated to determine the strength of the correlations between the frailty phenotype score and both socio-demographic and clinical variables. The coefficients were interpreted as follows[13]: < 0.3) = weak correlation, 0.3 to 0.59 = moderate correlation, 0.6 to 0.9 = strong correlation and 1.0 = perfect correlation. Logistic regression analysis was used to determine the effect of socio-demographic and clinical variables on frailty. The level of significance for the statistical tests was α = 0.05 (p ≤ 0.05).

This study received approval from the Human Research Ethics Committee of the Federal University of Carlos (UFSCar).

Results

Among the 107 interviewees, the majority was male (67.30%). Schooling ranged from 0 to 20 years (mean: 7.26 years). Mean time on dialysis was 48.91 (46.81) months (Table 1).

The prevalence of frailty, pre-frailty and non-frailty was 47.66% (n = 51), 44.85% (n = 48) and 7.49% (n = 8), respectively.

The participants with the highest degree of frailty had a poorer performance on the cognitive assessment (r= -0.30; p = 0.002), poorer functioning on instrumental activities of daily living (r = -0.41; p = 0.000) and a lower hematocrit level (r = -0.19; p = 0.04) (Table 2).

Older patients were at greater risk of being frail. Each year of life increased the chance of frailty by 3%. None of the other variables studied were significantly associated with the risk of frailty (Table 3).

Skin color, income per capita, time on dialysis, age and cognition (ACE-R) were associated with frailty in the bivariate analysis (p ≤ 0.20) and incorporated into the multivariate model. Using the stepwise backward method, independent variables with p > 0.05 were excluded from the final model, leaving only age.

Discussion

The term frailty has been employed to distinguish weaker, more vulnerable individuals. Re-

Table 1. Distribution of patients with chronic kidney disease according to socio-demographic and clinical characteristics (n = 107). São Carlos, SP, 2018.

Variable	Mean (SD†)	Median	Range	Distribution in categories	n	%
Sex	--	--	--	Male	72	67.30
				Female	35	32.70
Age (years)	54.30 (14.85)	56.00	22-85	20-29	7	6.54
				30-39	15	14.01
				40-49	22	20.56
				50-59	18	16.82
				60-69	25	23.36
				70-79	18	16.82
				80-89	2	1.89
Schooling (years)	7.26 (4.10)	8.00	0-20	0	3	2.80
				1-4	41	38.31
				5-8	18	16.82
				9-12	16	14.95
				13-16	28	26.16
				17-20	1	0.96
Time on dialysis (months)	48.91 (46.81)	36.00	6-264	6 ⊢ 18	26	24.30
				18 ⊢ 30	23	21.50
				30 ⊢ 42	8	7.48
				42 ⊢ 54	12	11.21
				54 ⊢ 66	12	11.21
				66 ⊢⊣ 264	26	24.30

† sd – standard deviation.

Table 2. Spearman correlation coefficients between frailty phenotype and socio-demographic/clinical variables of patients with chronic kidney disease. São Carlos, SP, 2018.

	Age	Cognition (ACE-R)	Functioning (Lawton)	Hematocrit
Phenotype				
r†	-0.15	-0.30	-0.41	-0.19
p‡	0.11	0.002	0.000	0.04
n§	107	107	107	107

†r = Spearman's correlation coefficient; ‡p = p-value; §n = number of participants.

cent national and international studies have contributed to a better definition of the clinical and physiological properties of frailty, highlighting the vulnerability of frail elderly individuals and the negative outcomes of this condition[7-14].

Although patients with CKD on dialysis at times have clinical signs and symptoms compatible with frailty, there is little information on the socio-demographic and clinical factors that may be associated with the condition in this population[15].

The identification of frailty and its predictors in the dialysis setting can potentially lead to the identification of patients at risk of adverse outcomes and who could benefit from interventions directed at preventing their decline[8].

In the present study, a large portion of patients with CKD on dialysis were frail and frailty syndrome was related to cognitive impairment, functional deficit, a lower hematocrit level and a more advanced age.

These findings are in agreement with data described in national and international studies, which report that frailty is more prevalent in this population[7,16-22]. Associated factors identified by other authors include peripheral vascular dis-

Table 3. Multivariate logistic regression of possible factors associated with frailty in patients with chronic kidney failure. São Carlos, SP, 2018.

Variables	Categories	p-value	OR†	95%CI OR‡
Skin color	White (ref)	0,44	0,71	0,30-1,69
	Non-white	0.44	0.71	0.30-1.69	0,82-1,40
Income per capita	Continuous variable	0.56	1.08	0.82-1.40
Age	Continuous variable	0.02	1.03	1.004-1.069
Time on dialysis	Continuous variable	0.07	0.99	0.98 – 1.00
Cognition (ACE-R)	Continuous variable	0.67	0.99	0.98 –1.01

†OR (OddsRatio) = Odds ratio for frailty; ‡95%CI OR = 95% confidence interval of odds ratio.

ease, heart disease, the black race and a lower concentration of serum albumin[15]; mortality and hospitalization[8]; number of hospitalizations and the risk of falls[17]; diabetes *mellitus*[18]; a high GFR[19]; the use of vitamin D and parathyroid hormone[7]; low physical performance and CKD severity[20]; poorer quality of life, sex and age[21].

However, the prevalence of frailty in the present investigation was higher than that reported in surveys of community-dwelling individuals, suggesting an increased health risk in this population, which has implications for health services and could lead to excessive burden on the part of health professionals at dialysis centers.

The limitation of the present study regards the cross-sectional design, which does not enable the determination of the cause-and-effect relationship. Thus, longitudinal investigations in this setting are needed for a greater understanding of the genesis of this syndrome in patients with CKD.

The identification of health status related to pre-frailty can favor the planning and implementation of care for adults and seniors in this context.

Considering the scarcity of Brazilian studies on this issue, the present findings broaden knowledge on the socio-demographic and clinical factors associated with frailty in the nephrology setting.

Thus, these findings can assist in the establishment of preventive health actions aimed at delaying the emergence and progression of frailty. There is a need for reflection on the healthcare system in terms of addressing the needs of adults and seniors with CKD in light of the negative impact of frailty syndrome on this population.

Conclusion

The prevalence of frailty was high among individuals with chronic kidney disease on dialysis. Moreover, frailty was negatively correlated with cognition, functioning on instrumental activities of daily living and hemotocrit level. This condition was also associated with a more advanced age.

Collaborations

GD Gesualdo contributed substantially to the planning, analysis and interpretation of the data. In addition, contributed significantly to the elaboration of the article. Also participated in the approval of the final version of the manuscript. JG Duarte contributed significantly to the elaboration of the article and the critical review of the content. MS Zazzetta contributed substantially to the preparation of the article and the critical review of the content. L Kusumota contributed substantially to the elaboration of the article and the critical review of the content. FS Orlandi contributed substantially to the conception, planning, analysis and interpretation of the data. In addition, contributed significantly to the preparation of the article and critical review of the content. All authors participated in the approval of the final version of the manuscript.

Acknowledgments

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